

18th World Sleep Congress

Singapore 2025 **WORLD SLEEP** September 5-10



ABSTRACTS

Abstracts

Singapore 2025
WORLD SLEEP
September 5-10

World Sleep Society is pleased to share the abstracts presented at the 18th World Sleep congress, which was held in Singapore over September 5 – 10, 2025. Researchers from over 80 countries gathered in Singapore to present the 1700+ abstracts now published in this supplement. We thank the World Sleep community for its contributions to the World Sleep 2025 scientific program and to the advancement of sleep health.

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Aging and Developmental Issues

Age-related Changes in Sleep Characteristics and Chronotype, and Their Associations with Physical Frailty: A Longitudinal Study

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Introduction: Sleep phenotypes and circadian manifestations are closely linked with physical frailty. However, the associations between sleep traits, chronotype, and the impact of chronological changes in these factors on frailty remain underexplored.

Materials and methods: A total of 292,940 UK Biobank participants were included for association analysis. Among, 34,157 participants were used for transition analysis. Self-reported continuous sleep duration (short (≤ 6 h) and long (≥ 9 h) sleep durations), insomnia, and chronotype were treated as exposures. Physical frailty was assessed by Fried five criteria, including weight loss, exhaustion, low physical activity, slow walking speed, and low grip strength. Multinomial logistic regression (MLM) and Two-stage regression (2SLS) were applied to analyze the associations. Transition analysis examined the effect of changes in sleep traits and chronotype on frailty risk.

Results: In both MLM and 2SLS models, each additional hour of sleep was associated with a lower risk of frailty (MLM: OR 0.92, 95% CI 0.91-0.94; 2SLS: OR 0.58, 95% CI 0.45-0.73). Short sleep duration (MLM: OR 1.96, 95% CI 1.88-2.05; 2SLS: OR 5.89, 95% CI 2.84-12.18) and insomnia (MLM: OR 2.72, 95% CI 2.61-2.83; 2SLS: OR 2.44, 95% CI 1.37-4.36) were associated with increased frailty risk. Morning chronotype was linked to a lower risk of pre-frailty (MLM: OR 0.94, 95% CI 0.93-0.94; 2SLS: OR 0.93, 95% CI 0.90-0.97). Transition analysis revealed that maintaining healthy sleep patterns (7-8 hours of sleep, no insomnia, and morning chronotype), along with improvements in insomnia and chronotype shifts, were associated with reduced frailty risk.

Conclusions: Multiple sleep and circadian phenotypes including short sleep duration, insomnia, and late chronotype may predispose physical frailty, and improvements in these factors overtime can reduce frailty risk. This underscores the need for widespread attention to sleep and circadian health.

Age related changes in sleep quantitative EEG brain activity and longitudinal relationship to cognitive function

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Introduction: Sleep microarchitecture including spindle characteristics evolves with normal ageing, and cognition declines with age. Sleep disturbance is a risk factor for cognitive impairment, however the underlying pathophysiology remains incompletely understood. Altered sleep spindle metrics have been shown to be associated with an increased risk of mild cognitive impairment in cross-sectional studies, however the longitudinal relationship between sleep neurophysiology and cognition in middle-to-late life is unclear. This study examined sleep microarchitecture measured by single channel (F4-M1) EEG and cognitive performance assessed with the trail-making test (TMT) part A and B and mini-mental state examination (MMSE) in a cohort of community dwelling men from the Florey Adelaide Male Ageing Study (FAMAS) over an 8-year period. The objectives of the study were to examine changes in sleep microarchitecture, and changes in cognition over eight years, and to investigate the longitudinal relationship between sleep microarchitecture and cognition.

Materials and methods: Participants from the FAMAS with no reported previous diagnosis of OSA underwent home-based PSG and cognitive testing at baseline and at follow-up, approximately eight

years apart. Power spectral analysis of EEG recordings was performed. Baseline and follow-up sleep parameters including sleep spindle characteristics and power spectra, and baseline and follow-up cognition were compared using paired t-tests, and associations were examined using Pearson's correlation.

Results: NREM (267.6 vs 299.2 minutes) sleep was higher during follow up PSG compared to baseline ($p < .001$). NREM spindle events (257.5 vs 351.7) and density (0.95 vs 1.17 events/ minute) were higher at follow up ($p < .001$). TMT performance declined (TMT-A: 15.4 vs. 38.7 seconds, TMT-B: 74.9 vs. 93.7 seconds, $p < .001$). There was no change in MMSE. The change in sleep spindle metrics and cognition were not correlated.

Conclusions: In this community-dwelling cohort of men, significant differences were observed in sleep spindle metrics and cognitive function at follow-up compared to baseline. No longitudinal relationship between sleep microarchitecture and cognitive function was observed.

Amplitude fluctuations of cerebrovascular oscillations and CSF movement desynchronize during NREM3 sleep

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Introduction: Sleep is a natural, reversible, and repeating neuro-behavioral state characterized by distinct coordinated cellular, circuit, and system level changes intended to optimize physiology, behaviour, and health. In mammals, sleep is broadly divided into different states – non-rapid eye movement (NREM) and rapid eye movement (REM) sleep with NREM sleep further divided into NREM1, NREM2 (collectively called light sleep), and NREM3 (deep sleep). During sleep, an individual cycles between these states which are characterized by distinct patterns of neural activity, muscle tone, breathing, and systemic physiology - including cerebrospinal fluid (CSF) movement.

Fluctuations in cerebral blood volume (CBV) are a dominant mechanism aiding CSF movement in the brain during wakefulness and non-rapid eye movement (NREM) sleep. However, it is unclear if the amplitudes of CBV oscillations also change in proportion to the changes in amplitude of CSF movement across specific NREM sleep states. It is also not known if the coupling strength between them varies between NREM sleep states. To investigate these relationships, we measured cerebral hemodynamics and cranial CSF movement at the fourth ventricle simultaneously during wakefulness and NREM sleep states using concurrent Electroencephalography and functional Magnetic Resonance Imaging.

Materials and methods: Ten healthy participants (6 females) aged 19 – 24 (20.90 ± 1.59) years were included in this study. The wake/sleep cycles were continuously monitored via actigraphy for a minimum of four days prior to the experimental session to ensure that they maintained regular habitual sleep schedules. In addition, they were also asked to listen to sound recordings from the MR scanner to acclimate to the sound. Further, on the day of the scan, participants were asked to wake 3 hours earlier than usual and the scan sessions were initiated an hour past their typical bedtime to build homeostatic and circadian sleep pressure. All participants' structural and functional MRI data were acquired using a 3T SIEMENS MRI scanner with a 64-channel head coil. 32-channel Electroencephalography (EEG) was concurrently acquired to allow for sleep stage scoring.

Results: We found that the amplitude fluctuations of cerebral hemodynamics and CSF oscillations desynchronize from one another only during deep NREM3 state, despite the strong mechanical coupling between CBV changes and CSF movement, which was consistent across all states. Deep NREM3 sleep marked a period of significant reduction in the amplitude fluctuations of only the cerebral hemodynamics, without any similar reductions in CSF inflow to the brain compared to light sleep. Interestingly, we also found the coupling between cerebral hemodynamic changes and CSF inflow continues to remain strong during NREM3 sleep, despite a significant reduction in cerebral hemodynamic fluctuations.

Conclusions: Our results suggests the existence of a different mechanism, linked to the cortical interstitial volume/resistance change, that regulates the NREM3 CSF inflow into the brain.

Acknowledgments: NIH R21 AG077461 Schwichtenberg, Tong (Co-PI)

Sleep, breathing, hemodynamic oscillations, and cerebrospinal fluid movements - Building toward a novel treatment approach for Alzheimer's disease.

An integrated analysis of rhythmic ageing markers, targets of anti-ageing compounds, and metabolic pathways for unraveling the circadian impact on ageing

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Introduction: Circadian rhythms have pronounced impacts on human health, diurnally synchronising physiological and behavioural processes. Circadian dysfunction can cause a multitude of physiological and metabolic irregularities, neurodegeneration, oxidative damage, and reduced lifespan. Ageing enhances these disruptions, leading to diverse chronic diseases. Therefore, it is crucial to investigate the molecular underpinnings and markers of ageing and their effects on circadian dysregulations. Also, compounds with evidence of prolonging lifespan are now well-reported; however, the effects of geroprotectors on circadian behavior remain poorly understood from a clock-controlled perspective. Our study addresses these gaps by a) creating a comprehensive map of circadian ageing markers across the mammalian system, b) identifying chrono-geriatric targets for ageing attenuation, and c) elucidating the effects of geroprotectors on circadian behavior across different aged *Drosophila*.

Materials and methods: In this study, we performed an *in-silico* analysis from a circadian perspective to identify ageing markers and chrono-geriatric targets for ageing attenuation. We curated a comprehensive map of human ageing markers (besides homologs in mice and *Drosophila*) from the Human Aging Genomic Resources, Aging Atlas, and Digital Aging Atlas databases. Another aspect of our study was curating anti-ageing drugs utilising the DrugAge and Ageing Atlas databases and their targets from Drugbank. We identified 24-hour rhythmic transcripts using CircaDB at the transcriptome level across the mammalian system for both the ageing markers and targets of anti-ageing pharmacological compounds (<http://circadb.hogeneschlab.org/>). Using the DAVID (<https://david.ncifcrf.gov/>) resource system, we conducted a functional analysis of the ageing-related rhythmic transcripts and robustly rhythmic compound targets (Period 24±3 hr, JTKQ < 0.1) to map the enriched pathways (FDR<0.01). On examining compounds with secondary clock targets and evidence of lifespan extension, we selected resveratrol as a candidate compound. The effects of resveratrol were investigated in different age groups of *Drosophila*.

Results: 50% of ageing genes investigated across the mammalian systems exhibit 24-hour rhythmic oscillation at the transcriptome level. The key physiological pathways associated with prevalent rhythmic genes were the longevity-regulating pathway, the AGE-RAGE signaling pathway, and pancreatic cancer in humans. The convergent biological process corresponding to oscillating targets of anti-ageing compounds was lipid metabolism. Resveratrol treatment was found to enhance locomotor activity with ageing, besides its sleep-altering effects when administered early in life.

Conclusions: The robustly rhythmic molecular components associated with the Absorption, distribution, metabolism, and excretion (ADME) process of geroprotectors converged to the biological process of lipid metabolism, a potential target for future chrono-geriatric treatments. Additionally, our investigations portray anti-ageing compounds' role in altering clock-controlled behavioural rhythms.

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Association Between Functional Dyspepsia and Sleep Architecture Disruption in Geriatric Patients: A Comprehensive Cohort Study

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Introduction: Sleep disorders and functional dyspepsia are prevalent comorbidities in patients with geriatric syndrome. The co-occurrence of functional dyspepsia and sleep disturbances demonstrates significant epidemiological overlap, with sleep disruptions frequently triggering emotional disturbances

and exacerbating gastrointestinal symptoms. Further investigation into the bidirectional pathophysiological interplay between these conditions is warranted to advance clinical risk stratification and therapeutic decision-making.

Materials and methods: A cohort of 400 elderly patients (aged ≥ 65 years) treated in Shijiazhuang People's Hospital, Hebei Province, P. R. China, from January 2022 to December 2023 was prospectively analyzed. Participants were stratified into sleep disorder ($n=281$, PSQI ≥ 8) and normal sleep groups ($n=119$, PSQI ≤ 7) using Pittsburgh Sleep Quality Index (PSQI) criteria. Comparative analysis of clinical characteristics was performed, followed by multivariate logistic regression to identify sleep quality determinants. The sleep disorder cohort was further subclassified by functional dyspepsia (FD) status into FD group ($n=224$) and non-FD group ($n=57$), with FD severity stratified into mild and moderate-severe subgroups. Polysomnography (PSG)-derived sleep architecture parameters were compared across groups. Spearman's rank correlation analyzed FD severity-PSQI associations.

Results: Significant intergroup differences emerged in marital status, smoking history, chronic gastrointestinal disorders, SDS scores (≥ 53), SAS scores (≥ 50), and FD prevalence (all $P<0.05$). Multivariate analysis identified SDS ≥ 53 (OR=2.41, 95%CI 1.62-3.58), SAS ≥ 50 (OR=1.97, 95%CI 1.28-3.04), chronic gastrointestinal comorbidity (OR=3.12, 95%CI 1.89-5.15), and FD diagnosis (OR=4.05, 95%CI 2.47-6.63) as independent risk factors for sleep disorders. The FD subgroup demonstrated elevated PSQI scores (14.3 ± 3.2 vs 8.1 ± 2.7 , $P<0.01$) and increased N1+N2 sleep stage proportion ($68.4\%\pm 9.1$ vs $59.2\%\pm 8.3$, $P<0.001$) compared to non-FD counterparts. PSG analysis revealed obstructive sleep apnea (OSA) severity stratification: no OSA (4.2%), mild OSA (13.9%), moderate OSA (22.1%), and severe OSA (59.8%), with significant PSQI elevation in moderate-severe OSA groups ($P<0.05$). Strong positive correlation emerged between FD severity and PSQI scores ($r=0.625$, $P=0.021$).

Conclusions: Progressive sleep architecture disruption in elderly patients demonstrates significant associations with FD severity, modulated by psychological parameters (SDS/SAS thresholds) and gastrointestinal comorbidity. These findings advocate integrated sleep-gut axis evaluation in geriatric care protocols.

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Association Between Sleep Duration and Sarcopenia in Korean Older Adults: Evidence from the 2022 KNHANES

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Introduction: Sarcopenia, defined as the combined loss of muscle mass and strength, is a significant health problem among older individuals, and is associated with impaired mobility, falls, and increased mortality. Although there is growing evidence that sleep duration is associated with reduced risk for sarcopenia, the evidence has been inconsistent, and there has been a lack of studies examining the relationship between sleep duration and risk for sarcopenia in Asian populations, including Korean older adults. Here, we utilize nationwide representative data from Korea to analyze the relationship between sleep duration and sarcopenia.

Materials and methods: We used the 2022 Korea National Health and Nutrition Examination Survey (KNHANES) data, consisting of a total of 2,544 adult subjects 65 years of age and older. Sarcopenia was defined based on the 2019 Asian Working Group for Sarcopenia (AWGS) definitions: low grip strength (≤ 28 kg in men and ≤ 18 kg in women) and low appendicular skeletal muscle mass index ($ASM/height^2 \leq 7.0$ kg/m² for men, ≤ 5.0 kg/m² for women). The sleep duration was performance into four categories: ≤ 5 hours, 5–7 hours, 7–9 hours (reference), and ≥ 9 hours. Multivariable logistic regression models were applied to assess the relationship between sleep duration and sarcopenia overall, while adjusting for sociodemographic, lifestyle, and clinical factors.

Results: The odds ratio of sarcopenia was 1.75 (95% CI: 1.02–2.99, $p=0.041$) in a participant who had 9 h or more sleep independent of reference group (7–9 h sleep). No such relations were found in the ≤ 5 h or 5–7 h groups. The sub-cohort analysis of men showed a similar trend (aOR=1.60) but it also did

not reach significance. For women, no significant relationship was observed between sleep duration and sarcopenia. U-type association between sleep duration and the risk of sarcopenia.

Conclusions: This is one of the first studies to examine the relationship between sleep duration and sarcopenia among Korean older adults based on nationally representative data. We found that long sleep (≥ 9 hours) was associated with an increased risk of sarcopenia, similar to those of previous studies for CHARLS and NHANES populations, respectively. These findings emphasize the need to consider sleep duration as a modifiable lifestyle factor in the prevention of sarcopenia and strategies for healthy aging among Korean older adults.

Associations between obstructive sleep apnoea risk and fall-related physical performance

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Introduction: Falls are a leading cause of injury, loss of independence and mortality in older people. Measures of physical performance, including balance, gait speed, and handgrip strength are significant predictors of falls. Emerging evidence suggests that obstructive sleep apnoea (OSA), a common sleep-related breathing disorder, may impair physical and cognitive performance in older adults, potentially through mechanisms including nocturnal hypoxemia, excessive daytime sleepiness, and impaired vasoreactivity. However, associations between the risk of OSA and fall-related physical performance remain unclear.

Materials and methods: Cross-sectional data from the 2016 Health and Retirement Study was analysed. OSA risk was derived using survey items aligned with the STOP-Bang questionnaire. Poor balance was defined as the inability to hold a semi-tandem stance for 10 seconds. Slow gait speed was defined as walking <0.8 m/s over 2.5 meters. Weak handgrip strength (HGS) was defined as HGS divided by body mass index (BMI) of <1.00 kg/BMI for males and <0.56 kg/BMI for females. Binomial logistic regression models were used to examine associations between high-risk OSA and physical performance measures. Potential confounders adjusted in the models include age, sex, BMI, physical activity, alcohol consumption, comorbidity burden, ethnicity, and treatment for sleep/snoring problems.

Results: Data from 6,911 participants (mean age 66 ± 11 years; 57% female) were analysed. The prevalence of high-risk OSA, poor balance, slow gait speed and weak HGS was 36%, 32%, 63% and 15%, respectively. High-risk OSA was significantly associated with higher odds of poor balance (OR: 1.23, 95% bootstrapped confidence interval (BCI): 1.07-1.39, $p=0.002$), slow gait speed (OR: 1.29, BCI: 1.06-1.56, $p=0.009$), and weak HGS (OR: 2.20, BCI: 1.86-2.60, $p=0.001$).

Conclusions: High-risk OSA is associated with higher odds of poor balance, slow gait speed and weak relative HGS, which are key predictors of falls. Co-screening of OSA and poor fall-related physical performance may support early detection and preventative strategies to improve safety and maintain functional independence in older adults.

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Associations Between Sleep Patterns and Estimated Pulse Wave Velocity From a Wearable Smart Ring in 500,000 Free-Living Adults

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Introduction:

Pulse wave velocity (PWV) is a well-established marker of arterial stiffness and a predictor of cardiovascular risk. Although conventionally assessed using tonometry or oscillometric techniques, recent evidence indicates that features derived from photoplethysmography (PPG)—a signal commonly

captured by consumer wearables such as smart rings—correlate strongly with PWV. This advancement supports the potential for continuous, passive vascular monitoring in real-world settings.

Sleep duration has shown a U-shaped association with arterial stiffness, with both short and long sleep linked to higher PWV. Beyond duration, lower sleep regularity, quantified by the Sleep Regularity Index (SRI), has been associated with increased PWV.

To address the need for validated wearable estimated PWV (ePWV) metrics, this study evaluates the accuracy of smart ring PPG-based estimates against a reference device and examines the relationship between ePWV and long-term sleep patterns in a large free-living cohort.

Materials and methods:

Carotid-femoral PWV (cf-PWV) was measured using the SphygmoCor XCEL system in a reference cohort of 300 healthy individuals. A model was trained on 200 participants using wearable-derived features and validated on the remaining 100.

We analysed anonymised and de-identified data from 500,000 Oura Ring Gen3 users with ≥ 14 days of valid recordings in September 2024. Daily sleep and ePWV estimates were averaged to produce monthly aggregates. ePWV delta was calculated as the difference between each user's estimated PWV and the age- and sex-specific average within the dataset.

Sleep metrics included total sleep time, awake time, sleep stage durations (light, deep, REM), and sleep onset and wake times, used to calculate the SRI. The difference between ePWV delta in binned sleep metric groups was evaluated using Kruskal–Wallis test.

Results: ePWV showed good agreement with cf-PWV ($R = .76$, mean difference = $.210$ m/s, $SD = .999$ m/s), meeting acceptable validation criteria (mean $\pm$ SD between 1.0 – 1.5 m/s). ePWV delta differed across total sleep duration groups, lowest at 7–9 hours; long sleep (>9 h) showed a greater increase than short sleep (<7 h). Kruskal–Wallis tests showed significant differences ($p < .001$) across all metrics. Increased deep and REM sleep were linked to lower ePWV delta, while increased awake time was tied to higher values. Light sleep duration showed a U-shaped pattern in ePWV delta. Higher SRI corresponded to lower ePWV delta.

Conclusions:

PWV estimates from a smart ring demonstrate acceptable agreement based on recommended validation guidelines. 7–9h sleep duration, regular timing, and more deep/REM sleep are linked to lower arterial stiffness (ePWV). In contrast, 4–7h and 9–11h sleep duration, irregular timing and more awake time are linked to higher ePWV. These findings demonstrate that PPG-based ePWV produces results consistent with prior research and provide a foundation for future large-scale studies investigating the complex relationship between sleep and arterial stiffness.

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Benzodiazepine Burden and associated Health Risks in geriatric Patients with Hearing impairment: A Population-Based Cohort Study

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Introduction: Benzodiazepine derivatives (BDZs) are commonly utilized as sedatives, hypnotics, muscle relaxants, and anticonvulsants. In South Korea, orexin receptor antagonists have not yet been introduced into clinical practice; thus, BDZs, along with Z-drugs, are prescribed in certain cases for the management of insomnia. Hearing loss is prevalent among older adults and is associated with an increased risk of falls, cognitive impairment, and mortality. BDZs may worsen these risks owing to their adverse effects to this age group with hearing loss. This study aims to investigate the association between prolonged BDZs use and the subsequent risks of falls, fractures, emergency department (ED) visits, dementia, and mortality in older adults with hearing loss in Korea.

Materials and methods: This population-based retrospective cohort study utilized data from the Korean National Health Insurance Database spanning 2018 to 2021. Participants included individuals aged 65 years or older who were diagnosed with hearing loss in the previous year, excluding those with cancer, genetic hearing loss, fractures, or dementia. The benzodiazepine burden was assessed using the approximate equivalent dose of 10 mg of diazepam (EDD10) and total standardized daily doses (TSDD). Cox regression analysis estimated hazard ratios (HRs) for falls, fractures, ED visits, dementia, and mortality, adjusting for covariates. The models used were as follows: Model 1 was unadjusted; Model 2 adjusted for age and sex; Model 3 further adjusted for alcohol consumption, smoking, and BMI; and Model 4 included adjustments for comorbid diseases associated with falls, fractures, and dementia.

Results: The final cohort consisted of 598,152 individuals. The group with a high benzodiazepine burden (TSDD $\geq$ 30, n=85,614) exhibited significantly increased risks for dementia (adjusted HR 1.197, 95% CI 1.162-1.215), ED visits (adjusted HR 1.051, 95% CI 1.016-1.079), and mortality (adjusted HR 1.127, 95% CI 1.09-1.164) compared to the group with no benzodiazepine burden (TSDD=0, n=370,665) after adjusting age, sex, alcohol use, smoking use, body mass index, comorbid diseases related to falls, fractures, and dementia. When the outcomes were falls and fractures, a significantly increased risk was observed in the group with a high benzodiazepine burden after adjusting for age, sex, alcohol use, smoking status, and body mass index. However, this association was no longer significant after further adjustment for comorbid conditions related to falls, fractures, and dementia. The Kaplan–Meier curves indicated a higher incidence of all outcomes, except mortality, in the high benzodiazepine burden group compared to the no burden group at all observed time points.

Conclusions: Prolonged benzodiazepine use in older adults with hearing loss is associated with an elevated risk of adverse outcomes, including dementia, ED visits, and mortality. When prescribing to this vulnerable population, the risk-benefit balance should be carefully considered and monitoring this population to mitigate potential harms. Further research is warranted to explore alternative therapeutic options and the underlying mechanisms contributing to these risks.

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Cerebral and Peripheral Hemodynamics across wakefulness and NREM Sleep

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Introduction: Wake/sleep state-related changes in cerebral hemodynamic oscillations are well established. However, similar changes in peripheral hemodynamics are vastly understudied. Importantly, the inter-relationships between cerebral and peripheral hemodynamics may change with wake/sleep states, given the fact that these oscillations in the low-frequency range are strongly coupled during wakefulness. The current study therefore investigates the temporal and spectral variations in cerebral and peripheral hemodynamics as well as the coupling between them in the low-frequency range across sleep-wake states.

Materials and methods: To study these, we concurrently measured cerebral hemodynamics and peripheral hemodynamics respectively using functional Magnetic Resonance Imaging of the brain and Near-infrared spectroscopy of the fingertips during wakefulness and non-rapid eye-movement sleep. This study included 10 healthy participants (6 females) aged 19 – 24 (20.90 $\pm$ 1.59) years. Actigraphy

was used to track each participant's sleep-wake cycles for at least four days before the experiment to ensure they adhered to their usual sleep schedules. Additionally, to allow for sound acclimation, they were instructed to listen to sound recordings from the MR scanner at bedtime for two to three nights before their scheduled bedtime scan. To capitalize on elevated homeostatic and circadian sleep pressures, participants were asked to wake up three hours earlier than usual the morning of their scan, and the scan sessions began roughly one hour after their usual sleep onset time. All MRI data were acquired using a 3T SIEMENS MRI scanner with a 64-channel head coil. Peripheral hemodynamics were recorded from two fingertips (fourth finger of both arms) using a Continuous Wave (CW) NIRS system with two laser sources, each combining two wavelengths (785 and 830 nm) and MRI-compatible NIRS probes with 10 m long optical fibers. For sleep scoring, a 32-channel Electroencephalography (EEG) was also simultaneously acquired using an MRI-compatible EEG system.

Results: Overall findings from the present study are twofold. First, hemodynamics in the brain remarkably differ in both oscillation amplitude and spectral power from peripheral hemodynamics during NREM sleep stages. Second, the LF coupling between cerebral and peripheral hemodynamics become desynchronized during NREM3 sleep.

Conclusions: Our data demonstrate the amplitude fluctuations of cerebral hemodynamics significantly increase during light NREM sleep (NREM1 and NREM2) and then decrease significantly during deep sleep (NREM3). Fluctuation levels of peripheral hemodynamics however stays the same from wake to NREM3. To our knowledge, this is the first study to report this discrepancy in hemodynamic fluctuation levels between brain and periphery during NREM sleep.

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Sleep, breathing, hemodynamic oscillations, and cerebrospinal fluid movements - Building toward a novel treatment approach for Alzheimer's disease.

Clinical Characteristics of pediatric Obstructive Sleep Apnea Hypopnea Syndrome After SARS-CoV-2 Exposure

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Introduction: Pediatric obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by recurrent episodes of partial upper airway obstruction, leading to oxygen desaturation and sleep disruption. Recent studies published between 2016 and 2023 have reported higher prevalence rates, ranging from 12.8% to 20.4%. Studies have demonstrated that persistent viral RNA can be detected in the tonsillar and adenoid tissues of children for weeks to months following acute SARS-CoV-2 infection. To investigate the incidence trends and clinical characteristics of pediatric obstructive sleep apnea (OSA) following exposure to SARS-CoV-2.

Materials and methods: This study enrolled a consecutive cohort of pediatric patients with polysomnography (PSG) recordings from the Sleep Medical Center of Beijing Tsinghua Changgung Hospital between January 2021 and November 2024. Patients who had severe concomitant pulmonary, neurologic, cardiovascular, or psychiatric disorders were excluded. The demographic and PSG characteristics were compared.

Results: 1. A total of 1,377 children were included in the study; a notable upward trend in the incidence of pediatric OSA was observed following exposure to SARS-CoV-2, with the pre-SARS-CoV-2 Exposure Group (pre-SCE) (n=496) and the post-SARS-CoV-2 Exposure Group (post-SCE) (n=881). After stratification by age, the incidence rose 1.06-fold in children <6 years and 2.09-fold in those aged 6-8 years. Strikingly, children > 8 years exhibited the most pronounced increase, with a 3.94-fold surge in the prevalence of OSA.

2. Pediatric OSA showed significant disease progression after SARS-CoV-2 exposure. The post-SCE group exhibited higher median values for the apnea-hypopnea index (AHI: 5.500 [2.750, 13.000] vs. 3.800 [1.900, 7.700]), hypopnea index (HI: 3.500 [1.400, 8.400] vs. 1.800 [0.600, 4.850]), and obstructive apnea-hypopnea index (OAHl: 4.150 [1.400, 10.675] vs. 2.000 [0.697-6.400]), $P < 0.001$.

3. PSG analysis indicated significant sleep architecture modifications post-SCE, with the arousal index increasing from 7.500 [5.100, 10.700] to 11.900 [8.700, 16.700], $P < 0.001$.

4. A comparative analysis of tonsillar and adenoid dimensions before and after viral exposure revealed a statistically significant rise in the proportion of grade 3 (36.49% vs 43.47%) and grade 4 (12.10% vs

14.42%) ($p < 0.05$) tonsillar enlargement following SARS-CoV-2 exposure. Within the age > 8 years group, the prevalence of adenoid tissue obstruction $> 75\%$ following SARS-CoV-2 exposure increased significantly from 11.90% to 22.05%, despite this age group typically exhibiting physiological adenoid involution.

5. Multivariate regression analysis revealed that children with grade 4 tonsillar hypertrophy demonstrated a significantly greater increase in the OAHl scores following exposure to SARS-CoV-2 compared to the pre-pandemic period ($\beta=3.40$, $p<0.001$).

Conclusions: Following exposure to SARS-CoV-2, there has been a notable increase in the incidence of pediatric OSA and the severity of the disease, which is associated with significant tonsillar hypertrophy and delayed adenoid regression.

Clinical Trial: Efficacy of Metered-dose Negative-Pressure Breathing Training in OSA Patients

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Introduction: Oliven et al (J Sleeping Res. 2018) found pharyngeal muscles response linearly to airway negative pressure change. We use that as a “dumbbell” load for exercise prescription. This study aims to assess the effectiveness of a resistance mask device (GST) for negative pressure breathing training in patients with obstructive sleep apnea (OSA).

The study plans to enroll 10 participants to assess the device's impact on respiratory muscle strength and sleep apnea symptoms.

One of the main contributors to sleep apnea is the collapse of upper airway muscles during sleep, resulting in breathing difficulties. Strengthening these muscles through targeted exercises could potentially alleviate symptoms and improve quality of life for patients with sleep apnea.

Materials and methods: * Participants diagnosed with sleep apnea will be recruited for the trial and provided with the mask device for daily use. The device GST utilizes resistance inspiration negative pressure with 10-40 hpa depending on the patient's condition to enhance the strength of upper respiratory dilator muscles during breathing exercises. Assessments of 4% ODI, questionnaire and visual analogue score will be conducted before and after using the device. Data analysis will focus on comparing pre- and post-treatment measurements to determine the device's efficacy in improving respiratory muscle function and alleviating sleep apnea symptoms. This study aims to provide valuable insights into the role of targeted muscle strengthening in managing sleep apnea and enhancing respiratory health.

Recruitment Criteria:

>Inclusion Criteria:

OSA patients aged 18-65, willing to participate, with a confirmed OSA diagnosis, and able to comply with the study protocol.

>Exclusion Criteria:

Abnormal PFT, acute illnesses, cardiovascular diseases, and uncontrolled allergic rhinitis or nasal obstruction diseases, BMI >30 , will be excluded

Results: 6 patients complete the trial

4% ODI: Decreased by an average of 29%

minSpO₂: Improved by 2%

Snoring Score: Totally reduced by 22%, very loud by 76%

Morning Symptoms: Headache and dizziness frequency dropped by 28%

Adherence: 100%

Training Load: 10–30 hPa, tailored per subject

Temporal Trends:

- ODI improvement occurred between Day 10–26

- Symptom relief noted after Day 32–40

- Snoring decreased after Day 7-25

Conclusions: Preliminary findings suggest GST is a promising adjunct to conventional OSA therapy, especially in enhancing patient tolerance and respiratory muscle endurance. GST's adaptability and high adherence rate support its feasibility. The initial clinical response appears temporally progressive and responsive to upper airway events, implying a muscle-based mechanism.

Metered-dose negative-pressure respiratory muscle training using the GST device shows early effectiveness in improving oxygenation, reducing snoring, and alleviating OSA-related symptoms. This pilot supports the rationale for broader trials and potential integration into multimodal OSA management.

Future Directions

- Expansion to full cohort with subgroup analysis
- Long-term follow-up on muscle strength and AHI
- Combination therapy with CPAP/APAP
- AI-guided personalization of pressure dosing

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Daytime Sleepiness is Associated with Poorer Driving Outcomes in Older Adults with SCD or MCI

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Introduction: Daytime sleepiness increases the risk of cognitive decline in older adults and separately has important implications for driving safety. To date, no research has investigated the association between sleepiness and driving behaviours in older adults with early stage cognitive decline: that is, subjective cognitive decline (SCD) and mild cognitive impairment (MCI). This study investigated how prodromal stages of dementia (cognitively healthy, SCD, and MCI) are associated with daytime sleepiness, self-reported driving behaviours, and the relationship between sleepiness and driving across the cognitive stages.

Materials and methods: Fifty-eight participants (mean age 71.34 ± 5.72 years) completed a neuropsychological assessment and were classified as cognitively healthy ($n = 21$), SCD ($n = 24$) or MCI ($n = 13$). The Geriatric Depression Scale (GDS), Epworth Sleepiness Scale (ESS) and the Manchester Driving Behaviours Questionnaire (DBQ) were also completed. The DBQ is categorised into lapses, aggressive violations, violations, and errors. Additionally, participants completed a driving diary for trips that were 15 minutes or longer, for two continuous weeks. This included the Karolinska Sleepiness Scale (KSS), Sleepiness Symptoms Questionnaire (SSQ) for sleepiness symptoms specific to driving, and any adverse driving events (i.e., sleep-related, inattention, hazardous, or violations).

Results: Relative to cognitively healthy participants, ESS scores were significantly elevated in SCD (156% increase, $p < .001$) and MCI (137% increase, $p = .014$) groups, adjusted for age, sex, and GDS. Similarly, driving diaries indicated that the SCD group reported 1.09x higher rates of sleepiness symptoms on the SSQ ($p = .004$) compared to cognitively healthy participants. For driving behaviours, the SCD group reported 2.77x more violations on the DBQ compared to the MCI group ($p = .032$), but did not differ to healthy controls. The SCD group also reported 7.51x greater inattention events on driving diaries compared to cognitively healthy participants ($p = .011$), adjusted for drive duration. Within group analyses showed that each unit increase in SSQ was associated with 1.34x more inattention events in the SCD group ($p = .004$) and 2.32x more inattention events in the MCI group ($p = .018$). Further analysis of specific SSQ items within the SCD group identified that "Reactions are slow" predicted 5.07x greater inattention events ($p < .001$), and "Difficulty keeping to the middle of the road" predicted 4.04x more inattention events ($p = .016$).

Conclusions: This was the first study to examine the relationship between sleepiness and driving in older adults at various prodromal stages of dementia. We show older adults with SCD and MCI report greater daytime sleepiness than those who are cognitively healthy, with sleepiness symptoms associated with more inattention driving events for both groups. These results suggest that daytime sleepiness may be early consequence of cognitive decline with implications for driver safety. Future work should examine whether targeting daytime sleepiness may improve driving outcome for those at

the early stages of cognitive decline, especially at SCD, which could prolong safe driving to preserve independence and social connectedness in older drivers.

Effect of sex hormones on sleep architecture in older women

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Introduction: Sleep in post menopausal elderly women is lacking in data as to how hormones effect their various stages of sleep. It has been shown that sex steroids Testosterone (T) and Estrone (E) increase with age with steady decline in DHEA. Sex hormones have been implicated in development of age related chronic diseases, including cancer, impacting overall longevity and quality of life. It has been established that decreasing levels of estrogen with increased testosterone levels affect development of cardiovascular diseases. Estrone is the major circulating estrone in post menopausal women. Post menopausal women have disturbed night time sleep with episodes of hot flashes that disrupt their sleep and leaves them tired and fatigued. they often complain of frequent awakenings, difficulty falling asleep, and poor overall quality of sleep. Each decade of post menopausal life has varying amounts of circulating sex hormones. Specifically in the seventh decade there is most significant changes observed in level of Estrone and testosterone. We hypothesized that changes in sleep architecture affected by circulating hormones will be observed in this age group of women.

Materials and methods: Twenty two post menopausal women between the ages of 55-79 were divided into two groups 55-69 and 70-79 underwent overnight polysomnography as indicated by their physicians. Data was collected on their age, BMI, chronic illnesses use of medications. Sleep stages of N1, N2, N3 and REM were measured and expressed in percentage of sleep. Total sleep time and time in bed was also measured. Data was collected and measured in percentage of sleep, Data analyzed as mean $\pm$ Std dev and t test conducted with $p < 0.05$ taken as significant.

Results: All twenty two postmenopausal women were diagnosed with sleep apnea. of the thirteen women in the 70-79 group, Eleven of these women were also diagnosed with diabetes and one was current smoker. Average BMI in the group was 32.1, Further N2 sleep was 60% and N3 and REM sleep were significantly reduced compared to women in the 55-69 age group, to 11% and 3 % of total sleep time with $p < 0.05$,

Conclusions: Post menopausal women have significant alterations in circulating sex hormones which among other things also significantly impacts their sleep architecture. Instead of putting all post menopausal women under one umbrella it would be helpful to cluster them in each decade of life and hence provide more appropriate supportive therapy as indicated by symptoms and circulating hormone levels. This study specifically looked at women in the seventh decade of life as literature shows that in this decade Estrone is the predominant circulating estrogen and levels of testosterone are not significantly different from premenopausal levels. So, could estrone be impacting sleep outcome, this needs further evaluation.

Elder Abuse, Age Discrimination, and Insomnia Among Frail Older Adults in India

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Introduction:

Elder abuse and age discrimination are growing public health concerns in India, particularly amid shifting family dynamics, changing caregiving roles, and persistent social stigma around aging. Insomnia is also highly prevalent among older adults, especially those who are frail, due to diminished physiological resilience and heightened vulnerability to psychosocial stressors. This study examined the associations of elder abuse and age discrimination with insomnia symptoms in a nationally representative sample of frail older adults in India.

Materials and methods: We analyzed data from the Longitudinal Aging Study in India (LASI), focusing on a sample of 8,901 older adults identified as frail. Frailty was measured using a modified version of the Fried Frailty Phenotype. To examine the association between elder abuse, age discrimination and

insomnia symptoms among frail older adults, we employed multivariable linear and logistic regression models.

Results: After adjusting for sociodemographic and health variables, including chronic conditions, both elder abuse (β : 0.35, 95% CI: 0.12, 0.57) and age discrimination (β : 0.23, 95% CI: 0.10, 0.36) were significantly associated with higher levels of insomnia symptoms among frail older adults. Specifically, elder abuse was associated with increased odds of difficulty initiating sleep (AOR: 1.57, 95% CI: 1.11, 2.22), difficulty maintaining sleep (AOR: 1.74, 95% CI: 1.28, 2.37), and early morning awakening (AOR: 1.44, 95% CI: 1.02, 2.03), though not with daytime unrested feeling. In contrast, age discrimination was significantly associated with difficulty maintaining sleep (AOR: 1.35, 95% CI: 1.11, 1.63), early morning awakening (AOR: 1.43, 95% CI: 1.17, 1.74), and daytime unrested feeling (AOR: 1.37, 95% CI: 1.13, 1.66), but not with difficulty initiating sleep.

Conclusions: Our findings highlight both elder abuse and age discrimination as significant risk factors for insomnia symptoms among frail older adults in India. Elder abuse was particularly associated with difficulties in sleep initiation and maintenance, while age discrimination was more strongly linked to difficulty maintaining sleep, early morning awakening, and daytime unrested feeling. These results underscore the need for policies and interventions that address elder mistreatment and age-based discrimination not only to safeguard the dignity and well-being of older adults but also to promote healthier sleep and overall quality of life in later life.

Enlarged perivascular spaces is associated with cognitive impairment in older adults with obstructive sleep apnoea

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Introduction: Obstructive sleep apnoea (OSA) is prevalent among older adults and is often linked to cognitive impairment when untreated. It is posited that the underlying pathology of OSA is connected to glymphatic dysfunction - a perivascular network in the brain responsible for metabolic waste removal. Although various methods have been proposed to index the perivascular spaces (PVS) as a promising imaging marker for the glymphatic system, these methods are often developed and tested on homogeneous datasets with high resolution scans, limiting its generalizability. Therefore, using a newly developed automated PVS segmentation method, this study aimed to determine (1) if PVS differs across OSA groups, and (2) if PVS is associated with cognitive impairment.

Materials and methods: Participants aged 50-80 with new onset cognitive or mood concerns underwent clinical and neuropsychological profiling at a memory clinic. Domain specific cognitive composites (i.e., verbal learning, verbal memory, executive function, processing speed and language) were created from neuropsychological tests, with age and education (where possible) adjusted. From polysomnography, apnea hypopnea index (AHI) was derived. Participants were categorized into normal (AHI<5; n=83), mild (AHI=5-14; n=92), moderate and severe (AHI≥15, n=111) OSA groups. PVS clusters and volumes were derived from a deep learning algorithm - Perivascular space Identification NnUNet for Generalised Usage (PINGU). Regions of interests (ROIs) included the Basal Ganglia, frontal lobe and Thalamus due to their functional relevance for sleep and cognition. One-way analysis of variance (ANOVA) and Spearman's rho were used to estimate group differences and correlations, adjusted for age, sex and body mass index.

Results: After adjusting for covariates, PVS clusters and volumes in all ROIs showed no differences among the three OSA groups. Across the whole sample, PVS was not associated with cognitive outcomes. However, in the mild OSA group, enlarged PVS in the Basal Ganglia was associated with impaired language ability (Clusters, $r=-.227$, $p=.042$; Volumes, $r=-.25$, $p=.023$). Enlarged PVS in the Thalamus was associated with lower performance in verbal learning (Clusters, $r=-.285$, $p=.010$; Volumes, $r=-.289$, $p=.009$), verbal memory (Clusters, $r=-.221$, $p=.049$; Volumes, $r=-.225$, $p=.043$), executive function (Volumes, $r=-.283$, $p=.012$) and processing speed (Volumes, $r=-.231$, $p=.039$).

Conclusions: This study, utilizing a new model of PVS processing pipeline, indicates that while OSA severity alone does not globally correlate with PVS enlargement or broad cognitive deficits in older adults, localized PVS changes in specific brain regions may influence domain-specific cognitive impairments, particularly in mild OSA. Early-stage OSA might trigger glymphatic dysfunction in cognition-critical regions, potentially masked or compounded by other pathological mechanisms in

moderate/severe OSA. The Thalamus and Basal Ganglia, crucial for sleep regulation, memory, and executive function, appear susceptible to PVS-related changes, highlighting their role as neural hubs where glymphatic disruption may disproportionately impact cognition. The PINGU tool allowed detection of subtle, region-specific PVS-cognition relationships, emphasizing the value of advanced segmentation techniques in heterogeneous clinical populations.

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Evaluating Sleep Architecture Variability in Older Adults with Cognitive Decline

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Introduction: Neurodegenerative disorders are characterized by cognitive deficits and sleep disturbances with abnormal sleep architecture. The interpretation and clinical application of sleep biomarker quantification for use in subtyping neurodegenerative disorders requires an understanding of how variability might impact the findings. In this study we investigated two factors that could influence the in-home sleep biomarker variability in older adults with cognitive decline.

Materials and methods: 23 women and 12 men (ages 71.5±8.5 years, 30 diagnosed with mild cognitive impairment and 5 with Alzheimer's dementia) completed two-night in-home recordings with the Sleep Profiler™ with 4 women and 6 men repeating the procedure one-year later, for a total of 45 recordings. The studies were auto-staged and then edited using procedures developed to visually verify accuracy. Intra-class correlations (ICC) and Bland-Altman (BA) analyses were used to compare Night-1 versus Night-2 variability obtained with auto- and then edited staging, followed by comparison of auto- versus edited staging by night.

Results: The consistency between Nights-1 versus Night-2 sleep times were poor for both auto- and edited-staging (ICC=0.39 and 0.31, $p<0.025$), and fair for recording times (ICC=0.50 and 0.40, $p<0.005$) and sleep efficiencies (ICC=0.46 and 0.47, $p<0.001$).

Between-night variability was exacerbated after the auto-staging was edited for REM time (ICC=0.55 and 0.47, $p<0.001$) and N1 time (ICC=0.59 and 0.49, $p<0.0005$), while pre- and post-edited consistencies were equivalent for %REM (ICC=0.54 and 0.55, $p<0.0001$) and %N1 (ICC=0.55 and 0.54, $p<0.0001$).

Between-night consistencies were good for auto- and edited times in stage N2 (ICC=0.68 and 0.69, $p<0.0001$), and increased to excellent for %N2 (ICC=0.80 and 0.80, $p<0.0001$). For stage N3, the variabilities were similar based on time (ICC=0.74 and 0.77, $p<0.0001$) and percent-time (0.74 and 0.74, $p<0.0001$).

Auto-staging biases resulting from detection of lower sleep efficiencies, decreased %REM, and increased %N2 on Night-1 (Bias=-2.38, -1.50, and 1.81%) were reduced after editing (Bias= -1.43, -0.72%, and 0.67%). These edits, however, contributed to an increased stage %N3 bias (Bias=0.03 and 0.59%).

The auto- versus edited recording times were excellent for Night-1 (ICC=0.84) and good for Night-2 (ICC=0.67). Sleep efficiency concordances were equivalent when auto- versus edited-staging were compared for Nights-1 and -2 (ICC=0.93 and 0.92, $p<0.0001$), however the bias on Night-1 was almost two-times greater than Night-2 (Bias=-0.92 to -0.49).

With the exception of Stage N1, the auto- versus edited consistencies were excellent across all stages, (all ICCs > 0.84, $p<0.0001$). Concordances were fair for time N1 and good for %N1 on Night-1 (ICC=0.53 and 0.69, $p<0.0001$) and excellent on Night-2 (ICC=0.78 and 0.91, $p<0.0001$).

The number of epochs edited from stage N2 to REM were greater on Night-1 and resulting in biases of -1.23% and 0.67%, respectively, versus 0.09 and -0.17 during Night-2.

Conclusions: Important night-to-night variability was observed in all sleep architecture measures except %N2. These findings point to a first night effect and suggest multiple nights would be useful in evaluating patients with cognitive impairment in their home. Technical edits to the auto-staging most prominently impact stages N1 and REM, primarily during Night-1.

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Evaluation of the effect of sleep apnea syndrome, as well as its therapeutic interventions, on hearing level

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Introduction: Obstructive sleep apnea (OSA) is one of the most common respiratory disorders characterized by intermittent upper airway obstruction during sleep resulting in episodes of apnea and/or hypopnea and awakenings associated with a respiratory event (RERA). While, the sense of hearing is based on the transmission of sound through the auditory pathway. It is a complex and quite sensitive pathway that begins from the external ear and ends in the auditory cortex of the brain, mediated by structures very sensitive to vascular insufficiency and hypoxemia such as the hair cells of the cochlea.

Materials and methods: In this prospective study we measured the hearing level of individuals with a new onset OSAS. For the purposes of the study, patients who, after a sleep study, will receive a diagnosis of sleep apnea syndrome will undergo a thorough ENT clinical examination and audiological examination. The participating patients will be re-evaluated three and six months after the initial diagnosis, a period that will coincide with the start of appropriate treatment (CPAP or surgery). Based on the results of the audiological tests at months 0, 3 and 6, we will attempt to test the correlation between treatment (CPAP or surgery) and prevention or improvement of the hearing threshold. In addition, the goal is to find the parameter that can best predict the degree of hearing loss in relation to the severity of sleep apnea. In this direction, we will look for the existence of a correlation between the degree of hearing loss and each of the following parameters of the sleep study: 1) Mean Spo2 of the study, 2) $\Delta\text{SpO}_2 = \text{resting} - \text{min sleep}$, 3) Total apnea time (minutes of sleep with saturation <90%), 4) Noise caused by snoring (dB), 5) AHI (apnea-hypopnea index) and 6) OSA questionnaires (Epworth Sleepiness Scale, Stop-Bang Questionnaire, OSA50, Berlin Questionnaire)

Results: Twenty two participants, (16 men, 6 women) with a mean age of 50.8 years old were included in the study. These individuals did not refer previous otologic history or any systematic disease associated with hearing problems. Clinical examination, otoscopy and tympanometry were normal. The pure tone audiogram revealed a slight sensorineural hearing impairment in both ears. A gradual deterioration was observed in high frequencies. The mean hearing level for 4kHz was 35dB for the right ear and 40dB for the left ear, while the hearing level for 8kHz was 45dB for both sides.

Conclusions: A few studies, with inconsistent results, have examined the possibility that nocturnal obstructive apnea-hypopnea affects the auditory pathway, however literature lacks consistency regarding the relationship between sleep apnea and hearing loss. Our study for correlation between OSAS and hearing loss was held at a clinical and not an experimental level. Audiological data are primarily based on subjective measurements of the pure tone audiogram. This fact decreases the degree of objectivity of the findings, however it allows speed, convenience and zero cost in data collection.

Lights Out, Waste Out: Dynamic Changes in Slow Wave Sleep Drive Peripheral Clearance of AD Biomarkers in Older Adults

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Introduction: There are currently 50 million people worldwide with dementia, with Alzheimer's Disease making up 60-80% of all cases. Convergent evidence suggests that slow wave sleep (SWS) is critical for brain health and cognition, and plays a potential role in neurodegeneration: for instance, SWS is associated with memory consolidation and frontal 'executive' function and shows a consistent decline with age, which is exacerbated in those with AD. Moreover, in a non-human model, SWS has been shown to clear AD-related waste products such as amyloid via the glymphatic system. More recently, dynamic changes in SWS across the night have been linked to plasma amyloid levels in providing evidence of SWS-related clearance of AD-related proteins in a human model. We aimed to extend this work by examining the association between SWS and other plasma biomarkers of AD in a cohort of older adults.

Materials and methods: Twenty-four cognitively intact older adults aged 60-76y (13 female) were recruited from the community and a large existing cohort (AIBL). Participants underwent simultaneous overnight polysomnography and blood sampling, whereby blood samples were collected every 30min remotely without awakening the participant, across an 8h sleep opportunity and for 1h post-wake. Plasma levels of AB40, AB42, pTau181, pTau217, GFAP and NfL were quantified using a SIMOA-HD, and modelled with slow oscillations (0.5-1Hz), slow wave activity (0.5-4Hz), and slow wave sleep minutes and proportion per 30min interval, across time lags of 0-120min.

Results: Linear mixed models revealed AB40, AB42, and pTau181 were significantly associated with several slow wave sleep dynamics at lags of 90-120 min. Moreover, repeated measures correlations show positive association between these markers and slow wave dynamics across the night, particularly at 120min lag. While pTau217 trended toward significance (for mixed models and correlations), overall plasma levels were extremely low, with less variability between participants or samples. In contrast, plasma GFAP and NFL levels were not significantly associated with slow wave dynamics. These results remained stable after accounting for baseline plasma levels, associated with cortical amyloid burden.

Conclusions: Slow wave sleep dynamics were significantly associated with peripheral levels of amyloid and p-Tau181 (p-Tau217 less consistent), but not GFAP and NfL. Given the established link between slow wave and glymphatic clearance, these peripheral markers *may* indicate glymphatic clearance, which in humans remains difficult to capture. These are preliminary data and further work is needed to establish (a) the causal role of slow wave on glymphatic clearance and (b) the use of this approach as a measure of glymphatic clearance.

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Multi-organ sleep age derived from polysomnography and risk of dementia and mortality

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Introduction: Chronological age is a major risk factor for dementia and mortality, but may not capture differential biological aging across organ systems. Multimodal physiological signals obtained from polysomnography (PSG) probe widespread physiological networks, and provide a unique opportunity to evaluate organ-specific ages: the electroencephalogram (EEG), electrocardiogram (ECG), and respiratory effort signals can serve as proxies for the sleep-derived ages of the brain, heart, and lungs, respectively. Given complexity of such data, artificial intelligence (AI)-derived multi-organ ages generated from PSG signals could predict dementia or mortality risk.

Materials and methods: We trained deep neural networks on 60,968 PSG recordings to predict chronological age and applied them to an independent test set of 3,110 recordings. Data were drawn from the National Sleep Research Resource cohorts and from the Massachusetts General Hospital (MGH), Sir Run Run Shaw Hospital, and Shanghai Sixth People's Hospital. We estimated brain, heart, and lung age from the EEG, ECG, and abdominal belt-derived respiratory effort signals, and computed brain age index (BAI), heart age index (HAI), and lung age index (LAI) as the difference between each organ's AI-predicted age (derived from its corresponding PSG modality) and chronological age. We examined associations between the three age metrics and the risk of dementia and mortality, using data from 7,395 MGH patients who underwent in-laboratory PSG. Dementia was identified using ICD-9 and -10 codes and mortality from the Massachusetts death registry and MGH electronic health records. For the dementia analysis, individuals with prevalent dementia at the time of PSG were excluded, resulting in a sample of 7,384 participants. Multivariate Cox regression models were performed. Death was treated as a competing risk in the dementia analysis using the Fine-Gray subdistribution hazard models.

Results: Participants had a mean chronological age of 50.3 (± 15.7) years, 50.8% were women, and 18.8% were non-White. Brain, heart, and lung ages were estimated with mean absolute errors of 4.41, 5.01, and 5.43 years, and corresponding Pearson correlation coefficients of 0.97, 0.96, and 0.96. HAI correlated moderately with LAI ($r = 0.26$), whereas BAI showed weaker correlations with both HAI ($r = 0.13$) and LAI ($r = 0.15$); all $p < 0.001$. Over a median follow-up of 9.5 years [range: 0.02–16.1], 182 participants developed dementia and 207 died. After controlling for sociodemographics, sleep medications, apnea-hypopnea index, and health covariates, each 10-year increase in BAI, HAI, and LAI were associated with a higher risk of dementia of 172% (Hazard ratio (HR)=2.72, 95% confidence interval (CI)= 2.0-3.94), 32% (HR=1.32, 95% CI=0.98-1.75), and 32% (HR=1.32, 95% CI=1.04-1.65), respectively. Similarly, higher BAI, HAI, and LAI were associated with increased mortality risks of 87% (HR=1.87, 95% CI=1.43-2.43), 59% (HR= 1.59, 95% CI=1.26-2.00), and 38% (HR=1.38, 95% CI=1.09-1.75), respectively.

Conclusions: Accelerated brain, heart, and lung age, as captured from PSG, are associated with increased risks of dementia and mortality over 10 years. Brain age showed the strongest association with both outcomes, while heart age was especially predictive of mortality. These organ-specific age metrics may serve as early markers of vulnerability to aging-related disease and potential targets for intervention.

Nocturnal Hypoxic Burden Is Associated with Brain Structural Alterations in Older Adults with OSA

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Introduction: Intermittent hypoxia in obstructive sleep apnea (OSA) is often underestimated by the conventional apnea-hypopnea index (AHI), which quantifies discrete respiratory events without quantifying their physiological severity. Hypoxia burden, defined as the area under the oxygen desaturation curve offers a more accurate measure of the intensity and duration of hypoxic stress. However, the association between hypoxia burden and brain structural changes has not been thoroughly investigated in older adults with OSA. The aim of the study was to study the association between hypoxia burden and brain structural changes in older adults with OSA

Materials and methods: This study analyses data from SOLACE cohort. A subpopulation of 55 older adults (aged 51-80 years) with obstructive sleep apnea and without dementia were selected based on the availability of brain MRI scans. Flow events and oxygen saturation values were extracted from overnight polysomnography, and hypoxia burden was computed using a custom MATLAB script. brain structure volumes were assessed using voxel-based morphometry on 3T MRI scans.

Results: The final sample included 55 participants (mean age 64.98 ± 7.21 years; 83.6% male, median AHI 17.10 (3-.23-13.13). Hypoxia burden was significantly correlated with left hippocampus volume, $r(53) = -.2788$, $p = 0.039$ and left amygdala, $r(53) = -.324$, $p = 0.036$.

Conclusions: In older adults with OSA, greater hypoxia burden is significantly associated with reduced volumes of the left hippocampus and left amygdala, suggesting a potential link between nocturnal hypoxemic stress and brain structural alterations.

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Orexin receptor antagonism rescues sleep and improves anxiety in tau-transgenic mice, but only improves cognition sex-dependently

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Introduction: Alzheimer's disease (AD) is one of the largest public health issues facing societies with aging populations, affecting females more than males. Disordered sleep is a well-known AD risk factor, symptom and bidirectional pathological contributor to disease progression. Dual orexin receptor antagonists (DORAs) block signalling of both orexin 1 (Ox1R) and 2 (Ox2R) receptors, and are the only hypnotics approved for use in AD. Yet, preclinical evidence indicates a blunted response to selective Ox2R antagonists (2-SORAs) in female rodents with tauopathy. Therefore, we aimed to compare the effects of DORAs and 2-SORAs on sleep, cognition, and anxiety in tau-transgenic PS19 male and female mice.

Materials and methods: We performed two experiments in PS19 mice. Experiment 1 assessed the baseline relationship between sleep and behaviour. Mice underwent monthly polysomnographic EEG recordings and locomotor assays at 7, 8 and 9 months of age, and Barnes maze cognitive testing at 7 and 9 months. Experiment 2 assessed the effects of the DORA "DORA-22" (100 mg/kg) and 2-SORA "MK-1064" (40 mg/kg) after 6 weeks of chronic, oral dosing. Sleep, via polysomnographic EEG recordings, cognition via Barnes maze, and anxiety/agitation via locomotor and stress-induced hyperthermia (SIH) assays were assessed after 6 weeks of dosing.

Results: Experiment 1 revealed tau-transgenics were awake for 154.8 minutes more than WT, with loss in NREM and REM sleep. Tau-transgenics spent an average of 118.7cm in outer region of locomotor cells; indicating increased anxiety. This phenotype was significantly more pronounced in tau-transgenic males. PS19s demonstrated similar learning effects to WT in Barnes maze probe trial performance. Experiment 2 revealed the relationship between sleep and cognition differed markedly between genotype and sex. Vehicle-treated PS19s lost 82.9 and 135.9 minutes of TST in females and males (respectively) compared to WT. DORA-22 treatment rescued 71.4 and 73.8 minutes of TST in females and males, respectively. MK-1064 rescued 86.9 and 42.9 minutes of TST in females and males, respectively. Both treatments reduced numerous locomotor hyperarousal measures manifesting in females, alongside anxiety measures in SIH. Lastly, treatment with either DORA-22 or MK-1064 rescued Barnes Maze cognitive performance to WT-levels in male tau-transgenic animals, but did not improve female cognitive performance.

Conclusions: DORAs and 2-SORAs improved sleep and neuropsychological outcomes in tau transgenic mice. Initial research emerging from the clinical sector parallels these findings. However, cognition was only rescued in male tauopathic mice; demonstrating a tau-dependent disconnect between sleep and cognition in females. The present data support ORAs as a non-invasive AD therapeutic with relatively minimal side effects. However, ORAs appear less/ineffective for cognitive rescue in female tauopathic mice. This may have clinical translational implications and potentially hints to an understudied mechanism of female vulnerability to AD tau pathology. Overall, the potential of ORAs for improving the wellbeing of AD patients is growing and is supported by the current studies.

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Polygenic scores for sleep traits and dementia incidence: Findings from the Swedish Twin Registry

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Introduction: There is evidence that poor sleep is related to an increased risk of dementia. But findings might be influenced by reverse causation. This study aimed to examine the association between genetically predicted sleep traits and incident dementia to explore the role of genetic background in this association.

Materials and methods: We used cohort data from Swedish twins born before 1958 or earlier (Screening Across the Lifespan Twin Study (SALT study)) who had participated in data collections (1998/2002) including genotyping. Participants who had diagnosis of dementia at baseline were excluded. Of the 44,919 twins who participated in the SALT study, 17,284 had genotyping data available for the construction of polygenic scores (PGS) for sleep traits (sleep duration, insomnia symptoms, chronotype, snoring, daytime sleepiness, additive sleep health score, daytime napping). PGSs were computed using Plink 2.0. Prior to analysis, the PGS for sleep traits were adjusted for genetic ancestry by regressing out the first five principal components from the score, and standardized. Tertile of PGSs were used to categorize the genetically predicted low, middle, or high sleep trait. Cox proportional hazard models were used to examine the association between the genetically predicted sleep traits and incident dementia. Age was used as timescale.

Results: In the Swedish Twin Registry, 16,397 dementia-free twin individuals (mean age = 55.4 [standard deviation (SD) = 8.0] years) at baseline were followed for average of 16.0 (SD = 2.0) years. A total of 689 cases of dementia were detected. There was no association between PGS for sleep duration, insomnia, chronotype, snoring, daytime sleepiness, additive sleep health score and dementia. Compared to participants in the low PGS category for daytime napping, those in the high category was associated with 30% increased risk of dementia (Hazard ratio: 1.30, 95% Confidence Interval: 1.03 - 1.64), independently of sociodemographic, lifestyle -and health-related factors. While analyzing the PGS for daytime napping as a continuous variable, the association was in the same direction, but weaker.

Conclusions: These findings indicate that genetic predisposition to daytime napping day might be related to higher risk of all-cause dementia.

Predictive factors of sleep-related accidents in a large population of retired regular highway drivers

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Introduction: Sleepiness at the wheel is a well-known risk factor for traffic accidents. The aim of this study is to explore the prevalence of sleepiness at the wheel and the risk factors associated with driving near misses and road accidents in regular French highway users who declared they were retired.

Materials and methods: Regular French highway users were invited to participate in an internet survey between April-May and October-November, 2024. A total of 14,046 retired drivers (mean age: 69.9 ± 6.2 years, 25.1% female) answered questions on socio-demographic characteristics, sleep behaviors, sleep disorders, lifestyle and health, substance use, driving habits, and near-accident and accident conditions.

Results: 14.9% reported at least one near-miss accident, and 4.5% reported at least one accident in the previous year. More than one out of three drivers (22.3%) experienced at least one episode of severe drowsiness at the wheel during the previous year (i.e., making driving difficult or forcing the driver to stop driving). Among these sleepy drivers, 26.6% reported at least one near-miss accident and 6.0% an accident in the past year. 67.2% of near-misses or accidents linked to sleepiness occurred on highways, and 68.7% on trips of over 2 hours. 67.2% of sleep-related near-misses and accidents occurred in a monotonous context (low traffic).

After adjustment for age, gender, mileage exposure and self-reported psychiatric disorders, the best predictive factors for accidents were: being widowed or divorced [adjusted OR 1.7, 95% CI, 1.3-2.2, P <.001], reporting at least one episode of severe sleepiness at the wheel in the past year [adjusted odds ratio (OR) 1.4, 95% confidence interval (CI) 1.1-1.8, P<.01], an Epworth score ≥11 [adjusted OR 1.5, 95% CI, 1.1-2.0, P <.01], being treated with hypnotics [adjusted OR 2.0, 95% CI, 1.1-3.7, P<.001] and having ever reported a near miss within the year [adjusted OR 6.6, 95% CI, 5.3-8.1, P<.001].

Conclusions: Occurrence of sleepiness at the wheel still constitute a major risk factor for near misses and accidents on highway in retired drivers. Having pathological excessive daytime sleepiness, being treated with hypnotics, reporting episodes of severe sleepiness at the wheel in the past year, and the reporting of a near miss in the past year, are major risk factors for near misses and road accidents in retired drivers.

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Quantitative EEG Analysis Reveals Early and Progressive Sleep Dysfunction in Premanifest and Manifest Huntington's Disease

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Introduction: Sleep disturbances are common in Huntington's disease (HD) and have recently been recognized by our group to precede manifest disease onset. Quantitative EEG (qEEG) analyses provide sensitive tools for detecting subtle changes in brain oscillatory dynamics, which can reflect underlying neuropathological processes. This study is the first to longitudinally investigate sleep qEEG changes from premanifest to early manifest stages of HD, exploring their association with disease progression and cognitive impairment.

Materials and methods: Participants included 13 HD gene carriers and 9 age- and sex-matched healthy controls who underwent polysomnographic assessments at two points over a 12-year interval. 8 HD gene carriers developed manifest disease and 5 remained premanifest. qEEG analysis included spectral analysis using Welch's method to compute frequency band-specific relative power. Automated detection of sleep microstructures utilized an MNE-Python toolbox 'YASA' to identify sleep spindles, slow waves, and sigma-slow-oscillation phase-amplitude coupling and circular mean phase. Exploratory tests included topographical tests, coherence analysis and aperiodic PSD metrics such as spectral slope. Statistical analyses included ANCOVA with backward covariate selection to measure cross-sectional group differences. Longitudinal group differences were calculated by conducting repeated measures general linear models to identify significant group*time interactions.

Results: Cross-sectionally at follow-up, HD patients showed pronounced reductions in theta power, decreased slow-wave amplitude, and increased spindle density and amplitude, including the emergence of "giant" spindles. Theta power loss and slow-wave amplitude reduction were progressive-highest in controls, intermediate in premanifest HD, and most pronounced in early manifest HD-suggesting stepwise deterioration with disease advancement. Longitudinally, loss of theta power and slow wave amplitude were steepest in individuals who converted to manifest HD, compared to both controls and those who remained premanifest. Increased spindle density and amplitude were already evident at baseline in gene carriers, particularly in those who converted to manifest HD, indicating that heightened spindle activity may serve as an early electrophysiological marker of dysfunction. Over time, spindle density and amplitude declined at rates similar to controls, but remained consistently higher in HD patients. Theta loss correlated significantly with deficits in psychomotor speed, attention, executive function, and increased depression and impulsivity scores. Elevated spindle density was associated with better performance in attention and executive domains and lower disease burden, whereas increased spindle amplitude correlated with worse cognitive performance. Supplementary analyses showed decreased coherence in the delta band and spectral slope flattening, reflecting a shift toward higher-frequency "noise" and reduced low-frequency synchrony.

Conclusions: HD is associated with early alterations in sleep EEG microarchitecture, including increased spindle density and amplitude and decreased slow-wave amplitude and theta power, detectable even in premanifest stages. The combination of these results suggest dysfunction in overlapping hippocampal-entorhinal cortex circuits and thalamocortical systems affected by HD pathology. These findings support sleep qEEG markers as sensitive indicators of compensatory and progressive network dysfunction. The association between electrophysiological changes and cognitive outcomes suggests that modulating sleep physiology may represent a potential strategy to improve cognitive function in HD. Sleep EEG may thus serve as a valuable non-invasive biomarker for early detection, monitoring, and therapeutic intervention in Huntington's disease.

Sleep and care burden of informal caregivers of people with dementia: an interim exploratory analysis of the ICare.IT-AvereCura study

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Introduction: Although informal caregivers of people with dementia play a crucial role in maintaining the well-being and residual autonomy of their care-receivers, their own well-being is relatively understudied and often neglected. In particular, the links between sleep and the care burden perceived by family caregivers of people with dementia remain insufficiently understood. ICare.IT-AvereCura is a longitudinal study aimed at monitoring the the well-being of family caregivers of people with dementia, focusing on psychological, physiological, socio-relational, and occupational aspects. The study combines self-administration of online questionnaires with the use of wearable sensors to monitor physical activity, sleep, and heart rate for one-week periods at baseline and after 6 and 12 months.

Materials and methods: We aimed to perform an interim exploratory analysis of the ICare.IT-AvereCura study results. The analysis included data at baseline from the first 68 consecutively recruited caregivers. The caregivers' sleep was assessed subjectively, with the Pittsburgh Sleep Quality Index (PSQI) and a sleep diary recording the time spent in bed (TIB) with lights out, and objectively, with data from an accelerometer (GeneActive, Activinsights, UK) on the non-dominant wrist analyzed with a validated algorithm in the GGIR R package. The perceived care burden was assessed with the Zarit Burden Interview (ZBI). The caregivers' anxiety and depression were evaluated with the Hospital Anxiety and Depression Scale subscales (HADS-A and -D, respectively). Data are reported as median (interquartile range, IQR) and analyzed with Spearman's correlations (ρ).

Results: The recruited caregivers (75% females) were aged 59 (14) years, perceived moderate care burden (ZBI: 39 (21)), mild levels of anxiety (HADS-A: 8 (3)) and depression (HADS-D: 8 (7)), and poor sleep quality (PSQI: 10 (5)). They reported a TIB of 7.4 (1.3) hours, while their total sleep duration (TST) estimated with sleep actigraphy aided by sleep log was 6.2 (1.3) hours. The ZBI score correlated positively and significantly with PSQI score ($\rho = 0.42$, $p = 0.005$), HADS-A, and HADS-D ($\rho = 0.49$, $p < 0.001$) and, marginally, with age ($\rho = 0.28$, $p = 0.052$), but not with TIB or TST ($\rho = -0.09/-0.16$, $p = 0.522/0.291$). The PSQI score correlated significantly with HADS-A ($\rho = 0.49$, $p < 0.001$) and marginally with HADS-D ($\rho = 0.31$, $p = 0.043$).

Conclusions: These interim exploratory results of the iCARE-IT-AvereCura study suggest that higher care burden perceived by family caregivers of people with dementia may be associated with worse subjective sleep quality and symptoms of anxiety and depression, but not with reduced objective sleep time.

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Sleep EEG-Based Brain Age Index as a Biomarker of Cognitive Function

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Introduction: Sleep quality and architecture are known to influence cognitive processing, and growing evidence links sleep disruption to neurodegenerative diseases and cognitive decline. Our group recently introduced the brain age index (BAI), a novel biomarker derived from sleep EEG, which has shown associations with cortical thinning. This study examines whether the sleep EEG-based BAI can serve as an indicator of brain health, specifically by evaluating its association with cognitive function

Materials and methods: We retrospectively analyzed polysomnography (PSG) data from 128 individuals (89 with obstructive sleep apnea [OSA], 39 healthy sleepers) who also completed neuropsychological assessments. Sleep EEG data were transformed into scalograms and input into a 3D deep learning model to predict brain age. BAI was calculated as the difference between predicted and

chronological age. We performed correlation and mediation analyses to evaluate the role of BAI in linking sleep features and cognitive outcomes.

Results: BAI showed negative correlation with attention and executive function in both overall subjects and the OSA subgroup. Mediation analysis revealed that BAI significantly mediated the relationship between sleep EEG microstructure and attention/executive function, as well as between sleep macrostructure (N3%, sleep efficiency) and attention/executive function.

Conclusions: This study demonstrated that sleep EEG based-BAI could be a promising biomarker for assessing cognitive impairment in patients with sleep disorders. Furthermore, BAI may serve as a mediator in the relationship between sleep and cognitive function, offering novel insights into the pathophysiology of neurodegenerative diseases.

Sleep micro-architecture predicts magnetic resonance imaging markers of brain aging in the general population

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Introduction: Sleep micro-architecture is a time-resolved assessment believed to underlie the beneficial processes of sleep on cognitive functions. We hypothesise that polysomnography (PSG) sleep micro-architectural features could be a valuable biomarker of one's cognitive health and brain aging, quantified by magnetic resonance imaging (MRI) measurements.

Materials and methods: 747 individuals from the Study of Health of Pomerania-Trend baseline, a population cohort, had PSG and MRI measurements, alongside other demographic and health variables assessed. Extracted micro-architecture consists of spindles, slow oscillations (SO) and spindle-SO coupling features. Brain structural measures included an individualised Alzheimer's disease score (AD score), mean cortical thickness (CT) and brain volume (BV), as proxies of brain aging. Regional associations of segmented CT, white matter (WM) area and subcortical areas using the Desikan-Killiany atlas were also evaluated. 476 individuals further underwent a 7-year follow-up MRI assessment on whom we performed longitudinal analysis of the same outcome variables.

Results: Exploratory findings across all sleep micro-architecture and whole-brain structural outcome pairs revealed that fast and slow spindle (FS and SS) powers were strongly and positively associated with BV (FS: $3.5e4$ [$2.2e4$, $4.8e3$], $fdr=4.8e-6$; SS: $3.7e3$ [$2.3e3$, $5.1e3$], $4.8e-6$). SS frequency was associated with AD score (0.33 [0.12 , 0.54], $fdr=0.029$) and SS power was positively associated with CT (0.0052 [0.0016 , 0.0088], $fdr=0.046$). SO frequency was positively associated with BV ($3.5e4$ [$9.8e3$, $6.1e4$], $fdr=0.027$). Against our assumptions, slow oscillations (SO) density was positively associated with AD score (0.2 [0.083 , 0.32], $fdr=0.01$) and negatively associated with mean CT (-0.015 [-0.026 , 0.0051], $fdr=0.02$). SO frequency was associated with BV ($3.5e4$ [$9.8e4$, $6.1e4$], $fdr=0.027$), while SO amplitude was surprisingly positively associated with WHM (0.0021 [$3.9e-4$, 0.0038], $fdr=0.049$). FS-SO coupling density was positively associated with BV ($-8.2e3$ [$-1.2e4$, $4.2e3$], $fdr=0.0013$). Despite multiple cross-sectional associations, there were no significant whole-brain associations longitudinally. In the sensitivity analyses, metabolic factors modified the strengths of the relationships. Presence of diabetes modified the effect sizes of 4 (of 10) associations, and total cholesterol/HDL ratio negated the association between SO amplitude and WMH.

In the region-wide association, we observed multiple significant micro-architectural-brain region pairs both cross-sectionally and longitudinally. The 162 regional metrics (68 GM thicknesses, 68 WM volumes, 26 subcortical volumes), and 19 micro-architectural features yielded 3078 associations. Multiple testing corrections were applied within each micro-architecture feature, across the 162 regions. Fisher's exact test revealed that significant associations were more likely to occur in AD-

vulnerable regions (Odds ratio=1.78 [1.15, 2.7], $p=0.0072$), which were: entorhinal cortex, parahippocampal gyrus, hippocampus, posterior cingulate cortex, precuneus, fusiform gyrus, amygdala, middle temporal gyrus, inferior temporal gyrus and inferior parietal lobe. These regions were more highly enriched in the longitudinal MRI dataset (Odds ratio=2.76 [1.53, 4.92], $p=4.28e-4$).

Conclusions: Our findings demonstrated associations of sleep micro-architectural characteristics with general, whole-brain measures of brain aging and regional structural correlates. Longitudinal analysis revealed limited associations with general brain-aging metrics, but regional associations were more pronounced. While the interpretation of these results would rely on further understanding of underlying neurophysiology, our results indicate that micro-architecture could potentially explain structural brain correlates of brain aging and neurodegeneration.

Sleep-related Cerebrospinal Fluid Dynamics in Young and Mature Adults

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Introduction: Cerebrospinal fluid (CSF) dynamics during sleep are a key portion of the glymphatic system (GS) and typical age-related data are needed to inform pathology development (i.e., neurodegeneration). CSF movement is directed both caudally (downward) and cranially (upward) building on the pulsatory nature of heart-rate and respiration. Using a developmental pathology approach, this study compared two groups of healthy adults (young and mature) to assess how CSF sleep-related dynamics change with age.

Materials and methods: In two groups of healthy adults, young ($n = 8$, age $M(SD) = 21(1.69)$ years) and mature ($n = 10$, age $M(SD) = 37.5(5.86)$ years), we measured CSF dynamics at the fourth ventricle during wakefulness and NREM sleep states using concurrent polysomnography (PSG) and functional magnetic resonance imaging (fMRI). Indices of average CSF movement, CSF fluctuation range, and CSF fluctuation standard deviations (across recorded 30 second epochs) were extracted from MR data and stratified by PSG-verified stages (Awake, NREM-N1, NREM-N2, NREM-N3). A series of ANOVAs were conducted to compare groups.

Results: A clear age effect emerged - total CSF movement decreased with age across all assessed stages (eta-squared range .49 - .46). There is some evidence of CSF fluctuation range increase with age during sleep - most notably during NREM-N2 (eta-squared = .30). CSF fluctuation SD did not vary by age or sleep stage.

Conclusions: Changes in CSF movement with age could reflect changes in cardiac or respiratory function - or change could reflect other, yet unknown, factors. Although sleep is highlighted by several recent papers as influential in CSF movement and ultimately GS function, the present data highlight that the impact of age may be more robust and considerations based on sleep stage alone may not be sufficient to capture meaningful differences.

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Sleep spindles and slow oscillations predict neurofilament-light, neurogranin 36, Chitinase-3-like protein-1 and cognition in mild to moderate Alzheimer's Disease

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Introduction:

Sleep is essential for brain health, including the clearance of β -amyloid ($A\beta$) and tau-hallmarks of Alzheimer's disease (AD). Sleep physiology can predict levels of these biomarkers and cognitive decline in persons with mild-to-moderate AD (Paez, 2025). However, there is a need for complementary biomarkers of neurodegeneration and neuroinflammation that reflect distinct aspects of AD pathology and improve diagnosis, staging, and prognosis. These include neurofilament light (NfL), a marker of axonal damage; chitinase-3-like protein-1 (YKL-40), a marker of neuroinflammation; and neurogranin (NG-36), associated with synaptic dysfunction and brain atrophy specific to AD. While linked to AD progression, these biomarkers have primarily been studied in at-risk but cognitively unimpaired older adults, not in those with established AD. It remains unclear how sleep physiology (microarchitecture) relates to these biomarkers, which sleep characteristics predict them, and whether they, in turn, predict cognitive or neuropsychiatric decline.

Materials and methods: We analyzed data from our prospective cohort of persons with mild-to-moderate AD (n=60; mean age 74.7; 30 female) in Lleida, Spain. Baseline assessments included overnight polysomnography (PSG), cerebrospinal fluid (CSF) and blood sampling for $A\beta$ 42, phosphorylated tau (pTau-181), total tau, NfL, YKL-40, and NG-36, as well as cognitive and neuropsychological testing at baseline, 12, 24, and 36 months using the Mini-Mental Status Examination (MMSE), California verbal learning test (CVLT), Rey-Osterrieth Complex Figure Test (ROCF), Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), and Neuropsychiatric Inventory (NPI).

PSG was scored per AASM guidelines. Sleep spindles and slow oscillations (SO) were analyzed using in-house, validated open-source algorithms. Generalized linear models (False Discovery Rate-adjusted) tested associations between sleep parameters, AD biomarkers, cognition, and neuropsychiatric symptoms, controlling for age, sex, and apnea-hypopnea index (AHI).

Results:

We found previously unreported associations between spindle and SO characteristics, NfL, YKL-40, NG-36, NfL/ $A\beta$ 42 ($\beta=-.0029$, $p=0.001$), YKL-40/ $A\beta$ 42 ($\beta=0.0004$, $p=0.003$) and cognition in persons with AD. These biomarkers predicted worse cognitive performance (higher ADAS-cog [$\beta=2.28$, $p=0.004$], lower MMSE scores [$\beta=-2.42$, $p=0.01$]) from baseline to 36-months, and a significant increase in neuropsychiatric symptom severity (NPI $\beta=16.93$ $p<0.001$). CSF NfL/ $A\beta$ 42 also mediated the effects of spindle activity on cognitive performance on the ADAS-cog ($p=0.041$) and MMSE ($p=0.0019$), while NfL, YKL-40, NG-36, NfL/ $A\beta$ 42 also moderated the relationships between spindle and SO activity on cognition, and spindles and SO moderated the relationships between these biomarkers and cognition.

Conclusions: Our novel findings demonstrate that spindle and SO activity are robustly associated with NfL, YKL-40, and NG-36, and cognitive decline, constituting predictive, non-invasive biomarkers of neurodegeneration, cognition, and mental health in AD. NREM spindle and SO activity can act as complimentary, non-invasive markers of neurodegeneration and potential therapeutic targets for sleep-related interventions designed to monitor or slow AD symptom progression. They add further evidence for links between NfL, NG-36, YKL-40, sleep, and cognition, and their role as supplemental AD biomarkers and biomarkers of susceptibility to neurodegeneration in cognitively unimpaired persons at higher risk of AD. They also constitute potential targets for sleep-related interventions for cognition in the context of AD and other neurodegenerative disorders.

The effect of yoga on sleep quality and menopausal symptoms in menopausal women: a systematic review and meta-analysis

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Introduction: Menopausal women often experience sleep disturbances and menopausal symptoms that significantly affect their quality of life. Recent studies have suggested that yoga may also positively

affect sleep quality by promoting relaxation and reducing stress, making it an appealing option for managing menopausal symptoms. We conducted a systematic review and meta-analysis of menopausal women to assess the effect of yoga on sleep quality and menopausal symptoms.

Materials and methods: PubMed, Scopus, Ovid, The Cochrane Library, and Google Scholar were searched through July 2023. Randomized controlled trials (RCTs) that evaluated the effects of yoga in menopausal women and reported quantitative data on sleep quality and menopausal symptoms were included. The study protocol was registered on PROSPERO (CRD 42023464468).

Results: Thirteen RCTs (1649 patients) were eligible for meta-analysis. The meta-analysis of six RCTs (591 patients) did not demonstrate a statistically significant difference in the total score of the Pittsburgh Sleep Quality Index (PSQI) (mean difference -1.39; 95% CI (-3.69, 0.92); $P = 0.24$). On the contrary, the meta-analysis of eight RCTs (1065 patients) revealed a significant improvement in the total score of the Menopausal Rating Scale (MRS) (mean difference -7.10; 95% CI (-11.27, -2.93); $P = 0.0008$). There were significant differences in the subscale of each symptom including somatovegetative, psychological, and urogenital subscale (somatovegetative subscale: mean difference -2.64; 95% CI (-4.93, -0.35); $P = 0.02$, psychological subscale: mean difference -3.43; 95% CI (-5.76, -1.11); $P = 0.004$, urogenital subscale: mean difference -1.25; 95% CI (-2.30, -0.21); $P = 0.02$).

Conclusions: The pooled results did not demonstrate the significant benefits of yoga on sleep quality in menopausal women. Conversely, the remarkable advantages of yoga in relieving menopausal symptoms were illustrated. To further explain the benefit of yoga on sleep quality in menopausal women, additional, longer-duration yoga training or longer-term studies are required.

The Relationship Between Napping and Memory Varies as a Function of Genetic Risk for Alzheimer's Disease

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Introduction: Habitual daytime napping is a significant aspect of many older adults' sleep-wake cycle. Growing evidence links napping and cognitive abilities in the context of Alzheimer's Disease (AD), yet little is known about how genetic risk influences this relationship. This study investigates the interactions between genetic risk for AD and self-reported daytime napping on the cognitive performance of 1655 non-clinical middle-aged to older adults.

Materials and methods: Cognition was assessed using a self-administered online battery and reduced to three variables: memory, visuospatial abilities and executive function. Sleep parameters were obtained via self-reported questionnaires. Genetic risk was assessed with the presence of the apolipoprotein (APOE) $\epsilon 4$ allele, the strongest known genetic risk factor for AD, and with polygenic risk scores (PRS; excluding APOE), with a low score indicating a lower risk for AD. The interactions between habitual napping duration and genetic risk on cognitive performance were assessed using analyses of covariance, adjusting for age, sex, education and body mass index (BMI).

Results: Participants were aged between 42 and 75 years (70.2% female), with 31.2% being APOE $\epsilon 4$ carriers (i.e., with at least one $\epsilon 4$ allele). APOE $\epsilon 4$ carriers who reported habitual long naps ($M = 0.32$, $SE = 0.16$) demonstrated better memory performance ($p = .003$) than non-carriers who also reported long naps ($M = -0.27$, $SE = 0.12$). Among APOE $\epsilon 4$ carriers, those who napped for ≥ 1 hour ($M = 0.32$, $SE = 0.16$) performed better ($p = .048$) than those reporting shorter naps ($M = 0.09$, $SE = 0.05$). This was not the case for non-carriers. In a separate analysis, low PRS ($M = 0.12$, $SD = 0.06$) was related to better memory performance than high PRS ($M = -0.13$, $SD = 0.68$) among those who did not nap ($p = .007$). Within the low PRS group, participants who did not nap ($M = 0.12$, $SD = 0.06$) outperformed ($p = .049$) those who reported short naps ($M = -0.18$, $SD = 0.10$). These results remained significant after accounting for self-reported overnight sleep efficiency.

Conclusions: The results of this study suggest that the relationship between napping and memory varies as a function of genetic risk for AD. Notably, it is possible that for those at a higher genetic risk for AD, napping provides a compensatory mechanism to adjust for deficiencies in nocturnal sleep. As such, our findings do not support a one-size fit all approach to sleep advice that long naps may be

detrimental, including for cognitive abilities. The current results could inform future studies investigating personalised preventative treatment, such as behavioural interventions modifying the sleep wake cycle, based on genetic profiles.

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The Sleep Detectives: a co-designed protocol for longitudinal tracking of sleep health, sleep neurophysiology and cognition in children and young people at risk of neurodevelopmental disorders

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Introduction: Several chromosomal deletions and duplications – including 22q11.2 and 1q21.1 deletion and 16p11.2 duplication – are associated with high risk of neurodevelopmental and psychiatric outcomes. Many people living with these copy number variants (CNV) present with insomnia and fragmented sleep, which are associated with symptoms including ADHD and anxiety. Sleep and circadian disruption are a key concern for children and their families/carers, and may present opportunities for early diagnosis and treatment, alongside offering insights into neurobiological mechanisms of psychiatric risk. However, harnessing these opportunities requires robust, longitudinal measures of sleep health, sleep neurophysiology (EEG) and rest-activity rhythms that are accessible and acceptable to children and young people.

Materials and methods: Working with a Lived Experience Advisory Panel of children and young people, parents, carers and support charities, we co-designed a protocol combining questionnaires, wrist-worn actigraphy (Fitbit Inspire 3), wearable EEG (Muse S headband) and gamified cognitive tasks (<https://osf.io/f78bq/>). The protocol was piloted with a representative sample of 28 school children (8-12 years) over 7 consecutive days/nights. We also report further analyses of cross-sectional data from wrist-worn actigraphy (Philips Actiwatch, 14 days/nights, 29 probands with 22q11.2 deletion syndrome [DS] and 22 siblings, 8-20 years) and/or high-density sleep EEG (60 channels, 1 night, 28 probands with 22q11.2DS and 17 siblings, 6-20 years) and polysomnography (PSG) in children and young people with 22q11.2 deletion syndrome (PMID: 31144615, 36039635).

We developed an open-source pipeline that uses the Fitbit Web API to extract, preprocess, and report longitudinal sleep and activity data (<https://github.com/sleepdetectives/fitbit-data-pipeline>). The pipeline facilitates derivation of Rest-Activity Rhythm metrics, an actigraphic proxy of circadian rhythms. EEG analyses leveraged computational modelling to infer the synaptic basis of sleep EEG alterations in 22q11.2DS using a Dynamic Causal Model (DCM) of thalamocortical circuits underpinning the hallmark oscillations of sleep EEG.

Results: Our pilot protocol was acceptable to school children and their families. The Muse S headband was well-tolerated and enabled characterization of spindle and slow-wave events, though signal quality tended to degrade over the course of each night.

Based on actigraphy and diaries, children with 22q11.2DS spent significantly longer in bed and asleep than siblings (total sleep time 517 vs. 475min, $p < 0.001$), but reported slightly reduced sleep quality ($p < 0.05$). These differences in sleep duration were not replicated with EEG/PSG. Rest-activity rhythms were altered in 22q11.2DS, with reduced amplitude and Midline Estimating Statistic of Rhythm ($p < 0.001$).

DCM showed that synaptic dysfunction in 22q11.2DS was most prominent during sleep, with constellations of parameters varying across non-REM and REM stages. Increased thalamo-cortical drive during N3 associated with reported sleep problems. Simulating increased NMDA receptor-mediated

gain showed potential to align 22q11.2DS EEG with neurotypical patterns. The largest effect sizes were particularly evident at slow-wave and spindle frequencies during non-REM.

Conclusions: Our multi-modal toolkit proved acceptable to children and young people, enabling integrated, multiscale analyses extending from qualitative descriptors of sleep quality to predictions of synaptic mechanisms. Using these approaches has allowed detection of potential biomarkers of thalamocortical network dysfunction in 22q11.2DS; current work is extending to other CNV.

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Trait-Like Slow-Wave Activities Link to Cognition: Multi-Night At-Home Wireless EEG Study in Older Adults

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Introduction: In-laboratory polysomnography remains the gold standard for studies examining associations between sleep and cognition. However, a single night of sleep – particularly in a new environment does not capture the extent of naturalistic night-to-night variability in sleep parameters and may contribute to inconsistent results across studies. In the present study, we computed variability across sleep stages and relative power spectra over multiple nights of sleep at home using a wireless headband to identify trait-like metrics that would be most reliably associated with cognitive function in older adults.

Materials and methods: A total of 49 free-living older adults (Age range: 71-80) with no self-reported sleep disorders. They wore a wireless sleep headband (Dreem Headband, Beacon Diagnostics, USA) over 4-8 nights of sleep. Night-to-night variability of sleep parameters was determined using the coefficient of variation (CV). Trait-likeness was defined as having CV under 20%. Cognition was assessed via a comprehensive neuropsychological battery. A composite global cognition score was computed from the battery. Correlation analyses examined the associations between trait-like sleep metrics and global cognition. Both the average across days and single nights of trait-like sleep metric were examined for correlation with cognition.

Results: Night-to-night variability in the current sample (n = 49; 302 nights) was high for N3% (CV=47%), medium for REM% (CV=22%), and low for N2% and relative power from all bands (CV=3-17%). Only relative Delta power (0.8- 4.5 Hz) was significantly associated with global cognition, both when considering average ($r=0.51$, $p<0.001$) and single night ($r=0.3-0.4$) assessments.

Conclusions: Delta band power demonstrated clear trait-likeness across nights and strong associations with cognition in free-living older adults. These results highlight the underestimation of night-to-night variability in objective sleep metrics when only using one assessment night and the importance of assessing slow-wave activity instead of N3% in examining sleep-cognition associations in older adults.

Tunable Lighting to Improve Sleep and Cognition Performance in Elderly Population in Nursing Homes

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Introduction: Depression is a common symptom among older adults with an estimated prevalence of 5% - 15% among those who are community-dwelling. In older adults, depression is associated with cognitive impairment and could approximately double the risk of dementia [3]. Moreover, these depressive symptoms could place additional stress on caregivers in both institutional and home settings.

Materials and methods: Lighting interventions included two whole-day lighting schemes with varying illuminance levels and/or CCTs. Both lighting schemes were designed based on available research to

meet circadian lighting needs of older adults. We perceived from prior literature indicates that an optimum lighting solution for circadian entrainment should provide:

- High levels of bright blue illuminance (high intensity + high CCT (or blue-enriched spectrum)) early in the morning to phase advance the circadian clock.
- Medium to high levels of illuminance (medium to high intensity + medium CCT (neutral white)) in the afternoon to increase alertness without exerting substantial phase shifting effects on the circadian clock
- Dimmed illumination (low intensity + low CCT (yellowish white light)) in the evening to avoid disruption of circadian rhythms and unwanted phase delay.

Results: The patterns of the depression scores across the study are illustrated in Figure 1. The general pattern is similar for the two groups; namely, depression scores decrease with the L1 intervention, decrease even more with the L2 intervention, and start returning to baseline levels after the intervention has been discontinued. These general trends were assessed with an independent *t*-test statistical analysis to determine the effectiveness of the experimental whole-day lighting interventions on depression among older adults. Data were managed and analyzed using IBM SPSS 22.0 statistical software.

Baseline measurements revealed that the mean GDS score in group A was 4.71 points higher than group B. After 9 days of exposure to the L1 and L2 interventions, we observed more reduction from the baseline 1 in mean depression scores in group A compared to group B (Table 5). However, an independent *t*-test showed no significant difference in the mean GDS score between groups in baseline 1 ($t = 2.12, P = 0.05$), L1 ($t = 1.11, P = 0.29$), L2 ($t = -0.08, P = 0.94$), and baseline 2 ($t = 0.56, P = 0.58$).

Conclusions: During the L2 intervention, we added tuning spectrum quality to the ambient illumination with varying illuminance levels to provide a bright cool light in the morning and a dimmed warm light in the evening. L2 intervention reduced mean depression score in participants by 60% in group A and 30% in group B, which were significantly higher than L1 intervention in both groups. This supports the idea that adding tuning spectrum to the environmental lighting quality provides additional benefits to reduce depression in older adults and improve their mood and well-being; hence, the color of light also matters.

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Basic Research

A Bistable Stochastic Model Quantifies Performance Degradation And Individual Vulnerability To Sleep Deprivation

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Introduction: Sleep deprivation impairs vigilance, increasing the frequency of very long reaction times (> 500 ms) and slowing average response speed on the psychomotor vigilance task. Vulnerability of sustained attention impairment due to sleep deprivation is trait-like, with some individuals consistently more vulnerable than others. However, the mechanisms behind vulnerability traits are not known, and no gold-standard method exists for classifying individuals according to their vulnerability. The objectives of this study were to (i) characterise and quantify sustained attention impairment during sleep deprivation and (ii) develop a mathematical model that accounts for these characteristics, as a step towards a vulnerability classification system.

Materials and methods: Young, healthy, male participants ($N = 321$, age 22.1 ± 2.7) underwent 40 hours of sleep deprivation under a constant routine protocol (dim light < 5 lux, constant posture and meals) starting from their habitual wake time. Participants performed a 10-minute psychomotor vigilance task every 2 hours, and saliva melatonin was collected every hour. Reciprocal reaction time

data was referenced to dim light melatonin onset and aggregated over individuals in 2-hour bins (group-aggregated data). To characterise vulnerability, for each individual, data was aggregated across baseline (2 – 16 h since awakening) and sleep deprivation (18 – 40 h since awakening). In all cases, we analysed distributions of reciprocal reaction times. Our bistable stochastic model was fit to all aggregated datasets using the maximum likelihood method.

Results: We observed that group-aggregated reciprocal reaction time distributions exhibited (i) a primary peak centered at 3.05 s^{-1} , and (ii) a secondary peak centered at 0.16 s^{-1} emerging 6 h after and persisting until 22 h after dim light melatonin onset. The secondary peak corresponds to very long reaction times, which can be characterised as period of unresponsiveness. We proposed a bistable stochastic model that accurately reproduced the experimental group-aggregated data (Kolmogorov distance between model and data was 0.009 ± 0.003). Analysis of model fits to baseline and sleep deprivation distributions for each individual revealed heterogeneous responses to sleep deprivation, where effects on individuals' primary and secondary peaks were decoupled. We found that participants can be split into groups based on the presence of the secondary peak at baseline and during sleep deprivation. A typical resilient person does not demonstrate a second peak at either baseline or during sleep deprivation, while a typical vulnerable person develops a second peak during sleep deprivation. However, shifts in the primary peak were often substantial and led to large increases in the frequency of reaction times $> 500 \text{ ms}$ even when no secondary peak developed, indicating that susceptibility to critical response slowing is distinct from susceptibility to periods of unresponsiveness.

Conclusions: A secondary peak in the reciprocal reaction time distribution differentiates very long responses from average response speed, and is predicted by bistability in a mathematical model. Individual responses to sleep deprivation are heterogeneous, and both peaks must be accounted for in order to properly characterise individual vulnerability.

A Case Study---Improving Sleep Quality and Glycemic Biomarkers in Patients with Obstructive Sleep Apnea and Type 2 Diabetes through Long-Term Use of Continuous Positive Airway Pressure Therapy

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Introduction: Obstructive Sleep Apnea (OSA) and Type 2 Diabetes Mellitus (T2DM) frequently coexist and exacerbate each other. OSA leads to intermittent nocturnal hypoxia and sleep fragmentation, which can worsen insulin resistance and glycemic control. Studies have shown that long-term use of Continuous Positive Airway Pressure (CPAP) therapy significantly improves sleep quality, reduces hypoxic episodes, and helps stabilize key biochemical markers in T2DM patients, such as fasting glucose, HbA1c, and insulin sensitivity. As a non-invasive intervention, CPAP presents a promising adjunctive treatment for patients suffering from both OSA and T2DM.

Materials and methods: This single-case study involved a patient with type 2 diabetes and insomnia, diagnosed with severe obstructive sleep apnea (AHI > 100), a body mass index (BMI) over 40, and an HbA1c level above 10. The patient underwent a two-month intervention using a Continuous Positive Airway Pressure (CPAP) device, worn nightly. Sleep quality and type 2 diabetes-related biochemical markers—including fasting glucose, HbA1c, and insulin sensitivity—were regularly monitored to evaluate the clinical impact of sustained PAP therapy.

Results: Before intervention, the patient's AHI exceeded 100 and HbA1c was over 10. After two months of continuous positive airway pressure therapy, AHI dramatically decreased to below 20. HbA1c levels significantly dropped, BMI showed a downward trend, and sleep quality improved markedly. Additionally, glycemic control became more stable.

Conclusions: These findings suggest that continuous positive airway pressure therapy has beneficial clinical and metabolic effects in patients with severe obstructive sleep apnea combined with type 2 diabetes, offering a promising adjunctive treatment approach.

Acknowledgments: Key Word: Obstructive Sleep Apnea (OSA), Type 2 Diabetes Mellitus (T2DM), Continuous positive airway pressure (CPAP), Apnea-Hypopnea Index (AHI), Sleep Quality, Hemoglobin A1c (HbA1c)

Acetate improves neurocognition in sleep-deprived male Wistar rats via modulation of xanthine oxidase/uric acid-driven oxidative stress and NFkB-dependent inflammation, and caspase 3-mediated apoptosis

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Introduction: The global rise in sleep deprivation (SD) is alarming, as reports show that an increasing number of individuals suffer from SD in at least 3-4 days per week due to work shifts, stress, and anxiety. SD alters several biological processes, including neurocognition, via the induction of oxidative stress. However, acetate confers cellular protection by modulating oxidative stress-sensitive signaling. Notwithstanding, the effect of acetate on SD-induced neurocognitive deficit is still unknown. Therefore, this study investigated the effect of acetate on SD-induced neurocognitive deficit. Also, the roles of xanthine oxidase (XO)/uric acid (UA) and NFkB/caspase 3 pathways were probed.

Materials and methods: Forty 10-week-old male Wistar rats of similar weights were randomly allotted into four groups (n=10): vehicle-treated control (0.5 mL of water), sodium acetate (200 mg/kg), SD, and SD + acetate. SD was induced by exposing the rats to continuous SD for 72 hr using the modified multiple platform technique. Acetate treatment was *per os* and lasted for 72 h. After this period, biochemical and histopathological parameters were evaluated in the serum and hippocampal and cortical tissues.

Results: SD led to neurocognitive deficit (evidenced by impaired parameters from novel object recognition, Y maze, and open field tests). In addition, SD increased hippocampal and cortical XO, UA, and MDA levels but reduced GSH, SOD and catalase. SD also elevated TNF- α , IL-1 β , IL-6, NF-kB, and caspase-3 in these tissues. These alterations were accompanied by a rise in lactate, lactate dehydrogenase, and creatinine kinase, and distorted hippocampal and cortical histo-architecture (pyknosis and neurodegeneration). However, acetate administration attenuated SD-driven hippocampal and cortical biochemical and histological derangements.

Conclusions: In conclusion, these findings revealed that SD induced neurodegeneration and cognitive deficit via the upregulation of XO/UA and NFkB/caspase 3 signaling. More so, acetate ameliorated SD-induced hippocampal and cortical biochemical and histological derangements by downregulating UA generation, NFkB-mediated inflammation, and caspase 3-dependent apoptosis.

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A cross-sectional observational study on sleep parameters in Indian males and females

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Introduction: Nearly all living organisms spend a fraction of their lives in a reversible, unconscious, coma-like state. It is still unclear why exactly organisms sleep but it is related to health and well-being. Disturbed sleep has negative effects on mental and physical health. Sleep has gender difference as well. The aim of the present study was to understand and compare sleep pattern of adult Indian males and females.

Materials and methods: A cross-sectional observational study was conducted on 301 participants presenting to a tertiary care centre in India. Participants were bystanders of patients representing the community and were not suffering from any known medical or psychiatric disorder. The participants were assessed on their socio-demographics, sleep profile and substance use profile with the help of Pittsburgh Sleep Quality Index (PSQI), Sleep -50, Epworth Sleepiness Scale (ESS), sleep Hygiene and The Alcohol Smoking and Substance involvement screening test (ASSIST).

Results: 187 males and 114 females participated in the study. Nearly half of the sample was married and nearly 60% of the sample were employed. Most of the sample belong to urban locality and middle socio-economic status. Only five percent of the sample reported lifetime use of tobacco and three percent reported current tobacco use. No participant reported use of any other substance. There was no difference in socio-demographics in males and females except for employment status as most of the females in our study were housewives. The mean age of the total sample was 31.2 (10.2) years. The mean subjective sleep latency and total sleep time of the sample were 30 (15,60) minutes and 417.3 (70.7) minutes. Near about 30 percent of the sample has PSQI>5. Females reported more sleep disturbance (n=37,33%) than males (n=53,28.8%) in terms of total PSQI score>5, however it was not statistically significant. The median PSQI score of the sample was 4(2,6). The median sleep latency was found to be same for males and females (30(15,60) minutes vs30 (15,30) minutes). The median ESS scores for males was 3.5 (0,7) and for females was 4 (1,9). The mean total sleep latency for males and females was 417.2 (73.7) minutes and 418.4 (67.1) minutes respectively. Most of the patients had normal day time sleepiness (n=268,89%). Only three percent of the participants (n=8) reported moderate to severe day time sleepiness. No significant difference was observed between subjective sleep latency, subjective total sleep time, total PSQI scores and total ESS scores between male and female participants. A significant negative correlation was observed between marital status and sleep latency in males but not in females. A significant positive correlation was observed between total ESS scores and type of employment in males but not in females.

Conclusions: The general adult population in India has a sleep of around seven hours. Females had more sleep disturbance than males although difference was not statistically significant. Married males had earlier onset of sleep.

Acute sleep deprivation causes rats' soleus muscle neuromuscular junction to undergo synaptic plasticity

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Introduction: Sleep is crucial for both cognitive and physical performance. Sleep deprivation impairs not just brain function but also causes physical exhaustion. A good night's sleep cures the functional abnormalities produced by sleep deprivation. Sleep's influence on brain function has been thoroughly explored. However, its role in the functional anatomy of the neuromuscular junction or skeletal muscle morphology is poorly understood, although skeletal muscle atonia and suspended thermoregulation during rapid eye movement sleep may provide a favorable environment for muscle rest and repair, similar to slow-wave sleep for synaptic downscaling.

Materials and methods: The Institutional Animal Ethics Committee's rules were followed throughout the investigation. A total of 18 rats were randomly assigned to three groups: control, 24-hour sleep deprivation, and 24-hour recovery sleep. After 24 hours of sleep deprivation utilizing a modified multiple-platform approach, animals were euthanized, and tissues were collected and analyzed for neuromuscular junction architecture and neurochemistry using electron microscopy and immunohistochemistry in the rat soleus muscle. A similar analysis of the neuromuscular junction was done in rats after sleep recovery given to the rats exposed to 24-hour sleep deprivation.

Results: Acute sleep deprivation changed synaptic ultrastructures, including mitochondria, synaptic vesicles, synaptic proteins, basal lamina, and junctional folds required for neuromuscular transmission. Furthermore, acute sleep loss causes depletion of the neurotransmitter acetylcholine and overactivity of its degrading enzyme, acetylcholine esterase, at the neuromuscular junction. The effects of sleep deprivation on synaptic homeostasis in the brain have lately been widely studied. Interestingly, in the sleep recovery group, the altered parameters at the neuromuscular junction was brought back to near normalcy.

Conclusions: The data from our research provides important insights into how sleep affects the homeostasis and functionality of neuromuscular junctions.

Acknowledgments: Current data from our research provides new perspectives into how sleep affects neuromuscular junction homeostasis and function.

A Digital, Real-Time, History-Based Sleep-Management Tool to Enhance Alertness

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Introduction: Chronic sleep disruption and circadian misalignment have become pervasive in today's 24-hour society, contributing to impaired cognitive performance, increased risk of accidents, and long-term health consequences. Yet, most sleep management strategies rely on one-size-fits-all recommendations that overlook individual variability, resulting in suboptimal and/or impractical solutions.

Materials and methods: To address this gap, we developed a real-time, personalized sleep scheduling framework that tracks dynamic sleep pressure and circadian rhythms using a mathematical model. This framework was implemented as a mobile application, SleepWake, which delivers individualized sleep recommendations based on continuously updated sleep data. We evaluated its effectiveness through two studies: a retrospective analysis of 71 female shift workers from a previous clinical trial, followed by a prospective clinical study involving 19 male shift workers.

Results: The analysis revealed that greater adherence to SleepWake's recommendations was associated with significantly improved alertness, even when total sleep time was comparable. These benefits were driven by two key innovations: real-time supplemental sleep prescriptions informed by recent sleep history, and personalized sleep timing aligned with each individual's circadian rhythm.

Conclusions: This study provides the first direct evidence that continuously updated, personalized sleep schedules can enhance alertness and sleep health in real-world environments. By integrating sleep physiology with evidence-based mathematical modeling, SleepWake offers a scalable tool to promote health, safety, and well-being in shift-working populations and beyond.

Adiponectin ameliorates chronic intermittent hypoxia induced insulin resistance by modulating macrophage polarization in visceral white adipose tissue

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Introduction: Chronic intermittent hypoxia (CIH) caused by obstructive sleep apnea (OSA) is an independent risk factor for insulin resistance (IR) in non-obese individuals, yet its underlying mechanisms remain unclear. Visceral adipose tissue (vWAT) is a central driver of insulin resistance, and its dysfunction is closely associated with IR. Adiponectin (Ad), one of the key adipokines secreted by adipose tissue, playing a key role in metabolic regulation. This study investigated how IR was induced by CIH and ameliorated by Ad through modulating macrophage polarization in vWAT.

Materials and methods: This study successfully set up a lean murine CIH-IR model, C57BL/6J mice were divided into normoxic control (NC) group, CIH-exposed (CIH) group, and Ad-intervened CIH-exposed (CIH+Ad) group (10 mice / group) .

Glucose metabolic parameters were measured to evaluate systemic glucose homeostasis.

Subsequently, epididymal white adipose tissue (eWAT) was collected for comprehensive analysis. Macrophage infiltration and polarization status were assessed using a combination of immunofluorescence (IF) staining, flow cytometry, and ELISA. In parallel, RNA sequencing (RNA-seq) was conducted to identify differentially expressed genes in the adipose tissue, followed by Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis to elucidate significantly altered biological pathways. To further investigate the pathway, Western blot (WB) analysis was performed to examine key proteins in the insulin signaling pathway.

Results: It was found that the serum Ad level was significantly reduced in CIH group compared with the NC group, while accompanied by clearly increased Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). When Ad was administered to CIH mice twice a week for 10 weeks, we

observed reductions in HOMA-IR.

Transcriptomic sequencing identified the top 100 differentially expressed genes (DEGs) in eWAT among three groups. KEGG pathway enrichment analysis revealed significant alterations in the PI3K-AKT signaling pathway. Western Blot (WB) analysis demonstrated that p-PI3K and p-AKT protein expression was downregulated in the eWAT of CIH group, and improved by Ad complementation. The IF tests of F4/80 in mouse eWAT indicated that the proportion of F4/80-positive cells in the CIH group was significantly higher than that in the NC group and CIH+Ad group. Flow cytometry analysis revealed that the number of F4/80 and CD11b double-positive cells in the single-cell suspension of the stromal vascular fraction (SVF) from eWAT was remarkably increased in the CIH group compared to the NC group, while it was decreased after Ad intervention. Meanwhile, it showed a higher M1/M2 ratio in the CIH group compared to the NC group, while a reduced M1/M2 ratio was identified in the CIH+Ad group.

The levels of TNF- α , IL-6, and IL-1 β in the eWAT suspension of the CIH group were significantly higher compared to the NC group, whereas these inflammatory cytokines were lower in the CIH+Ad group.

Conclusions: CIH might impair insulin signaling pathways in mouse eWAT by promoting M1 polarization of eWAT macrophages, which is probably an important mechanism of CIH-induced insulin resistance. Furthermore, it is hypothesized that Ad alleviates CIH-induced insulin resistance in mice by regulating eWAT macrophage polarization and restoring insulin signaling pathways.

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AI-Driven Contactless Sleep Monitoring Using Smart Mattress and Machine Learning to Predict Obstructive Sleep Apnea and Sleep Quality in Military Personnel

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Introduction: Obstructive Sleep Apnea (OSA) significantly impairs sleep quality and daytime alertness, especially in military personnel who face high operational and cognitive demands. Polysomnography (PSG), while being the diagnostic gold standard, is impractical for large-scale or continuous monitoring. This study aims to develop and validate a contactless sleep monitoring system using AI-enhanced smart mattress data integrated with machine learning (ML) algorithms to classify OSA severity and estimate sleep quality among hospitalized military personnel.

Materials and methods: Sleep data from military inpatients will be collected using a smart mattress system (Huijia Health Life Corporation) that records physiological signals (heart rate, respiratory rate, body movement) simultaneously with PSG. Supervised ML models-random forest, support vector machines, and deep neural networks-will be trained to classify OSA severity and predict sleep quality. SHAP values will be applied to interpret model outputs and identify key contributing features.

Results: We expect to establish a high-performing and interpretable model capable of classifying OSA severity with high accuracy and estimating sleep quality non-invasively. The model may also uncover latent relationships between OSA and degraded sleep, enabling early intervention and clinical decision-making.

Conclusions: Integrating smart mattress technology with ML provides a novel, non-contact, and scalable solution for OSA risk detection and sleep quality assessment. This approach could transform sleep monitoring and enhance military healthcare strategies.

Acknowledgments: Keywords : Obstructive Sleep Apnea; Smart Mattress; Machine Learning; Sleep Quality; Military Personnel

A Machine Learning-Derived Transcriptomic Risk Model Linking DEHP and Sleep-Disordered Breathing to Cancer Prognosis and Immune Dysregulation

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Introduction: Both sleep-disordered breathing (SDB) and exposure to environmental toxicants such as di(2-ethylhexyl) phthalate (DEHP) are associated with chronic inflammation, immune dysfunction, and tumor progression. However, their combined molecular impact remains poorly understood. Clarifying this relationship may uncover novel mechanisms linking environmental and physiological stress to cancer outcomes.

Materials and methods: Thirteen overlapping genes related to both DEHP and SDB were identified via transcriptomic analysis and literature mining. A DEHP-SDB score was developed using LASSO Cox regression in The Cancer Genome Atlas (TCGA) pan-cancer cohort. Risk groups were compared across survival endpoints (OS, PFI, DSS). Functional enrichment and immune microenvironment analyses were conducted to interpret the biological relevance of the score.

Results: The DEHP-SDB score was significantly associated with poor survival in multiple cancers (- LUAD, KIRC, COAD, and ACC). High-risk tumors showed activation of epithelial-mesenchymal transition, IL-17 signaling, and the p53 pathway. These tumors also had increased immune checkpoint expression and stromal activation. A prognostic nomogram incorporating the score achieved an AUC of 0.81 for 5-year survival prediction.

Conclusions: We propose a novel DEHP-SDB transcriptomic signature that integrates environmental and sleep-related stressors into a unified prognostic model. This risk score not only predicts survival outcomes but also reflects immune and inflammatory remodeling, offering new insights for cancer risk stratification in vulnerable populations.

Acknowledgments: We sincerely thank the Kaohsiung Armed Forces General Hospital for providing clinical resources and institutional support. We also acknowledge Huijia Health Life Corporation for supplying the smart mattress system used in this study. Special thanks to Bo-Sheng Chen for his technical expertise in AI model development and implementation.

Aperiodic EEG activity in rodents as a potential marker for human hyperarousal

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Introduction: Insomnia and anxiety-related disorders account for one-third of the mental disorder burden in society. This situation is likely related to a limited understanding of the complex biological mechanisms underlying their symptoms, which in turn results in a poor prognosis and limited treatment effectiveness for these conditions. A common key marker of severity and treatment resistance in both disorder types is hyperarousal. Here, we aim to study potential electrophysiological markers of altered monoaminergic activity across sleep stages in rodents and study its relation to hyperarousal in humans.

Materials and methods: Our work employs a systems neuroscience approach in mouse sleep to investigate the aperiodic activity of mice across sleep stages, their spatial features, and their dependency on recording conditions. We study their alterations upon optogenetic manipulation of the Locus Coeruleus (LC) noradrenergic (NA) system, sleep restriction, and stress.

Results: The intercept and slope of aperiodic activity across sleep stages are highly dependent on the spectral band analyzed and the type of signal studied, specifically whether it is cortical EEG or high-impedance Local Field Potentials (LFP). Stimulation of LC activity significantly alters the aperiodic features of the EEG and LFP, rendering them more "wake-like" compared to sham manipulations. In contrast, inhibiting these cells has a negligible effect on aperiodic features. Interestingly, a stressful experience, resulting in increased LC activity, produces a more non-rapid-eye-movement sleep-like aperiodic features in comparison to baseline or gentle sleep deprivation.

Conclusions: This work focuses on the aperiodic activity of the EEG and LFP in mice upon artificial or behavioral manipulations of LC-NA activity. These experimental conditions are related to the theoretical mechanisms of the overlapping symptom of hyperarousal in humans. We demonstrate that LC-NA activity is linked to the aperiodic component of electrophysiological activity in the sleeping brain, and we highlight the importance of technical considerations when conducting this type of analysis, as it may have potential consequences for the study of hyperarousal in humans.

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Aperiodic neural activity reflects subjective sleep depth

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Introduction: The feeling of being well-rested is essential to proper everyday functioning, however, the neural correlates of subjective sleep depth are still being established. A serial awakenings experiment (Stephan et al., 2021) found that subjective sleep depth was lowest during the early NREM sleep, the time when slow wave activity is highest. Furthermore, subjective sleep depth inversely correlated with fast high-frequency EEG activity as measured by the conventional band-based spectral approach. We use a part of the same dataset and calculate the aperiodic component of the EEG signal, a strong marker of objective sleep depth and stages. We explore whether, similarly to objectively measured sleep, aperiodic spectrum steepens as subjective sleep depth increases.

Materials and methods: We re-analyzed a part of the data reported by Stephan et al., 2021, where serial awakenings were carried out in 20 healthy subjects during two night's sleep with high-density EEG. Two-minutes EEG epochs were extracted before awakening. Participants reported whether they felt asleep or awake and the depth of the experienced sleep. To control for the effect of time of night and sleep stages, only awakenings from the first two hours of the night were included (n = 146). The aperiodic component of spectral power was calculated using the Irregular Resampling Auto-Spectral Analysis method with 4-s windows. Then, a piecewise-defined linear regression was applied in the log-log domain in the fitting range of 1–30Hz, resulting in a pair of low and high bands separated by the breaking frequency that differed for each epoch. Aperiodic slopes and intercepts were calculated and compared between epochs corresponding to the reported feeling asleep vs feeling awake for N2 (33 asleep, 8 awake reports) and N3 (69 asleep, 26 awake reports) separately, using the permutation test with the correction for multiple comparisons. To keep the number of awake and asleep reports balanced, the equal number of asleep epochs were randomly selected for each stage. Likewise, we correlated aperiodic parameters with the reported sleep depth on a scale of 1–5 ("5" being the deepest sleep).

Results: Upon awakening from N3 but not N2, EEG segments associated with subjective reports of feeling asleep showed steeper aperiodic slopes and higher intercepts in the low (but not high) domain in the occipito-parietal region compared to reports of feeling awake with medium to large effect sizes (Cohen's d's = 0.5–1.3, p's < 0.005). Furthermore, in N3, deeper subjective sleep was associated with steeper aperiodic slopes.

Conclusions: Beyond being noticeably distinct in different sleep stages, aperiodic neural activity also reflects modulations in perceived sleep depth, where steeper aperiodic spectral decay corresponds to deeper subjective sleep during early N3 sleep.

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Reference

Stephan AM, Lecci S, Cataldi J, Siclari F. Conscious experiences and high-density EEG patterns predicting subjective sleep depth. *Curr Biol.* 2021 Dec 20;31(24):5487-5500.e3. doi: 10.1016/j.cub.2021.10.012. Epub 2021 Oct 27. PMID: 34710350.

Assessing sleep quality and sleepiness among nursing undergraduates: A cross-sectional survey

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Introduction: Background: Sleep quality is crucial for health and quality of life, especially for nursing students. Daytime sleepiness is uncontrollable tiredness and snoozing during the day. Poor sleep quality and excessive daytime sleepiness that might have negative impacts on nursing students in terms

of poor academic and clinical practicum performance, mental health problem e.g., insomnia and depression, and further affect patient care.

Aims: This study was to assess the sleep quality and daytime sleepiness among nursing undergraduates.

Materials and methods: A cross-sectional questionnaire study was employed to recruit year 2 to 5 nursing undergraduates studying in the Caritas Institute of Higher Education (CIHE), Hong Kong. Approval was granted from the Research and Ethics Committee of CIHE. A total of 129 nursing undergraduates were invited to complete an online questionnaire, including demographic variables, Sleep Quality Scale (SQS) and Epworth Sleepiness Scale (ESS) from 06 November 2023 to 30 December 2023. The collected data was analysed using Pearson chi-squared test and correlation tests to investigate the relationship between sleep quality and daytime sleepiness.

Results: This study revealed a significant relationship between sleep quality and daytime sleepiness with a significant score of $r = 0.264$ (1), $p = 0.003$. The Pearson Chi-Squared test coefficients for 6 factors of SQS (Daytime dysfunction, restoration after sleep, difficulty in falling sleep, difficulty in getting up, satisfaction with sleep and difficulty in maintaining sleep) and ESS (Daytime sleepiness) indicated non-significant results. Only year 5 students had scores of $r = 0.413$ (1), $p = 0.014$ showing a significant relationship between sleep quality and daytime sleepiness.

Conclusions: There was a significant positive correlation between sleep quality and daytime sleepiness, indicating that higher levels of daytime sleepiness were associated with poorer sleep quality. The findings highlight the need to address sleep hygiene and promote optimal sleep quality for overall student well-being and alertness in clinical practicum for patient safety especially for final year students. Further research and interventions are necessary to better understand and improve sleep health in academic settings to acknowledge the limitations of the study, including its reliance on self-reported measures. Future research should aim to incorporate objective measures and expand the participant pool to enhance generalizability of findings.

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Assessment of sleep quality among heavy truck, shift work drivers in Erdenet Mining Company of Mongolia

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Introduction: The working conditions of truck and heavy vehicle drivers, such as shift work, long driving hours, and irregular sleep patterns, are among the highest risk factors for sleep deprivation. Shift workers are at increased risk for sleep disorders due to disrupted circadian rhythms and reduced sleep duration to less than 7 hours per 24-hour period.²¹ Shift work of more than 12 hours, early work start times before 6 am, and shifts that start at night have been shown to negatively impact sleep quality.

Objectives: To assess the sleep quality, and lifestyle using a questionnaire.

Materials and methods:

The study followed a cross-sectional, descriptive design. Demographic, anthropometric, and sleep questionnaire surveys were done on 300 drivers and shift workers from November 3, 2023, to December 5, 2023. From the 300 operators who participated in the survey, 20 operators at risk were selected and polysomnography was conducted.

Results: 88% of the mine operators were male with a sex ratio of 4:1, mean age 39.2, and 80% of the operators were aged 30-49. 87% of the respondents were smokers, and 50% had a history of alcohol consumption. 28% of the operators had worked in the mine for 5-10 years, and increasing age was directly related to increasing years of work. Anthropometric indicators showed that 74% were overweight or obese, with neck circumference and waist circumference 3-5 cm larger than the average

Mongolian, and an average of 1st-degree hypertension. Anthropometric indicators differed by the workshop, with overweight and hypertension being more common among drivers. 76% of all operators are at risk of having one or more sleep disorders, 44% are excessively sleepiness, and 38% have poor sleep quality. Sleep disorders, drowsiness, and poor sleep quality are directly related to having a high BMI, large neck and waist circumference, high blood pressure, and high heart rate, and are also associated with years of work. In polysomnography, 99% of all operators have sleep disorders or poor sleep quality, of which 10% have insomnia as the main diagnosis, 65% have sleep apnea, and 20% have periodic limb movement disorder. Noteworthy that 80% have two or more types of sleep disorders combined.

Conclusions: Obesity, alcohol consumption, and insufficient sleep and rest time among mining operators and workers are major risks to the normal functioning of the work-life balance. Therefore, increasing sleep time is not only important for safety but also for individual health, and has many benefits for improving labor productivity and stable work. We propose measures that include organizational and individual participation from the organization.

Acknowledgments:

1. Bauerle T, Dugdale Z, Poplin G. Mineworker fatigue: A review of what we know and future decisions. *Min Eng.* 2018;70(3):33.
2. Richter K, Acker J, Adam S, Niklewski G. Prevention of fatigue and insomnia in shift workers review of non-pharmacological measures. *EPMA J.* 2016;7(1):16.
3. Garbarino S, Guglielmi O, Sannita WG, Magnavita N, Lanteri P. Sleep and Mental Health in Truck Drivers: Descriptive Review of the Current Evidence and Proposal of Strategies for Primary Prevention. *Int J Environ Res Public Health.* 2018;15(9):1852.

Assessment of sleep quality and its association with mental status and physical activity among medical undergraduates

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Introduction:

Sleep is vital for overall health and well-being. Sleep improves cognition, learning and memory, and academic performance. It also brings behavioural and emotional control and fosters positivity, thus improving the overall quality of life (QoL). Chronic sleep deprivation worsens health and emotional well-being and leads to self-criticism, internalising symptoms and risk-taking behaviours escalating to mental illness, self-harm and suicidal tendencies if unattended. The majority of the young population, in their peak productive period, neglect sleep and suffer from insufficient sleep syndrome due to academic and work demands. Therefore, the present study was planned to assess sleep quality and its association with mental status and physical activity among medical undergraduate students.

Materials and methods:

Undergraduate Medical students (N=345) of either sex between the age group 18 and 25 years were recruited for the study. The data was collected online by Google form and self-reported questionnaires of the Pittsburgh Sleep Quality Index and Depression Anxiety Stress Scales, Epworth Sleepiness Score and International Physical Activity Questionnaire were used to measure the Sleep quality, Depression, Anxiety and Stress levels, Daytime sleepiness and Physical activity respectively

Results:

The average age of the Study participants (n=345) was 20.36 ± 1.135 years. Of the total, 184 (53.3%) were male and 161 (46.7%) were female. Sleep quality data revealed that 146 (42.3%) had good sleep, while 199 (57.7%) experienced poor sleep. Additionally, participants with poor sleep quality had significantly higher levels of depression ($p < 0.001$), anxiety ($p < 0.001$), stress ($p < 0.001$), and daytime sleepiness ($p < 0.001$), along with a significant decrease in physical activity ($p = 0.009$), compared to those with good sleep quality.

Conclusions:

Poor sleep quality is high among medical students and is significantly associated with depression, anxiety, and stress. However, structured physical activity of moderate to severe degree proves beneficial in improving sleep quality

Acknowledgments:

I express our gratitude to the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, for granting permission to conduct this study in medical undergraduates. This helped us to estimate the sleep quality and the determine the prevalence of poor sleep quality among medical undergraduates

Beyond Sleep Duration: The Critical Role of Sleep Stages in Cardiovascular Disease Risk: Insights from two community-based cohort study

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Introduction:

While most studies have focused on conventional self-reported measures such as sleep duration and quality, emerging evidence highlights the physiological and clinical heterogeneity of sleep architecture. This study comprehensively investigated the linear and nonlinear associations between four polysomnography-derived sleep stages (N1, N2, N3/N4, REM) and long-term CVD incidence in two large independent cohort studies, focusing on effect modification by habitual sleep duration and obstructive sleep apnea (OSA) status, as well as the mediating pathways exploration.

Materials and methods: We recruited 5,804 middle-aged and elderly individuals from the Sleep Heart Health Study (SHHS) and 1,416 individuals from the Wisconsin Sleep Cohort (WSC). Sleep stages were assessed objectively using in-home polysomnography. Multivariable Cox regression models were employed to calculate hazard ratio (HR) for CVD, coronary heart disease (CHD), and stroke, adjusting for demographics and other sleep metrics. Subgroup analyses stratified by habitual sleep duration and OSA status were conducted. Mediation analysis was used to quantify the mediating effect of six modifiable cardiometabolic biomarkers.

Results: A total of 4,042 participants from SHHS and 600 participants from WSC were included in the analysis, with a mean follow-up of 11.0 (SD=2.7) and 8.8 (SD=2.6) years, respectively. During the follow-up time, 695 and 60 CVD cases occurred in SHHS and WSC. After adjustment for potential confounders, each standard deviation (SD) increase in N2% was associated with a 17% increase in CVD risk (adjusted hazard ratio (AHR)=1.17, 95% CI: 1.08–1.27), while each SD increase in REM% was associated with an 11% reduction in CVD risk (AHR=0.89, 95% CI: 0.83–0.96). Sleep duration shows a significant modification effect for REM% (P for interaction=0.008), while OSA status shows a significant modification effect for N2%, N3/4%, and REM% (All for interaction<0.05). Restricted cubic spline curves indicate U-shaped associations of N3/4% with CVDs (P for non-linearity<0.001). Mediation analysis shows BMI and SBP are the main mediators, accounting for 13.1% and 5.5% for N2% and 13.9% and 7.4% for REM% sleep.

Conclusions: Our study demonstrates that a higher proportion of N2 sleep and a lower proportion of REM sleep are associated with increased CVD risk, especially in individuals with short habitual sleep duration and non-OSA populations. The BMI reduction and SBP control for CVD prevention may warrant prioritization, targeting the adverse effects of unfavorable sleep stage proportion.

Bidirectional Relations of Insomnia with Anxiety and Depression symptom networks and Moderating Role of Fatigue

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Introduction: Insomnia is closely associated with anxiety and depression, forming a complex bidirectional relationship. Although previous research has demonstrated that fatigue is a core and bridge symptom within this complex relationship, its potential moderating role in their interaction remains unexplored. This study employs symptom network analysis to explore the Moderating role of fatigue, aiming to identify core symptoms and their interactions.

Materials and methods: 544 participants (37.86 ± 11.41 , 210 males) diagnosed with chronic insomnia disorder were participated in the study. The Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Hamilton Anxiety and Depression Scales (HAMA and HAMD-17), were used to assess symptoms. Network analysis was conducted using hierarchical LASSO to estimate symptom networks, with O3(fatigue) as a moderating variable.

Results: Our study revealed significant bidirectional relationships among insomnia, depression, and anxiety symptoms, such as S5 with O2, and O4 with D2. Fatigue played a crucial moderating role, particularly in strengthening the relationships between sleep maintenance difficulties and circadian rhythm features, S2 (sleep satisfaction) and D2 (weight changes), A2 (somatic anxiety) and O1 (daytime dysfunction). Centrality analysis identified mental anxiety (A1), the impact of insomnia on quality of life (S6), and sleep interference with daytime function (S5) as core symptoms in the network.

Conclusions: We identified significant bidirectional relationships between the symptoms of insomnia, depression, and anxiety symptoms and interaction terms moderated by fatigue. These findings provide valuable theoretical and practical insights for breaking the cycle between symptoms of insomnia, depression, and anxiety through intervention with fatigue.

Bilateral thalamic stimulation via TES-TI Enhances Sleep Spindle Activity during a Daytime Sleep Episode

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Introduction: Sleep spindles are transient electroencephalographic (EEG) elements named after their typical waxing and waning morphology. They represent a defining characteristic of non-rapid eye movement sleep in mammals. The rhythmic interaction of the thalamic reticular nucleus with the thalamocortical relay neurons constitutes the core neurophysiological mechanism underlying spindle generation. Sleep spindles activity exhibits correlations with memory performance, while their deficit has been reported in patients affected by schizophrenia in association with decreased cognitive abilities. Here, we demonstrate Transcranial Electrical Stimulation with Temporal Interference (TES-TI) ability to enhance spindle activity bilaterally targeting the thalamus.

Materials and methods: 24 participants (age $27.2 \text{ ys} \pm 7.4 \text{ ys}$; 69.6% F) underwent thalamic TES-TI stimulation during daytime naps. Stimulation protocols were delivered during N2 sleep with the following parameters: three minutes duration, 15 kHz carrier frequency, 15 seconds ramping up/down periods. Three envelope frequencies were tested in random order: 10 Hz (TES-TI 10Hz), envelope frequency matched to each participant's sigma peak (TES-TI Peak), and 0 Hz (TES). Simultaneous 256-channel high-density EEG recordings were performed. Average spectral power in the sigma band (9-16 Hz) across all electrodes was compared before (PRE) and during the stimulation (STIM) using paired Wilcoxon test. Topographic patterns of sigma power modulation during the stimulation were assessed using a non-parametric cluster-based permutation test. Spindle density and power were quantified using an automated spindle detection algorithm and compared between STIM and PRE using paired Wilcoxon tests.

Results: TES-TI 10Hz stimulation was associated with a significant increase in sigma power ($\Delta\mu_{\text{STIM-PRE}} = 0.36 \log_{10}\mu\text{V}^2$, $p = 0.042$), but not TES ($\Delta\mu_{\text{STIM-PRE}} = -0.17 \log_{10}\mu\text{V}^2$, $p = 0.23$) and TES-TI Peak stimulation ($\Delta\mu_{\text{STIM-PRE}} = -0.047 \log_{10}\mu\text{V}^2$, $p = 0.47$). Cluster-based analysis localized the increase over two frontal and centro-parietal electrode clusters ($p = 0.027$). TES-TI 10Hz stimulation was also associated with a significant increase in spindle power ($\Delta\mu_{\text{STIM-PRE}} = 0.035 \log_{10}\mu\text{V}^2$, $p = 0.0093$) and a trend towards an increase in spindle density ($\Delta\mu_{\text{STIM-PRE}} = 1.96 \text{ spindle/s}$, $p = 0.092$). No significant change in spindle characteristics was observed during TES-TI Peak (power: $\Delta\mu_{\text{STIM-PRE}} = -0.0042$

$\log_{10}\mu V^2$, $p = 1$; density: $\Delta\mu_{\text{STIM-PRE}} = -2.45$ spindle/s, $p = 0.20$) and TES stimulation (power: $\Delta\mu_{\text{STIM-PRE}} = -0.012 \log_{10}\mu V^2$, $p = 0.49$; density: $\Delta\mu_{\text{STIM-PRE}} = -2.79$ spindle/s, $p = 0.16$).

Conclusions: This study presents the first evidence supporting the successful use of TES-TI during sleep to target the thalamus and enhance sleep spindle activity. Stimulation at a fixed envelope frequency of 10 Hz effectively increased sigma band power, whereas stimulation matched to each participant's individual sigma band peak did not produce a comparable enhancement. Sigma power increase followed a pattern consistent with typical spindle topography in healthy adults and was associated with an increase in power of individual spindles. Further research is needed to investigate the cognitive and clinical impact of TES-TI-induced spindle enhancement.

BTBD9 Controls Sleep via Ubiquitination of IMPDH2 and Adenosine Modulation in the Basal Forebrain

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Introduction: BTBD9 has been established as a critical sleep-regulating gene, whose genetic variants are associated with human insomnia and restless legs syndrome (RLS), while its loss-of-function leads to disrupted sleep architecture in both mice and *Drosophila*. However, its precise molecular mechanisms remain elusive.

Materials and methods: We employed an integrated multidisciplinary approach: 1) AAV-mediated Cre/loxP system with stereotaxic injection for basal forebrain (BF)-specific genetic manipulation; 2) Long-term sleep monitoring and deprivation experiments using synchronized electroencephalography/electromyography (EEG/EMG) recordings; 3) Quantitative proteomics, ubiquitinomics, and bioinformatic prediction to identify key substrates; 4) Structural analysis, in vitro ubiquitination assays, and site-directed mutagenesis to validate molecular interactions; 5) Fiber photometry and tissue metabolome for neurotransmitter dynamics assessment; 6) AAV-delivered competitive interfering peptides for in vivo functional rescue experiments.

Results: We discovered that BF-specific *Btbd9* knockout induces a previously-unexpected pro-sleep phenotype mediated by elevated adenosine levels. IMPDH2, the rate-limiting enzyme in *de novo* GTP biosynthesis, was identified as an evolutionarily conserved ubiquitination substrate of BTBD9, with lysine 195 (K195) being the critical modification site. BTBD9-mediated ubiquitination disrupts GTP-dependent feedback inhibition of IMPDH2, altering its enzymatic activity. Both pharmacological inhibition of IMPDH2 with MPA and conditional knockout in BF neurons recapitulated the sleep-promoting effects, increasing NREM sleep duration and slow-wave activity (SWA)—key markers of sleep pressure. Crucially, targeted disruption of the BTBD9-IMPDH2 interaction via AAV-delivered interfering peptides not only prolonged NREM sleep but also confirmed the druggability of this pathway.

Conclusions: Our study unveils the novel BTBD9-IMPDH2-adenosine axis in sleep regulation and proposes targeting this interaction as a promising therapeutic strategy for sleep disorders. These findings provide groundbreaking insights into the molecular pathogenesis of sleep disturbances.

Butyric Acid Suppresses Adipogenesis Triggered by Intermittent Hypoxia and Hypercapnia via sAC/cAMP/PKA Pathway Modulation

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Introduction: To explore whether intermittent hypoxia and hypercapnia i.e., intermittent hypoxic-hypercapnia (IHH), the main characteristics of obstructive sleep apnea (OSA), induce adipogenesis, and assess the inhibitory effect of butyric acid, (BA) on intermittent hypoxia or hypercapnia accelerated adipogenesis.

Materials and methods: To determine the potential impact IHH on adipogenesis, cells were exposed to simultaneous transient hypoxic-hypercapnia (4% O₂, 10% CO₂) for 48 hours. Intracellular lipid and triglyceride accumulation of groups above was observed using an Oil Red O stain and triglyceride assay. To clarify the underlying mechanism, the expression level of the pro-adipogenic markers including peroxisome proliferator-activated receptor (PPAR) γ , CCAAT/enhancer binding protein (CEBP) α , CEBP β and cAMP Response Element-Binding Protein (CREB) were measured. And the protein expression of soluble adenylyl cyclase (sAC) cyclic adenosine monophosphate (cAMP) and protein kinase A (PKA) was also assessed.

Results: IHH accelerated lipid accumulation, triglyceride formation, and protein expression of PPAR γ , CEBP α , CEBP β and CREB which were inhibited by butyric acid. Additionally, butyric acid suppressed the sAC/cAMP/PKA pathway protein expression in IHH-induced adipogenesis.

Conclusions: This study reveals that OSA-induced adipogenesis results from the synergistic effort of hypoxia and hypercapnia, also butyric acid could inhibit adipogenesis induced by hypoxic-hypercapnia via the suppression of sAC-dependent cAMP production and PKA activation.

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Can breaking up prolonged sitting with physical activity during simulated dayshifts and nightshifts improve sleep quality? A randomised controlled trial

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Introduction: Inadequate sleep is a global problem and contributes to poor health outcomes. Physical activity has a positive impact on sleep outcomes, however the prevalence of physical inactivity is increasing worldwide, coupled with the rise of sedentary behaviour at work. Interventions that promote physical activity and reduce sedentary behaviour are essential, as they can improve sleep. The current study investigated the effects of breaking up prolonged sitting with physical activity during the day or night on sleep architecture during a 9 h or 5 h sleep opportunity.

Materials and methods: Participants (n=125, 51% male, 23.4 $\pm$ 4.8 years of age) completed an in-laboratory sleep study. Participants completed five simulated shifts during the day or night. During the simulated work shifts, participants in the breaking up sitting conditions completed a 3-minute light walk (3.2km/h) on a treadmill every 30 minutes. Sleep opportunities were either 9 h or 5 h following each shift. Participants were allocated to one of six conditions, 1) Sedentary during the day and 9 h sleep; 2) Breaking up sitting during the day and 9 h sleep opportunity; 3) Sedentary during the day and 5 h sleep opportunity; 4) Breaking up sitting during the day and 5 h sleep opportunity; 5) Sedentary during the night and 9 h sleep opportunity; 6) Breaking up sitting during the night and 9 h sleep opportunity. Sleep outcomes were recorded using polysomnography (total sleep time, sleep onset latency, sleep efficiency, wake after sleep onset and percentage of time spent in stage N1, N2, N3, NREM and REM).

Results: In the analysis of day shifts, mixed model ANOVAs demonstrated a significant physical activity condition by sleep opportunity interaction for total sleep time ($p < 0.001$), sleep onset latency ($p < 0.001$), time spent in N2 ($p < 0.001$) and N3 ($p = 0.03$). Post-hoc analyses revealed that participants in the 9 h sleep conditions had longer total sleep time, shorter sleep onset latency, and more slow-wave sleep (N3) during sleep opportunities 1-4 but not sleep opportunity 5. There were no significant differences in sleep architecture by physical activity condition for the nightshift conditions.

Conclusions: Better sleep quality was seen in the 9 h condition compared to the 5 h condition, and breaking up sitting did not affect sleep. Given the benefits of breaking up sitting on health, our findings suggest a breaking up sitting intervention can be promoted without detrimental impacts on sleep.

CD169⁺ Macrophages Mediated Downregulation of Endothelial CX43 Expression Underlies Obstructive Sleep Apnea Related Cognitive Impairment

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Introduction: Objective: Obstructive sleep apnea (OSA) is an independent risk factor for cognitive impairment, with chronic intermittent hypoxia (CIH)-induced blood-brain barrier (BBB) injury being a critical mechanism. However, the specific pathways remain unclear. Macrophages may regulate BBB damage by influencing endothelial cell function. Macrophages exhibit heterogeneity, and tissue-resident macrophages in the brain (CD169⁺ macrophages) play a pivotal role in the early stages of disease. This study investigates the molecular mechanism by which CD169⁺ macrophages mediate OSA-related cognitive dysfunction through interactions with endothelial cells.

Materials and methods: Methods: A CD169⁺ macrophage-depleted mouse model was generated by intraperitoneal injection of diphtheria toxin (DT) into CD169-DTR mice. These mice were then subjected to chronic intermittent hypoxia stimulation to mimic OSA-related pathological conditions. Changes in blood-brain barrier permeability were quantitatively analyzed using two-photon fluorescence imaging. Cognitive dysfunction was assessed through behavioral tests, including the Morris Water Maze and Novel Object Recognition assays. Immunofluorescence staining was employed to determine the spatial localization of CD169⁺ macrophages in specific brain regions of CIH-exposed mice. Additionally, an *in vitro* co-culture system of CD169⁺ macrophages and endothelial cells was established to investigate the downstream molecular mechanisms mediated by the CX43-Claudin 5 pathway. Sequencing and pathway analyses were conducted to identify key gene expression changes and signaling cascades underlying macrophage-endothelial interactions.

Results: Results: CIH impaired learning and memory in mice and increased BBB permeability to 10-kDa small molecules. These effects were alleviated after CD169⁺ macrophage depletion. Under CIH, CD169⁺ macrophages proliferated in the hippocampal region and exacerbated neuroinflammation. The expression of chemokines CXCL3 and CXCL5, as well as inflammatory factors IFN β and IL-6, was significantly elevated in CD169⁺ macrophages. Sequencing results from the *in vitro* co-culture system revealed that CD169⁺ macrophages downregulated endothelial *Gja1* (encoding connexin CX43) expression. Pathway analysis showed that CX43 inhibited the expression of p38 α in the MAPK signaling pathway, thereby suppressing *Cldn5* gene transcription. This led to reduced levels of the tight junction protein Claudin 5, resulting in disrupted BBB integrity and increased permeability.

Conclusions: Conclusion: In summary, CIH promotes BBB injury and neuroinflammation, contributing to cognitive dysfunction via interactions between CD169⁺ macrophages and endothelial cells. CD169⁺ macrophages downregulate connexin CX43 expression in endothelial cells, suppress the MAPK pathway, and reduce Claudin 5 levels, ultimately increasing BBB permeability. Targeting CD169⁺ macrophages may provide a theoretical foundation for understanding the immunological mechanisms and therapeutic strategies for OSA-related cognitive impairment.

Chronic Intermittent hypoxia exacerbates the progress of periodontal disease via promoting inflammatory and microbial dysbiosis

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Introduction: Obstructive sleep apnea (OSA) has been suggested to be independently associated with periodontitis; however, the causal relationship between OSA and periodontitis remains unclear. This study aimed to investigate the effects of chronic intermittent hypoxia (CIH), a hallmark of OSA, on periodontitis.

Materials and methods: Eight six-week-old male Wistar rats were randomly assigned to two groups: normoxic group and CIH group. A periodontitis model was induced in both groups by ligating the maxillary second molars. The CIH group was exposed to a chronic intermittent hypoxic environment simulating OSA for five weeks. Gingival crevicular fluid was collected, and the microbiome composition was analyzed via pyrosequencing and bioinformatic analyses of 16S rRNA. Micro-computed tomography (micro-CT) was used to evaluate the relative cemento-enamel junction (CEJ) to the alveolar bone crest (ABC) distance, bone volume fraction (BV/TV), and trabecular thickness (Tb.Th). Histological

evaluations were conducted using hematoxylin and eosin (HE) staining, Masson's trichrome staining and tartrate-resistant acid phosphatase (TRAP) staining. Inflammatory markers, including HIF-1 α and IL-1 β , were quantified using enzyme-linked immunosorbent assay (ELISA) and real-time quantitative PCR.

Results: Clinical parameters showed that probing depth (PD) and bleeding index (BI) were significantly higher in the CIH group than in the normoxic group. Micro-CT analysis revealed a greater distance from the CEJ to the ABC in the CIH group, along with reduced Tb.Th and BV/TV. Histological analysis showed increased attachment loss and inflammatory cell infiltration in the CIH group. TRAP staining demonstrated a higher number of activated osteoclasts in the CIH group. Inflammatory markers HIF-1 α and IL-1 β were significantly elevated in the CIH group. At the phylum level, 16S rRNA analysis revealed an increased relative abundance of Proteobacteria, Firmicutes, Bacteroidota, and Deinococcota, with decreased relative abundance of Actinobacteriota in the CIH group.

Conclusions: Chronic intermittent hypoxia (CIH) aggravates the progression of periodontitis by elevating inflammatory factor levels, changing the composition of the subgingival microbiota, and accelerating periodontal tissue destruction.

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Comparison between Ultrasound and CBCT Measurements of Airway Anatomy in Adults with and without Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a significant public health concern linked to adverse cardiovascular, metabolic, cognitive, and mental health outcomes. While polysomnography (PSG) remains the diagnostic gold standard, it primarily captures physiological sleep data and lacks direct anatomical insight, limiting its ability to guide precision treatment. Identifying patient-specific anatomical contributors to OSA is essential for developing targeted, etiology-based therapies. Backscattered ultrasound imaging (BUI), particularly submental ultrasound (US), has emerged as a promising modality due to its portability, cost-effectiveness, and radiation-free nature. Prior studies have demonstrated that ultrasound can visualize the pharyngeal airway and detect dynamic changes in the retropalatal transverse diameter, facilitating the identification of severe OSA. Incorporating ultrasonography into routine evaluation may enable longitudinal, anatomy-driven care in a more accessible and cost-effective manner.

Materials and methods: A retrospective analysis was conducted on eight patients (mean age 38.8 $\pm$ 12.1 years; 3 females, 5 males), with or without a diagnosis of obstructive sleep apnea (OSA), screened at the University of the Pacific's graduate orthodontics clinic. Upper airway ultrasound imaging was performed using the AmCAD-UO system (AmCAD BioMed Corporation), measuring airspace width at the velum, oropharynx, tongue base, and epiglottis during tidal and Müller breathing. The system also generated a risk assessment for moderate/severe OSA (low, medium, or high). CBCT scans were acquired for all patients using the i-CAT FLX system (Imaging Sciences International), and corresponding airway measurements were obtained using the CBCT Airway Evaluation module in Dolphin Imaging software. Additionally, three patients underwent overnight home sleep apnea testing (HSAT) using the WatchPAT One device (Itamar Medical Ltd.), dispensed through the Stanford Sleep Medicine Center.

Results: Airspace width measurements during tidal breathing obtained via ultrasound imaging (US) were compared to CBCT-derived measurements at four anatomical levels. At the velum, mean widths were 2.5 $\pm$ 0.9 cm (US) and 2.8 $\pm$ 0.6 cm (CBCT); at the oropharynx, 3.1 $\pm$ 1.0 cm (US) and 2.8 $\pm$ 0.7 cm (CBCT); at the tongue base, 3.0 $\pm$ 0.6 cm (US) and 3.0 $\pm$ 0.7 cm (CBCT); and at the epiglottis, 2.9 $\pm$ 0.5 cm (US) and 3.2 $\pm$ 0.3 cm (CBCT). No statistically significant differences were observed, suggesting strong agreement between US and CBCT measurements during tidal breathing. Among the three patients who underwent home sleep apnea testing, ultrasound-based risk assessments were consistent with sleep study results.

Conclusions: This study highlights the potential of ultrasound imaging as a valuable diagnostic tool for screening and evaluating patients with obstructive sleep apnea (OSA). When compared to CBCT and home sleep apnea testing (HSAT), ultrasound demonstrated strong diagnostic concordance. Its fast, radiation-free assessment of dynamic upper airway anatomy enables accurate identification of anatomic sites of restriction, offering a practical and informative approach to guiding treatment planning and evaluating therapeutic outcomes.

Comparison of epilepsy mouse models induced by kainic acid through different administration routes

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Introduction: Epilepsy is a debilitating neurological disorder driven by abnormal excessive or synchronous neuronal activity in the brain, affecting about 50 million people worldwide according to the World Health Organization Report 2024. Over the last decades, different epilepsy models have been developed including injection of chemoconvulsants, traumatic brain injury, electrical kindling, and optogenetic kindling established more recently. The most widely used epilepsy model is created with kainic acid (KA) due to its convenience and robust phenotype mimicking the clinical symptoms observed in patients bearing epilepsy. However, a side-by-side comparison of sleep/wake pattern, and the implicated brain regions in epilepsy mouse models with KA administration through different routes remains underexplored. In this study, we administered KA/saline intraperitoneally or intrahippocampally, and compared their seizures, isolated spikes, and c-Fos expression pattern spanning the entire mouse brain at different time points in a systematical manner.

Materials and methods: Epilepsy mouse models were created through intraperitoneal injection of KA (IPKA, 20mg/kg, saline (0.9% NaCl) as solvent, IPS), or locally to dorsal hippocampal CA1 region (IHKA, 150ng, saline as solvent, IHS). EEG and simultaneous EMG were sampled at various times to monitor the dynamic changes of sleep/wake architecture, and the development of epilepsy. A subgroup of mice was perfused at different times following drug administration, and their brains were collected for immunohistochemical analyses to determine the contribution of dynamic neuronal activity during the development of epileptogenesis.

Results: We observed a more severe disruption of sleep architecture perpetuating for a longer time associated with seizures in the IHKA group. IHKA induced a more robust epilepsy pattern during the acute phase. Both IPKA and IHKA increased the amount of wakefulness and decreased non-rapid eye movement (NREM) sleep within a few hours after injection. REM sleep was completely abolished during the initial 5 hours in the IHKA group, whereas the absence of REM in the IPKA group lasted for a shorter time. A chronic epilepsy model was developed as seizures were observed up to 4 weeks in the IHKA group, but not in the IPKA group. Reduction of REM sleep remained 4 weeks after treatment of IHKA. IHKA induced more isolated spikes overall, and stabilized at 3 weeks after drug administration. Both IPKA and IHKA induced increased c-Fos expression within 3 hours after the drug administration as compared to their controls. Pearson correlation analyses among different brain regions expressing c-Fos revealed that IHKA primarily affected forebrain and midbrain, but IPKA implicated subnuclei across the entire brain despite c-Fos+ cell counts were less than the IHKA group.

Conclusions: Our results demonstrate that the IHKA induced a more robust epilepsy mouse model, which exhibited acute and chronic disruption of sleep/wake architecture, perpetuating seizures, and more isolated spikes. c-Fos expression analysis revealed that the correlation pattern of brain regions expressing c-Fos in the IHKA group is distinct from the correlation pattern in the IPKA group at the acute phase.

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Correlation between T3, T4, TSH and Qualitative and Quantitative Polysomnography Sleep Variables

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Introduction: Poor sleep quality is consistently noted in patients of hypothyroidism. People complained of sleeplessness, excessive day-time sleepiness, snoring, arousals and breathlessness. Decrease in quantity and quality of sleep occurred in various degrees of severity. These facts provided an impetus to assess the correlation between T3,T4 levels and TSH and Total Sleep Time, Sleep efficiency, Sleep stage percentage, Sleep onset latency, Arousal index, Apnoea-Hypopnea index, Oxygen desaturation index, Snoring index and Epworth Sleepiness Scale score.

Materials and methods: This cross sectional study was conducted in thirty patients of hypothyroidism who were in ages between 30 and 50 years. Polysomnography was conducted on these patients for studying the sleep architecture.

Results: There was positive correlation between T3 and sleeps parameters including total sleep time, sleep efficiency, sleep onset latency, apnea-hypopnea index, arousal index, snoring index, oxygen desaturation index and Epworth Sleepiness Scale score. A significant negative correlation was found between T4 and AHI and T4 and ESS. A significant positive correlation was found TSH and ODI, TSH and AHI.

Conclusions: These fact reveals that hypothyroidism affect sleep architecture leading to poor sleep quality.

Daflon attenuates sleep deprivation-induced neurocognitive deficit in male Wistar rat by activating AMPK/Nrf2/HO-1 and downregulating Bax/Bcl-2/caspase 3 apoptotic signaling

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Introduction: Sleep deprivation (SD) is a widespread global challenge, with recent surveys revealing that about one-third of individuals report difficulty falling or staying asleep multiple times per week, due to work shifts, anxiety, stress, and financial pressures. SD has been associated with neurocognitive deficit, which is mediated by oxidative stress signaling. On the other hand, daflon exerts antioxidant properties. However, the effect of daflon on SD-induced neurocognitive deficit has not been reported. Thus, this study investigated the effect of SD, with or without daflon, on neurocognition and the involvement of AMPK/Nrf2 and Bax/Bcl-2/caspase 3 apoptotic signaling as a possible mechanistic pathway.

Materials and methods: Thirty-two-week-old male Wistar rats weighing 200 ± 10 g were randomly allotted into vehicle-treated control (0.5 mL of water), daflon (100 mg/kg), SD, and SD + daflon. SD was induced by exposing the animals to continuous SD for 96 hr using the modified multiple platform technique, followed by a 72 hr recovery period (where they were allowed to sleep). This cycle continued for 4 weeks. Daflon treatment was daily and *per os*. Twenty-four hours after the experimental period, neurobehavioral studies such as Barnes', novel object recognition, Y maze, open field, and hanging wire tests were performed to evaluate cognition, motor function, and anxiety, while the cerebral cortex, hippocampus, and cerebellar cortex were excised for biochemical assays and histopathological examinations.

Results: Daflon improved cognition, motor function, and anxiety-like behaviour in SD rats. Also, daflon attenuated lipid peroxidation (MDA generation), and enhanced cellular antioxidant (GSH, SOD, and catalase), brain-derived neurotrophic factor (BDNF), dopamine, and acetylcholinesterase in SD rats. In addition, daflon upregulated AMPK, Nrf2, HO-1, and Bcl-2 but downregulated NF-kB, TNF- α , IL-1 β , IL-6, Bax, and caspase-3 in the brain tissues. Daflon also improved the histological alterations in the cerebral cortex, hippocampus, and cerebellar cortex, such as pyknotic neurons, vascular congestion, and inflammatory cell infiltration in SD rats.

Conclusions: In conclusion, this study revealed that daflon improves neurocognition in sleep-deprived rats by activating AMPK/Nrf2/HO-1 and downregulating Bax/Bcl-2/caspase 3 apoptotic signaling.

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Data-Driven Fatigue Management: Harmonising Predictive Models with Actual Pilot Data to Optimise Alertness and Performance

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Introduction: Fatigue remains a significant risk to pilot performance and safety. To proactively manage fatigue, Qantas utilises a comprehensive Fatigue Risk Management System (FRMS), incorporating biomathematical modelling to predict sleep, fatigue, and performance. Biomathematical models, however, are based on population-level data and may not reflect individual variability or unique operational contexts. Therefore, this study aimed to explore the sleep/wake behaviours of A330 pilots and harmonise actual versus predicted sleep/wake behaviour using biomathematical modelling. Harmonising the biomathematical models refers to refining and improving the accuracy for a specific operation. Refining these models ensures they remain aligned with operational realities and contemporary sleep science, which is critical for optimising scheduling, crew alertness, and safety outcomes.

Materials and methods: Twenty-six Qantas A330 pilots (10 Captains, 8 First Officers, 8 Second Officers), aged 33-60 years (median= 48.5 years), participated between 1–3 month period. Data from 299 flight sectors, both domestic (e.g. Perth, Melbourne) and international (e.g. Haneda, Shanghai) were analysed. Objective sleep throughout flight patterns were recorded using Dreem 3 EEG headbands and MotionWatch 8 actigraphy. Cognitive performance was assessed via the Psychomotor Vigilance Task (PVT), and subjective fatigue and sleepiness were measured using the Samn-Perelli Fatigue Scale and Karolinska Sleepiness Scale, respectively. Sleep diaries provided additional subjective data. Cognitive performance and fatigue/ sleepiness measures were taken Pre-Flight, Top of Climb, Pre-Rest, Post-Rest, Top of Descent, and Post-Flight, as well as for sleep outside duty periods.

Results: Pilots achieved the American Academy of Sleep Medicine (AASM) recommendation of 7h of sleep when at home, with reduced sleep at layovers and recovery after a flight. Sleep efficiency was sufficiently above 80% across all sleep periods except for in-flight. There were high levels of Stage 3 sleep across all sleep periods, indicating deep, restorative sleep at all times, including during in-flight rest. Subjective sleepiness and PVT performance deteriorated with time into flight, especially upon waking up from in-flight rest, and after the flight. Harmonisation of the biomathematical modelling improved Minimum Sleep/Wake Accuracy from 81.5% to 86% and Total Daily Sleep Accuracy from 82.1% to 99.2%, confirming model reliability with minor adjustments.

Conclusions: This study provides novel insights into the real-world sleep patterns of A330 pilots. Despite limited sleep opportunities during in-flight rest, restorative deep sleep was achieved. Harmonisation of biomathematical modelling improved prediction accuracy and led to the development of a fleet specific biomathematical modelling setup. These refinements enhance operational confidence in fatigue prediction and support better rostering, countermeasures, and crew safety. The integration of EEG in the field represents a major advancement in aviation sleep science. Continued research and education are vital to further strengthen fatigue risk management and pilot wellbeing.

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Day-time Napping: The Benefits of Well-Being and Productivity

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Introduction: Short day-time naps are increasingly recognised as effective strategies for improving alertness and well-being in workplace settings. While nature-based sounds (e.g., forest rain) are widely acknowledged for their relaxation benefits, their potential to enhance nap-related outcomes remains understudied.

Materials and methods: In a repeated-measures crossover design, 22 healthy adults (mean age: 30.1 ± 10.9 years) completed two 20-minute naps in a MetroNaps® EnergyPod®, once while listening to forest rain sounds (music condition) and once with noise-cancelling headphones (control condition), on separate days. Participants rated subjective sleepiness (Karolinska Sleepiness Scale; Åkerstedt & Gillberg, 1990), relaxation, productivity readiness, valence, and arousal immediately before and after each nap, following a 5-minute adjustment period to mitigate sleep inertia. Working memory (N-BACK) and basic reaction time (PVT) tasks were also administered pre- and post-nap. Subjective evaluations continued post-nap via a short-burst experience-sampling protocol delivered by text message, achieving a 95% completion rate. This protocol included three hourly follow-ups and an additional bedtime reflection regarding the perceived impact of the nap on work and personal productivity.

Results: Outcomes across the six timepoints (pre-nap, post-nap, and four follow-ups) were analysed using Linear Mixed Effects models with fixed effects for condition, timepoint, and their interaction. Interactions were non-significant across all models and were removed ($p > .555$). Follow-up contrasts were Holm-corrected for multiple comparisons. Naps significantly improved self-reported relaxation (pre-nap: 5.9, 95% Confidence Intervals [5.4, 6.4] vs. post-nap: 7.2 [6.67, 7.64]; $p < .001$, $d = 1.15$) and reduced arousal (pre-nap: 48.8 [40.1, 57.5] vs. post-nap: 34.7 [26.0, 43.4]; $p < .001$, $d = 0.963$). Valence did not change significantly (pre-nap: 72.5 [66.7, 78.3] vs. post-nap: 76.5 [70.7, 82.4]; $p > .999$, $d = 0.32$). A modest, non-significant increase in sleepiness was observed post-nap, consistent with sleep inertia (pre-nap: 4.1 [3.56, 4.62] vs. post-nap: 4.8 [4.29, 5.35]; $p = .056$, $d = 0.57$). Evening reflections indicated participants perceived the nap as improving work ($p < .001$, $d = 1.37$) and personal productivity ($p < .001$, $d = 0.87$), with no significant differences between music and control conditions ($p > .600$, $d < .118$). No changes in cognitive task performance were observed ($p > .091$, $d < .11$). Outcome measures were not influenced by auditory context (all $p > .11$).

Conclusions: Brief workplace naps improve subjective relaxation and reduce arousal, offering perceived benefits to productivity later in the day—regardless of auditory context. The lack of added benefit from relaxing music may reflect the effectiveness of the noise-cancelling control, which likely created a similarly tranquil environment. Future studies should explore personalised auditory contexts, as effects may vary based on individual preference, familiarity, and situational fit. Although no immediate cognitive improvements were observed, extending measurement later into the day may reveal protective effects of day-time napping on cognitive fatigue. Incorporating longitudinal and biometric measurements could further enhance understanding of nap effects. Brief naps represent a low-cost, scalable intervention for enhancing well-being and sustaining perceived productivity in real-world work settings.

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Differential histamine responses measured with biosensor in wild-type and orexin/ataxin-3 mice: genotype-specific pharmacological sensitivity

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Introduction: The histaminergic and orexinergic systems are key regulators of wakefulness. Orexin/ataxin-3 mice, which lack orexin neurons, exhibit sleep-wake fragmentation, cataplexy, and excessive daytime sleepiness—features resembling human narcolepsy type 1. By modulating these systems using TAK-925 (an orexin receptor 2 agonist) and pitolisant (a histamine 3 receptor inverse agonist/antagonist), we aim to investigate acute, compound-specific effects on extracellular histamine in wild-type and orexin/ataxin-3 mice.

Materials and methods: Orexin/ataxin-3 and wild-type littermates were implanted with a GPCR-activation based (GRAB) - HA1h biosensor and optic fiber in lateral hypothalamus, along electroencephalography (EEG) and electromyography (EMG) electrodes. Furthermore, accelerometer (Acc) and video data were collected. Recordings began at ZT10, followed by subcutaneous injection of

TAK-925, pitolisant, or vehicle at ZT12 (lights off). We recorded 4 hours of biosensor data and 21 hours of EEG/EMG/Acc and video data post-injection.

Results: Administration of TAK-925 (10 mg/kg) or pitolisant (10 mg/kg) increased relative histamine levels extracellularly ($\Delta F/F$ normalized to baseline) in both genotypes. Pitolisant increased histamine similarly in both genotypes with similar progressions in normalized $\Delta F/F$ over time. TAK-925 increased normalized $\Delta F/F$ histamine levels extracellularly more in orexin/ataxin-3 mice than in wild-type littermates and remained higher over a longer time-course.

Conclusions: The GRAB-HA1h biosensor enables real-time detection of compound-induced changes in extracellular histamine. The effects of pitolisant appear independent of orexin signaling, showing similar profiles across genotypes. In contrast, TAK-925 elicits a genotype-dependent histaminergic response, suggesting heightened sensitivity in the absence of endogenous orexin. These findings underscore distinct mechanisms by which these compounds influence arousal circuits.

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Dim light at night exacerbate Parkinson's disease through circadian rhythm related pathways in mice

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Introduction: Growing evidence suggests that exposure to dim light at night (dLAN) can disrupt circadian rhythms. Circadian disruption has been implicated in the pathogenesis of various neurological disorders, including Parkinson's disease (PD)—a prevalent, progressive neurodegenerative condition with no cure and a high risk of disability. While studies have established a close association between circadian rhythms and PD, direct evidence linking dLAN exposure to the onset or progression of PD remains limited. Thus, we investigated whether dLAN could exacerbate Parkinsonism and circadian rhythms induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.

Materials and methods: MPTP-induced PD mice were housed in either a light-dark cycle (LD; 12 h of 200 lux:12 h of 0 lux) or a light-dLAN cycle (dLAN; 12 h of 200 lux:12 h of 5 lux) during the experimental periods. Motor function was assessed by the pole test and rotarod test. Substantia nigra transcript profiles were examined using multi-timepoint transcriptome analysis to assess the effects of dLAN exposure.

Results: First, we observed that dLAN exacerbated motor dysfunction in PD mice. Next, we found that dLAN decreased the levels of dopaminergic fibers and neurons in the striatum and the substantia nigra, respectively. In addition, dLAN reduced the amplitude of circadian rest-activity behaviors and nighttime activity levels in PD mice. Moreover, dLAN disrupted the expression of circadian genes in the substantia nigra, particularly *Npas2* in PD mice.

Conclusions: These findings reveal that dLAN exacerbated motor dysfunction and dopaminergic neuron loss in MPTP-induced PD mice, with disruptions in circadian rest-activity rhythms and rhythmic gene expression likely mediating the adverse effects of dLAN on these behaviors.

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Does acute late sleep restriction impact placebo hypoalgesia?

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Introduction: Sleep plays a critical role in regulating physiological and cognitive functions, including pain processing and affective learning. Experimental sleep restriction has been shown to impair emotional regulation and stress reactivity. However, little is known about whether sleep loss can potentially impair the ability to induce placebo effects. The placebo effect is a psychobiological phenomenon that produces clinical benefits attributed to a wide range of neurobiological mechanisms. The relationship between sleep and placebo effects, especially placebo effects in pain, has received very little attention. This study aims to investigate if acute late sleep restriction affects the formation of observationally induced placebo effect.

Materials and methods: 20 healthy volunteers were randomly assigned to either a sleep restriction group or a control group with habitual sleep. The experimental setup took place in a controlled laboratory environment, where participants were required to sleep. Participants in the sleep restriction group had their natural night sleep shortened by 60% due to early wake-up, while those in the control group maintained their standard sleep duration. All participants underwent an overnight PSG recording. During the 7 days preceding the study, participants' sleep-wake cycle was monitored using wrist actigraphy combined with a sleep log. The start time of the study and the required sleep duration in both sleep restriction group and control group were determined individually and adjusted to each participant's circadian rhythm, based on the sleep log and actigraphy recordings.

In the morning participants from both groups underwent placebo hypoalgesia induction via observational learning. Participants were presented with a video depicting a model experiencing pain stimuli and rating them as less intense when applied with the placebo. The sham TENS device attached to the forearm was used as a placebo. Thermal pain stimuli of medium intensity were delivered to the participants' forearm before and after the observational learning phase to test learning effects. Pain intensity was rated on an 11-point Numeric Rating Scale (NRS), ranging from 'no pain' to 'the most intense pain tolerable', and recorded after each stimulus.

Results: Data collection is ongoing, the results will be presented on the poster.

These findings come from a pilot study conducted with 20 healthy participants. The results indicate that observational learning successfully induced placebo hypoalgesia in both sleep conditions. Participants in the sleep restriction group reported significantly lower pain during placebo trials ($M = 3.97$, $SD = 1.37$) compared to control trials ($M = 4.90$, $SD = 1.43$), $p < .001$. A similar effect was observed in the habitual sleep group (placebo: $M = 3.42$, $SD = 1.05$; control: $M = 4.14$, $SD = 1.13$), $p < .001$. No significant between-group differences were found, $t(18) = 1.27$, $p = .22$.

Conclusions:

Observational learning is effective in inducing placebo hypoalgesia. However, we found no evidence that acute late sleep restriction affects the placebo hypoalgesia. As a pilot study, these findings are preliminary and will be continued in a larger sample. Importantly, this is the first study to investigate the role of sleep restriction in the formation of placebo hypoalgesia through observational learning.

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Effect of sleep irregularity on driving simulator performance during extended wakefulness

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Introduction: Insufficient and irregular sleep are now well-established risk factors for adverse health outcomes. While the impact of insufficient sleep on driving performance is known to be substantial, the degree to which irregular sleep, independent of sleep duration, affects driving performance is far less understood. We examined whether habitual sleep irregularity in the lead up to acute sleep loss influences subsequent driving simulator performance during extended wakefulness.

Materials and methods: Thirty-eight healthy sleepers (23 females and 15 males, aged 31.0 ± 11.6 y) completed two weeks of sleep/wake monitoring (GENEActiv activity monitors) prior to undergoing 29 h laboratory extended wakefulness study. Five 60-minute driving simulator (AusEd) tests were completed: 1, 7, 13 h of wakefulness determined baseline rested performance, while 19 and 25 h determined performance while sleep deprived. Sleep irregularity prior to the laboratory was calculated using the standard deviation (SD) of sleep midpoint time and total sleep time, used to split participants into irregular ($n=11$) or regular ($n=27$) sleeper groups using two-step cluster analysis. Linear mixed

model analysis was used to test the effects of time awake (rested vs sleep deprived) and sleep irregularity (regular vs irregular) on driving simulator steering deviation. Binary logistic regression was used to examine the association between continuous sleep irregularity measures and incidence of driving crashes.

Results: Steering deviation significantly deteriorated throughout extended wakefulness (Mean $\pm$ SD, rested vs sleep deprived, 45.1 $\pm$ 27.9 vs 69.1 $\pm$ 37.5 cm, $F(1, 30.45) = 17.03$, $p < .001$), but there was no interaction ($F(1, 30.5) = 0.19$, $p = .665$) or main effect of sleep irregularity group ($F(1, 35.5) = 0.02$, $p = .901$). Binary logistic regressions revealed that when rested (i.e., 1, 7, and 13 hours after waking), neither irregularity in total sleep time (OR=1.85 [95% CI:0.67, 9.34], $p = .458$) nor irregularity in sleep midpoint timing (OR=0.59 [95% CI:0.14, 2.47], $p = .467$) were associated with crash incidence. However, when sleep deprived (i.e., 19 and 25 hours after waking), irregularity in total sleep time (OR=9.97 [95% CI:1.20, 85.67], $p = .033$) but not irregularity in sleep midpoint timing (OR=0.42 [95% CI:0.07, 2.40], $p = .325$) was associated with crashing events on the driving simulator.

Conclusions: These findings suggest that although sleep irregularity does not impact steering stability. Driving simulator crash events are indicative of alertness and performance failure, and hence our findings suggest that irregular sleep duration may predispose drivers to adverse effects of sleep loss by increasing the risk of a crash. Further studies are warranted to determine the relative impacts of habitual sleep irregularity, independent of sleep duration, to better understand impacts on road safety.

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Effects of chronic intermittent hypoxia during sleep on intraoral pain via hypoxia inducible factor-1 α in ovariectomized rats

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Introduction: Burning mouth syndrome (BMS) is a chronic pain condition characterized by a burning sensation or discomfort in oral mucosa without any visible lesions. In BMS, capsaicin, an agonist of transient receptor potential cation channel subfamily V member 1 (TRPV1), can exacerbate pain in the tongue and the oral mucosa. The etiology of BMS is thought to involve a complex interplay of multiple factors. The risk of developing BMS increases after menopause, a trend also observed in obstructive sleep apnea (OSA). Moreover, OSA has been reported as a potential risk factor for BMS. Therefore, we propose that there is a link between OSA and the development of BMS, with OSA-induced hypoxia serving as a contributing factor. Hypoxia-inducible factors (HIFs) serve as a sensor of hypoxia; under hypoxic conditions, HIF-1 α accumulates and is translocated to the nucleus, where it functions as a transcription factor that regulates genes related to the cellular responses to hypoxia. The HIF pathway has been implicated in various physiological and pathophysiological processes. Based on these, we hypothesized that hypoxia by OSA contributes to the accumulation of HIF, which then promotes TRPV1 expression in the trigeminal ganglion (TG), then enhancing the sensitivity to capsaicin and contributing to the development of BMS.

Materials and methods: Ovariectomized (OVX) rats were exposed to chronic intermittent hypoxia (CIH) (nadir O₂ 5%, 6-min cycles, 6 h/day, 14 days). Intraoral pain was assessed using a two-bottle preference drinking test with a capsaicin solution. Immunohistochemical staining was used to assess changes in the proportion of TRPV1-positive and HIF-1 α -positive cells in the ophthalmic, maxillary, and mandibular nerve branches of the TG. Additionally, a HIF-1 α inhibitor was administered to the TG to determine the effects on capsaicin sensitivity and the proportion of TRPV1-positive and HIF-1 α -positive cells.

Results: Capsaicin consumption was significantly lower in the OVX-CIH group than that in the control group. OVX-CIH rats showed a significantly higher number of TRPV1-positive, HIF-1 α -positive, and TRPV1+HIF-1 α co-positive cells in all branches of the TG. Furthermore, the administration of an HIF-1 α inhibitor to the TG of OVX-CIH rats alleviated intraoral sensitivity to capsaicin. The increase in the number of TRPV1-positive cells in the OVX-CIH group was suppressed by the HIF-1 α inhibitor administration.

Conclusions: These findings suggest that the CIH-induced stabilization of HIF-1 α in the trigeminal ganglion contributes to BMS-like intraoral pain by upregulating TRPV1.

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Effects of Chronobiologically Effective Lighting on Attention, Mood and Daytime Sleepiness

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Introduction: Light plays a crucial role in regulating the circadian rhythm, influencing sleep-wake cycles and various physiological processes. Research suggests that melanopically equivalent daylight illuminance (MEDI) levels exceeding 250 lx may enhance daytime functions, including mood, alertness, and reduce sleepiness. This study investigates the effects of different daytime lighting scenarios, applied under standardized conditions, on mood, alertness, and sleepiness.

Materials and methods: A randomized crossover design was employed with two 1-day sessions per participant, separated by a 1-week interval.

Data collection was conducted from June to November 2024. 20 healthy subjects (18–35 years) participated in the study and were exposed to two lighting Scenarios (under controlled laboratory conditions): Scenario 1: Reference Lighting (RL) = E: 123 lux | MEDI: 58 lx | T_c: 2816 K; Scenario 2: Chronobiologically Effective Lighting (CEL) = E: 739 lux | MEDI: 594 lx | T_c: 5422 K

Participants completed a neurocognitive test battery before and after 1 hour of light exposure. The tests included:

- Karolinska Sleepiness Scale (KSS)
- Profile of Mood States (ASTS)
- d2-R Attention and Concentration Test

Results: Prospective statistical analysis will test the following hypothesis:

Higher alertness and lower sleepiness under the CEL condition compared to the RL condition. Mixed linear regression analysis considering: (1) sequence of light scenarios and (2) time of day (morning, midday, afternoon)

Descriptive statistical analysis revealed the following: N = 20, mean age: 24 $\pm$ 3 year, ESS: 7 $\pm$ 2, ISI: 4 $\pm$ 2, PSQI: 4 $\pm$ 1, Chronotype (MCTQ): Mild late chronotype (MSF)

Conclusions: This study contributes to the development of individually adaptive lighting scenarios designed to support daily life, particularly in professional and social contexts. These scenarios aim to improve attention, enhance mood, and reduce sleepiness, offering potential benefits for managing challenges such as jet lag.

The research is part of a collaborative project to establish an Internet of Things (IoT) standard for individualized, adaptive, and chronobiologically effective lighting solutions, applicable in both mobility and everyday situations. For more information, visit www.chronolite.de.

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Effects of Combined Chronic Intermittent Hypoxia and Hypercapnia Exposure on Blood Pressure, Systemic Inflammation, and Oxidative Stress Levels in Rats

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Introduction: Chronic Intermittent Hypoxia (CIH), the most characteristic pathophysiological feature of obstructive sleep apnea (OSA), has been extensively documented in animal studies to induce multiple

OSA-associated adverse outcomes. Intermittent hypercapnia, another hallmark pathophysiological trait of OSA, however, has rarely been incorporated into OSA animal modeling paradigms. The purpose of this study is to investigate the effects of combined chronic intermittent hypoxia with hypercapnia (CIHHC) exposure on blood pressure, systemic inflammation, and oxidative stress (OS) levels in Sprague-Dawley (SD) rats, compared to chronic intermittent hypoxia (CIH) alone and chronic intermittent hypercapnia (CIHC) alone.

Materials and methods: Forty 6-week-old male SD rats were randomly divided into four groups (n=10 per group) and exposed for 8 hours daily to specific oxygen (O₂) or carbon dioxide (CO₂) partial pressure conditions: (1) Control group (O₂: 21%, CO₂: 0.3%); (2) CIH group (O₂ cycled every 60 seconds between 5% and 21%, CO₂: 0.3%); (3) CIHC group (O₂: 21%, CO₂ cycled every 60 seconds between 0.3% and 5%); and (4) CIHHC group (O₂ cycled between 5% and 21%, CO₂ cycled between 0.3% and 5% every 60 seconds). Tail artery systolic blood pressure (SBP) was measured pre- and post-30-day exposure. Post-exposure peripheral serum samples were collected to quantify levels of inflammatory biomarkers [tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6)] and OS markers [superoxide dismutase (SOD), malondialdehyde (MDA)].

Results: No significant differences in pre-exposure SBP (pre-SBP) were observed among the four groups. While post-exposure SBP (post-SBP) differed significantly ($P=0.002$), with the order CIH > CIHC > CIHHC > Control. Post-SBP increased significantly in all experimental groups but not the control group compared to their respective pre-SBP (all $p<0.05$). Post-exposure serum levels of TNF- α , IL-6, SOD, and MDA also differed significantly among groups (all $P<0.05$). TNF- α , IL-6, and MDA levels followed the order CIH > CIHC > CIHHC > Control, while SOD levels ranked Control > CIHHC > CIHC > CIH.

Conclusions: Both CIH and CIHC exposure significantly elevated blood pressure, systemic inflammation, and OS levels in rats. However, combined CIHHC exposure induced significantly milder effects compared to CIH or CIHC alone, suggesting that intermittent hypercapnia concurrent with CIH may exert a protective or ameliorative influence on these pathological processes.

Effects of Sleep Deprivation on Cognitive Performance and Neurovascular Coupling: A Functional Transcranial Doppler Study

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Introduction: Sleep deprivation (SD) disrupts neural homeostasis and compromises cognitive abilities, particularly attention and verbal fluency. Neurovascular coupling (NVC), the mechanism that ensures cerebral blood flow (CBF) matches neural metabolic demands, is crucial for sustaining cognitive functions. This study aimed to explore how 32 hours of total sleep deprivation affects cognitive performance across various task difficulties and the corresponding changes in cerebral blood velocity (CBv).

Materials and methods: Fourteen healthy participants, aged between 26 and 47 years, underwent functional transcranial Doppler (fTCD) assessments, during which bilateral cerebral blood velocity (CBv) in the middle cerebral arteries was continuously recorded. Measurements were obtained both during resting conditions and while performing two categories of cognitive tasks: Thai word-naming (NW), divided into easy (k/ sound), moderate (ph/ sound), and hard (f/ sound) levels, and serial subtraction (SS) tasks involving sequences such as 100–2, 100–7, and 1000–17. Each cognitive task was administered for 60 seconds, with CBv signals normalized against a 60-second resting baseline recorded before task initiation. According to data distribution, pre- and post-task comparisons were analyzed using either paired t-tests or Wilcoxon signed-rank tests. Furthermore, a two-way ANOVA was employed to examine interactions between task complexity and time segments under normal and sleep-deprived conditions, with multiple comparisons adjusted using Tukey's post hoc procedure.

Results: Resting CBv, mean arterial pressure, and heart rate showed no significant differences between the pre- and post-SD conditions ($p > 0.05$). At the start of all cognitive tasks, a significant bilateral increase in CBv was observed ($p < 0.001$). Post-SD, the CBv responses in the left hemisphere were

significantly influenced by the complexity levels of the NW tasks (interaction $p = 0.038$), with a notable increase particularly observed during the T3 phase ($p < 0.05$). Pre-SD, a clear dominance of the left hemisphere was evident during NW tasks; however, this lateralization effect diminished during SS tasks post-SD ($p > 0.05$). Additionally, no significant differences were found in CBv responses across the complexities of the SS tasks, pre- and post-SD ($p > 0.078$).

Conclusions: Thirty-two hours of SD selectively impaired NVC responses during verbal fluency tasks. This was indicated by noticeable increases in CBv in the left hemisphere, depending on the task complexity. These findings suggest that the brain employs compensatory hemodynamic strategies to maintain verbal fluency performance despite SD. However, attention-related tasks, such as SS, appeared less affected by the NVC disruptions caused by SD. Functional TCD provides a valuable, non-invasive method for detecting subtle changes in cerebral hemodynamics related to sleep loss, which has significant implications for monitoring cognitive health in clinical and research contexts.

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Efficacy and feasibility of light therapy glasses to mitigate fatigue in patients with multiple sclerosis: a randomised, placebo-controlled, crossover field study

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Introduction: Fatigue is a highly prevalent, clinically significant, persistent symptom in multiple sclerosis (MS), highlighting the need for effective countermeasures.

The objective of the present study was to evaluate the feasibility and short-term efficacy of light therapy in reducing MS-related fatigue.

Materials and methods: This single-blind, randomized, placebo-controlled crossover study included 20 patients with MS with high levels of fatigue (Fatigue Severity Scale [FSS] >36). Participants used active blue-enriched bright light (BL) glasses or placebo dim red light (DRL) glasses for 20 minutes daily after waking up. Each intervention lasted 1 week, separated by a 6-day washout period. Fatigue was the primary outcome (Visual Analogue Scale for Fatigue [VAS_F], immediately before and after each intervention, and at 13:00). Two additional fatigue measures (the FSS and the Daily Fatigue Impact Scale [DFIS]) and one quality of life measure (Multicultural Quality of Life Inventory [MQLI]) were rated four times per intervention week. Feasibility was evaluated using self-reported variables related to comfort, side effects, and sleep parameters.

Results: Both interventions significantly reduced fatigue ratings (VAS_F) immediately after the intervention and at 13:00 on the same day, with BL showing significantly more reduction compared to DRL (all $p < 0.05$). FSS scores significantly decreased on the sixth and seventh intervention days (follow-up) during both interventions (all $p < 0.05$), with BL inducing a clinically significant reduction on the sixth day. D-FIS and MQLI scores remained unchanged. Patients reported greater comfort and improved fitness, well-being, and reduced fatigue with BL (all $p < 0.05$). Both interventions showed low levels of side effects and no effects on subjective sleep parameters.

Conclusions: The findings of the present study provide initial evidence for blue-enriched bright light therapy administered via glasses as a feasible and immediately effective intervention for MS-related fatigue.

Acknowledgments: We are grateful to all patients who were interested in, willing to participate, and who did participate in our study.

Enhancing Pilot Performance and Alertness: A Survey of Fatigue Risk in Short-Haul Flight Operations

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Introduction: Fatigue within aviation presents a serious risk to pilot performance, safety, and wellbeing. While most research focuses on long-haul or ultra-long haul flying, critical gaps remain in understanding fatigue in short-haul contexts. Short-haul pilots face unique stressors including consecutive early starts, short turnarounds between multiple flights, and minimal rest periods between flying duties. Of particular focus are back of clock (BOC) operations, defined as flying for at least 2 hours between 01:00-04:59, which disrupt sleep and circadian rhythms. Controlled rest (brief, in-cockpit sleep) is a proposed fatigue countermeasure used by Qantas. The effectiveness of controlled rest, however, is limited by stigma, regulatory inconsistencies, and sleep inertia. This survey addresses the literature gap by exploring the fatigue experiences of Qantas B737 short-haul pilots, with a focus on BOC operations, use of controlled rest, and operational workload. The research aims to inform fatigue risk management strategies to enhance in-flight alertness, particularly considering the evolving aircraft fleets and flight schedules.

Materials and methods: A total of 124 Qantas B737 pilots (14.19% of all B737 Qantas pilots; 71 Captains, 53 First Officers), aged 26-69 years (median=45 years) completed an online survey via Survey Monkey. The survey took approximately 30 minutes to complete and included a total of 55 questions with both multiple-choice and open-ended questions on general operations, BOC duties, controlled rest, and workload. A thematic analysis was conducted on qualitative responses using Delve. Transcripts were first read for familiarity, then systematically coded. Codes were then organised into broader themes through iterative refinement and were supported by participant quotes to ensure accurate representation.

Results: Thematic analysis revealed several key contributors to fatigue in short-haul operations. The sleep opportunity is variable and mainly impacted by rostering and suboptimal sleep environments. Scheduling design, including the swapping between early to late starts and late to early starts, extended duties, and limited recovery is a source of fatigue. Circadian disruption persists during BOC operations, with pilots frequently reporting misaligned sleep with their circadian timing. In-flight rest is also hindered by cockpit discomfort, operational requirements, and cabin noise and distractions. Lifestyle factors, including exercise and personal routines, influenced fatigue resilience but are often compromised by work demands. Fatigue management strategies include caffeine use, strategic napping, and controlled rest. Uptake, however, was hindered by operational constraints and perceived stigma.

Conclusions: This study provides novel insights into the fatigue challenges specific to short-haul pilots, particularly during BOC operations. Key fatigue drivers included insufficient rest opportunities, underutilisation of controlled rest, and high workload. The findings support several actionable recommendations, including optimised rostering, improved controlled rest protocols, enhanced cockpit conditions, and enhanced fatigue education. These strategies aim to improve pilot alertness, reduce fatigue-related risk, and support safer, more sustainable short-haul operations.

Esketamine and Dexmedetomidine Co-Administration: A Novel Approach to Alleviating Depression and Insomnia in chronic restraint stress Mouse Models

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Introduction: Depression is often accompanied by insomnia, and conventional antidepressants have limited efficacy in addressing sleep disorder. This study investigates the therapeutic potential of combining esketamine and dexmedetomidine in a chronic restraint stress (CRS) mouse model of depression.

Materials and methods: We confirmed depression-like symptoms with behavioral tests and used functional magnetic resonance imaging (fMRI) to assess changes in brain activity, transmission electron microscopy to observe the ultrastructure of the brain, and combined with molecular biology to detect protein changes in the CA1 region of the hippocampus.

Results: The results showed that the functional connections of amygdala, hippocampus and lateral habenular nucleus were significantly changed after combination therapy, and demyelination changes

were reduced compared with the model group. In addition, combination therapy significantly upregulated the levels of brain-derived neurotrophic factor and its receptor TrkB in hippocampus. **Conclusions:** These findings suggest that the combination of esketamine and dexmedetomidine can alleviate depressive symptoms, improve brain functional connectivity, and repair ultrastructural damage, providing valuable insights into treatment strategies for sleep disorders associated with mood disorders.

Exercise improves sleep deprivation-induced cognitive impairment by upregulating brain-derived neurotrophic factor and restoring hippocampal synaptic plasticity

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Introduction: Sleep deprivation (SD) impairs hippocampal synaptic plasticity, reducing brain-derived neurotrophic factor (BDNF) and affecting cognitive and motor functions vital for neurorehabilitation. Exercise mitigates these deficits remains unclear. This study evaluates whether exercise alleviates SD-induced behavioral and synaptic deficits in rats.

Materials and methods: Eighteen male Wistar rats were divided into normal control (NC, n=6), sleep deprivation (SD, n=6), or SD with exercise (SD+Ex, n=6) groups. NC rats were housed under standard conditions, while SD and SD+Ex groups underwent 31-day SD using the multiple platform method. SD+Ex rats received an 5-day treadmill exercise intervention during SD. Behavioral, structural, and molecular outcomes in the hippocampus were assessed using the Morris Water Maze (MWM), Open Field Test (OFT), ELISA, Golgi staining, and Western blot.

Results: SD induced cognitive and motor deficits, with prolonged MWM escape latency ($P<0.05$), reduced reversal learning and locomotor activity ($P<0.05$), and decreased BDNF ($P<0.0001$), dendritic spine density ($P<0.05$), and synaptic function markers Synapsin ($P<0.05$) versus NC. Exercise restored hippocampal dendritic spine density ($P<0.05$) versus SD, significantly upregulated BDNF ($P<0.05$), increased LTP-related molecules NMDAR ($P<0.0001$) and CaMKIV ($P<0.05$), elevated synaptic function markers PSD-95, tyrosine hydroxylase ($P<0.05$), and enhanced reversal learning ($P<0.05$) and locomotor activity ($P<0.01$) versus SD.

Conclusions: Exercise mitigates SD-induced cognitive and synaptic deficits by enhancing BDNF-mediated synaptic plasticity and dendritic spine restoration, providing a potential non-pharmacological neurorehabilitation strategy for individuals with sleep disorders.

EXPERT SYSTEM FOR SLEEPINESS MONITORING

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Introduction: The purpose of the monitoring system is to determine the level of human sleepiness without interfering with the performance of actions, give recommendations for further action so that prevent falling asleep. The secondary objectives of the study are to orientate in the development of sleepiness, optimize the set of measured parameters, develop expert decision rules in a situation where most parameters are absent numerical value, but are verbal assessments given by experts.

Materials and methods: To achieve the goals, the monitoring system (MS) is designed as an expert a system that works with decision trees, production laws.

For understanding the development (pathogenesis) of sleepiness and the parameters to be measured

the topological method of functioning systems is used to select an optimized set modeling (TM). Subjective information is an input evaluated by expert ratings on point scales without a numerical equivalent. Decision making applies fuzzy logic and linguistic variable theory. Anticipatory alarm is realized by EEG signals.

Results: The MS “Non-intrusive human fatigue assessment” of sleepiness has been developed. The MS consists of 3 blocks: sleepiness determination, recommendations, anticipatory alarm. Blocks evaluate the objective and subjective information using the fuzzy set and the linguistic variable theory. Anticipatory alarm block that prevents a person from falling asleep, receives an EEG signal from 1 electrode in the forehead area. A single electrode EEG lead provides monitoring application of the system in practice. Realized MS interface system for the user (operator or driver) in the form of a mobile Application, where the user is supposed to enter questionnaire data, interactively perform fatigue detection test activities and visualize fatigue assessment, recommendations and alarm warnings. On the other hand, the implemented Expert system visualization interface is intended for direct interaction with each of the modules of the ES complex.

Conclusions: The application of topological modeling is justified by choosing a set of parameters optimized for sleepiness by their informativeness and detection options. Theory of expert systems with decision trees and product laws allow the level of sleepiness to be determined. Linguistic variables theory allows the evaluation of subjective information that does not contain numeric assessments. Adaptation of the system to the field of use is discussed by creating specific recommendations for car drivers and for the work of operators. Recommendations for reducing mental fatigue and alarming state assessments during monitoring and for a pre-flight survey tailored to operators or performing risky work are separately provided. On the other hand, monitoring for the detection of drowsiness has been implemented for the use of drivers, which is based on the data of wearable sensors with the possibility of providing a preventive alarm signal.

Exploration of Physiological Markers Sensitive to Sleep Restriction during the Maintenance of Wakefulness Test

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Introduction: Sleepiness resulting from sleep deprivation or sleep disorders is known to impair neurobehavioral performance, increasing the risk of traffic and occupational accidents. Objective assessments of sleepiness, such as the Maintenance of Wakefulness Test (MWT), are essential for identifying individuals with excessive daytime sleepiness. However, current assessment methods are limited by the need for specialized facilities, extended testing durations, and high cost. Therefore, there is a pressing need to develop more accessible and efficient approaches to assess sleepiness.

Objective:

This study aimed to identify electroencephalogram (EEG) and ocular markers that are sensitive to sleep restriction during the MWT, with the goal of contributing to the development of simpler and more practical sleepiness detection methods.

Materials and methods: This study was approved by the Ethics Committee of the Faculty of Medicine, University of Tsukuba (No. 2053). Healthy adults (target N = 20) participated in two sleep conditions: 8-hour (normal) or 4-hour (restricted) sleep, following an adaptation night. On the test day, participants completed four MWT sessions at 2-hour intervals. High-density EEG and ocular data were collected during each session. EEG analyses included microsleep frequency, microsleep latency, and Hori's EEG stages (Hori et al., 1994). Ocular indicators included the PERcent time of slow eyelid CLOSures (PERCLOS) and estimated response speed in the Psychomotor Vigilance Test (PVT), inferred from eyelid opening degree (Noguchi et al., 2024). Data from 19 participants (11 females; mean age = 25.4 ± 4.5 years; 136 trials) were analyzed. Hori's EEG stage data analyses were available for 15 participants (9 females; mean age = 25.5 ± 4.8 years; 120 trials).

Results: MWT sleep latency was significantly reduced following sleep restriction ($p = 0.002$, $d = 0.85$), and microsleep frequency significantly increased ($p = 0.003$, $d = 1.03$). Percentages of Hori's EEG stages 2 and 3 were significantly higher after sleep deprivation ($p = 0.004$ and 0.0006 ; $d = 1.13$ and 1.09 ,

respectively). Estimated PVT response speed also significantly declined following sleep restriction ($p = 0.02$, $d = 0.85$), whereas PERCLOS showed no significant change ($p = 0.48$).

Conclusions: Multiple physiological markers were sensitive to sleep restriction during the MWT. Among these, percentages of Hori's EEG stages 2 and 3 emerged as the most sensitive markers. A device that detects Hori's EEG stages holds promise for more practical and accessible methods for sleepiness detection in real-world settings.

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Glucose homeostasis during recurrent periods of sleep restriction and recovery in healthy young adults

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Introduction: Short sleep has been shown to impair glucose metabolism as indicated by increased plasma glucose concentrations and reduced insulin sensitivity; however, most existing studies do not consider that sleep curtailment typically occurs on weekdays, and have not examined how glucose homeostasis is altered during multiple weeks of sleep curtailment with intervening weekend recovery sleep. Furthermore, recovery sleep does not only take place on weekends, but can also occur on weekdays, thereby increasing intraindividual variability in weekday sleep duration. Therefore, this study aimed to investigate glucose homeostasis during recurrent periods of sleep restriction on weekdays and recovery on weekends – a typical sleep pattern among adults in many countries, and whether among sleep restricted individuals, glucose homeostasis would depend on the variability in sleep duration across weeknights.

Materials and methods: In this 15-night lab-based study, 48 healthy young adults (age: 21-28y; 24 males) underwent two baseline nights of 8-h time-in-bed (TIB), followed by two cycles of "weekday" sleep opportunity manipulation (control group's TIB: 8-h/night; stable short sleep group: 6-h/night; variable short sleep group: 8-, 4-, 8-, 4-, and 6-h from the first to the fifth night) and "weekend" recovery (all groups: 8 h). OGTTs were performed at the end of baseline and each manipulation period. Plasma glucose and insulin concentrations during fasting (0 min) and OGTT (15, 30, 60 and 120 min after 75g glucose solution consumption) were measured.

Results: At 2-h post-glucose load, the control group's glucose levels remained stable across the three OGTTs (mean $\pm$ SEM: between 5.28 ± 0.32 and 5.93 ± 0.32 mmol/L, $p > .08$), although their insulin levels increased from baseline (from 48.40 ± 13.61 to 81.19 ± 13.61 mIU/L, $p = .02$ and 93.92 ± 13.61 mIU/L, $p = .003$) probably due to the sedentary lifestyle in the laboratory. The stable short sleep group also showed increased insulin levels in the first week (from 69.06 ± 12.98 to 102.07 ± 12.42 mIU/L, $p = .02$), but their glucose levels still increased from baseline (from 5.68 ± 0.31 to 6.58 ± 0.29 mIU/L, $p = .02$). Importantly, in both weeks of sleep restriction, the variable short sleep group failed to elevate their insulin levels (between 64.09 ± 13.61 and 77.45 ± 13.61 mmol/L, $p > .30$); hence, their glucose was above baseline (baseline: 5.12 ± 0.32 ; week 1: 6.20 ± 0.34 mIU/L, $p = .01$; week 2: 6.49 ± 0.32 mmol/L, $p = .0005$).

Conclusions: Glucose homeostasis in healthy young adults is hampered during multiple nights of sleep restriction on weekdays despite weekend catch-up sleep, which may increase the risk of type 2 diabetes. Stable and variable short sleep schedules may cause such impairment through insulin resistance and impeding pancreatic beta-cell functions respectively.

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Hippocampal Activity Associated with Central Sleep Apnea Episodes

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Introduction: Breathing is primarily controlled by brainstem respiratory centers, but higher-order brain structures such as the amygdala, hypothalamus, and hippocampus also contribute to its regulation. These suprapontine areas can influence autonomic breathing during both wakefulness and sleep. Central sleep apnea (CA) is a temporary cessation of breathing during sleep due to a lack of central respiratory drive. CA can occur in healthy people and animals, as well as in association with neurological and cardiopulmonary disorders. Recent studies suggested a bidirectional relationship between hippocampal dysfunction and sleep-disordered breathing. We hypothesized that hippocampal activity may contribute to the initiation or modulation of CA episodes. In this case, hippocampal activity was expected to change not just during CA, but also before the onset of CA.

Materials and methods: Chronic electrophysiological recordings were performed in two adult cats across multiple natural sleep-wake cycles. We recorded single-neuron activity and local field potentials (LFPs) of the dorsal hippocampus along with EEG, ECG, eye movements, nasal airflow, and thoracic muscle activity, and identified naturally occurring CA episodes (duration > 3 sec). Neuronal spike rates (single- and multi-unit activities) were analyzed for the intervals before, during, and after apnea episodes, using sleep-stage-matched control periods for statistical comparisons (Wilcoxon rank-sum test). LFP segments for the analysis were selected based on EEG-defined sleep stability. Baseline neuronal activity was compared to the "pre-apnea" period, defined as the stable or transitional sleep phase preceding apnea onset based on EEG delta amplitude, and the "post-apnea" period, spanning from the last breath to the first recovery breath. These segments captured consistent physiological states for comparison with apnea-related changes.

Results: We recorded 71 CA episodes across all sleep stages. The majority occurred during transitions between sleep stages: 30 during slow wave sleep (SWS) to rapid eye movement (REM) transitions, 24 from REM to SWS, 12 within REM sleep, and 5 within stable SWS. Of the 238 recorded neurons, 88 (38%) exhibited significant ($p < 0.05$) changes in their firing rates related to CA episodes. Among them, 45% changed activity both before and after apnea, 22% only before, and 31% only after it. Most neurons showed increased activity prior to apnea onset and reduced activity following it. Multi-unit activity changed significantly in 19 of 27 recordings both before and after apnea. LFP analysis revealed consistent spectral changes as well. Before and during apnea, beta and gamma power increased, suggesting heightened local network excitability or arousal. Hippocampal delta power decreased both before and during apnea, while global EEG changed only after CA. Notably, theta power increased during apnea in both hippocampal LFPs and global EEG. Since hippocampal theta is associated with REM sleep, this may reflect a functional shift in brain state during respiratory arrest.

Conclusions: Our findings demonstrate that hippocampal activity reliably changes in association with CA episodes. Changes preceding CA suggest that the hippocampus may play a role in initiating or modulating these events, rather than merely responding to them. This supports our hypothesis and highlights the role of the hippocampus as a potential upstream modulator of brainstem respiratory centers.

Impact of Acute Sleep Restriction on the Resting Ventilatory Response to Normobaric Hypoxia and Its Relationship with Blood Cytokine Levels in Healthy Men

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Introduction: Exposure to the combined stressors of hypoxia and sleep restriction can occur in various contexts, such as during operational missions, trekking expeditions, and similar situations. This combination of stressors is also observed in obstructive sleep apnea. While the effects of hypoxia on

sleep have been previously investigated, the impact of sleep restriction on physiological responses to hypoxia remains unknown. This study aimed to evaluate the effects of acute sleep restriction on (i) the resting ventilatory response to normobaric hypoxia, (ii) plasma levels of pro- and anti-inflammatory cytokines, and (iii) their potential relationship. Interindividual differences related to genetics were assessed on the cardiac response.

Materials and methods: Seventeen healthy men were exposed to 5 hours of normobaric hypoxia ($F_{iO_2}=13.6\%$, $\sim 3,500$ m) in a crossover design, following either habitual sleep (HS HY, Total sleep time (TST) > 6 hours) or restricted sleep (SR HY, TST < 3 hours). Ventilatory parameters were measured after 1.5 hours (Quark CPET, Cosmed® device), and blood cytokine levels (TNF- α and IL-10) were assessed at 1.5 (BS +1h30) and 5 hours (BS +5h00) (Simoa® CorPlex™ Cytokine Panel-1 5-Plex Kit, ref.85-0353, Quanterix). Genotyping for the rs228697_PER3 C>G polymorphism was performed on blood cells using the LAMP-MC method

Results: Sleep restriction led to increased tidal volume (0.68 ± 0.36 vs. 0.63 ± 0.36 L, $p < 0.05$) and ventilatory equivalent for CO₂ (36.30 ± 5.93 vs. 34.40 ± 4.33 , $p < 0.05$). TNF- α concentrations were elevated following sleep restriction (0.98 ± 0.38 vs. 0.86 ± 0.41 pg·mL⁻¹ at BS+1h30; 1.00 ± 0.45 vs. 0.79 ± 0.35 pg·mL⁻¹ at BS+5h00; $p < 0.001$). IL-10 levels were significantly higher after 5 hours of hypoxia after sleep restriction (0.94 ± 0.65 vs. 0.83 ± 0.61 pg·mL⁻¹, $p < 0.05$), and exceeded those measured under habitual sleep (0.94 ± 0.65 vs. 0.78 ± 0.73 pg·mL⁻¹, $p < 0.05$). IL-10 concentrations positively correlated with ventilatory responses, regardless of sleep condition or exposure duration. Carriers of the C/G mutated genotype of the rs228697_PER3 polymorphism showed higher heart rates under hypoxia, independent of sleep condition.

Conclusions: This is the first study to isolate the impact of sleep restriction on ventilatory and cytokine responses to normobaric hypoxia. It highlights IL-10's potential role in hypoxic ventilatory regulation and suggests that sleep duration influences the ventilatory response. Given these sleep-related differences, future hypoxia studies should, at minimum, quantify sleep duration to enable proper control and comparison of physiological outcomes and cytokines responses.

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Investigating the Effects of Sedative-Hypnotic Drugs on Sleep and Autonomic Nervous System Function in Wild-type and Alzheimer's Disease Transgenic Mice

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Introduction: Patients with Alzheimer's disease (AD) often experience insomnia, and clinical management frequently involves the use of sedative-hypnotic drugs to alleviate sleep disturbances. However, previous studies have indicated potential negative consequences of long-term sedative use in patients. This study aims to explore the effects of single dose and long-term administration of sedative-hypnotic drugs on sleep patterns and autonomic nervous system function in APP/PS1 transgenic mice, a model of AD, during the pre-symptomatic stage.

Materials and methods: In this experiment, both pre-symptomatic APP/PS1 mice (17-18 weeks old) and wild-type (WT) control mice were orally administered different doses of Lorazepam (1, 2, and 4 mg/kg) and Zolpidem (5, 7.5, and 10 mg/kg) for a single dose. After one week, the mice were further administered Lorazepam (2 mg/kg) and Zolpidem (7.5 mg/kg) daily, along with a vehicle control, for two weeks. Each group consisted of 9 mice, and physiological signals such as EEG, EMG, and ECG were recorded continuously for 24 hours each week.

Results: Prior to drug administration, assessment revealed that APP/PS1 mice, compared to WT mice, exhibited poorer performance in quiet sleep (QS) duration (similar to human Non-REM sleep), sleep disturbances, and heart rate variability (HRV) parameters, including RR interval (RR), total power (TP), high frequency (HF), and normalized low frequency (LF%). Single-dose administration of Lorazepam and Zolpidem increased QS duration while reducing paradoxical sleep (PS) duration in both APP/PS1 and WT mice. Long-term drug use for two weeks showed that neither Lorazepam nor Zolpidem had a sustained effect on QS duration, and Lorazepam reduced PS duration in WT mice, while Zolpidem

reduced both QS and PS durations in APP/PS1 mice, along with an increase in awake time. Lorazepam significantly decreased HRV parameters (TP, HF, and LF%) during PS in APP/PS1 mice after a single dose, whereas Zolpidem had a smaller impact on HRV. However, after two weeks of continuous use, Zolpidem exhibited significant effects, particularly on PS sleep in APP/PS1 mice, approaching the impact observed with Lorazepam. Regardless of single or long-term administration, HRV in WT mice was less affected.

Conclusions: A single dose of Lorazepam and Zolpidem increased QS sleep in both WT and APP/PS1 mice, but this effect disappeared after two weeks of continuous administration, showing a trend of worsening sleep quality. Lorazepam, whether administered acutely or chronically, affected HRV during sleep in APP/PS1 mice, while Zolpidem had a minor impact with acute use, becoming more pronounced after two weeks of continuous administration, especially during PS sleep in APP/PS1 mice.

Investigating the impact of night-duty on sleep architecture and mental well-being in the security personnel: A quasi-experimental study

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Introduction: In a world that never sleeps, the role of security personnel is vital in maintaining order, safety, and peace. While the responsibilities of security professionals are diverse and multifaceted, one aspect of their job that often remains hidden in the darkness is the relentless demand for night-duty shifts. This research delves into the often-overlooked consequences of night-duty shifts on security personnel. The study aims to investigate impact of night shifts on the physical health, psychological well-being of security professionals. By exploring the disruptions to sleep architecture, such as stages of sleep (N2), sleep efficiency, and the potential mental health implications like mental well-being, the research seeks to enhance understanding of the physiological changes in these dedicated professionals

Materials and methods: Using a novel quasi-experimental design approach, the study was conducted in AIIMS Bibinagar. Polysomnography (PSG) was used to monitor and analyze the sleep patterns of security personnel on night-duty shifts compared to off-duty periods. Additionally, mental well-being was assessed through validated mini state mental examination scores as psychological questionnaire

Results: PSG parameters like sleep time have significantly decreased, sleep efficiency along with duration of sleep stages of N2 has significantly decreased. There is a notable rise in systolic blood pressure which can be correlated to a decrease in the sleep's efficiency and total sleep time. These changes attributed to physiological changes due to sleep deprivation for the security personnel post night-duty shifts.

Conclusions: In conclusion, the reviewed literature and our current study clearly demonstrates the detrimental impact of night-duty on sleep architecture and mental well-being among security personnel. This study aims to provide the necessary evidence to develop and implement interventions that ultimately enhancing both personal and public safety.

Acknowledgments: Prof. Dr. Vikas Bhatia (Executive Director) for his constant support and guidance.

Investigating the impact of night-duty on sleep architecture and mental well-being in the security personnel: A quasi-experimental study

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Investigation of the Role and Mechanism of the Der p1-IL-21 Axis in Adenoid Germinal Center Responses

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Introduction: Adenoid hypertrophy is a key etiological factor in obstructive sleep apnea-hypopnea syndrome (OSAHS), often associated with excessive germinal center (GC) proliferation. House dust mite (HDM) colonization, particularly by the allergen Der p1, has been implicated in this pathology, but its mechanistic role remains poorly understood.

Materials and methods: To investigate this, we established an innovative adenoid organoid model and utilized IL-21^{-/-} mice to evaluate the effects of Der p1 on GC responses.

Results: Our findings demonstrate that Der p1 stimulation significantly increased IL-21⁺ T follicular helper (Tfh) cells, which in turn enhanced GC responses. Notably, IL-21^{-/-} mice showed markedly reduced GC formation in the spleen.

Conclusions: These results suggest that the Der p1-IL-21 axis plays a critical role in promoting GC proliferation in adenoid hypertrophy, offering new insights into the pathogenesis of OSAHS and potential therapeutic targets.

I-SLEEPS: A Simplified and Accurate Approach to Sleep Disorder Prediction with Body Composition Metrics

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Introduction: Accurately predicting the risk of sleep disorders such as insomnia, obstructive sleep apnea (OSA), and comorbid insomnia and sleep apnea (COMISA) typically requires a costly and time-consuming process involving multiple questionnaires and polysomnography tests. As a simpler alternative for sleep disorder prediction, the SLEEPS algorithm uses only nine questions, which includes the body mass index (BMI) as a key feature. However, BMI alone fails to capture differences in body composition, as individuals with identical BMI values can exhibit significant variations in muscle and fat distribution. We aim to develop a machine learning algorithm that can accurately predict the risk of insomnia, OSA, and COMISA using body composition metrics.

Materials and methods: We applied a tree-based machine learning algorithm to a dataset of 3291 patients. Demographic data, sleep-related questions, and body composition metrics were evaluated as potential features for the model. The final feature selection was based on feature importance calculated by Shapley additive explanations (SHAP) method. Using the selected features, we developed a new machine learning algorithm for predicting insomnia, OSA, and COMISA, named I-SLEEPS (InBody-based Simple questionnaire Predicting Sleep disorders). The accuracy of the algorithm was evaluated using the area under the receiver operating characteristics curve (AUROC).

Results: A total of 10 features were selected to construct I-SLEEPS, including skeletal muscle index (SMI) and fat-free mass index (FFMI) instead of BMI, along with the original SLEEPS questionnaire items. I-SLEEPS achieved superior predictive accuracy (AUROC > 0.93 for OSA, COMISA and insomnia) compared to SLEEPS (AUROC > 0.90). Additionally, our approach significantly enhanced AUPRC values, which is critical for addressing the imbalanced datasets of COMISA and insomnia. Furthermore, our analysis revealed distinct relationships between muscle mass indices (SMI and FFMI) and the risks of OSA, insomnia, and COMISA, providing new insights into the role of body composition in sleep disorders.

Conclusions: By leveraging the accessibility of InBody analysis, I-SLEEPS offers a practical, non-invasive alternative for diagnosing and managing sleep disorders, improving upon traditional screening methods such as polysomnography.

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KLF9 Regulates Sleep Architecture via B-Mediated Excitability of VTA Dopaminergic Neurons

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Introduction: Sleep is a fundamental physiological process essential for physical and mental recovery, representing a state of comprehensive brain rest. In mammals, sleep is tightly regulated by a complex network of deep brain nuclei. However, the genetic and molecular mechanisms underlying this intricate regulatory network remain largely unknown. Genome-wide association studies have identified a significant association between genetic polymorphisms in Krüppel-like factor 9 (KLF9) and alterations in sleep architecture in patients with obstructive sleep apnea. Nevertheless, whether KLF9 plays a functional role in sleep regulation and the nature of its downstream mechanisms remain unclear and warrant further investigation.

Materials and methods: To investigate the role of *Klf9* in sleep regulation, we employed a combination of genetic, neurophysiological, and multi-omics approaches. A *Klf9* knockout mouse model was generated using CRISPR/Cas9 technology, while whole-brain neuronal overexpression of *Klf9* was achieved through retro-orbital injection of AAV-hsyn-*Klf9*. Sleep parameters were assessed using EEG/EMG recordings to evaluate the impact of *Klf9* manipulation on sleep architecture. To trace the spatial expression of KLF9 protein in the brain, we constructed an in-frame *Klf9*-HA knock-in mouse model for in situ labeling. Region- and cell-type-specific overexpression or deletion of *Klf9* was further accomplished via stereotactic injection of AAV vectors combined with the Cre-loxP system, enabling precise dissection of its function in specific brain regions and neuronal populations. To uncover the transcriptional network downstream of *Klf9*, we integrated single-nucleus RNA sequencing (snRNA-seq) with CUT&Tag profiling. The regulatory relationships between *Klf9* and its target genes were subsequently validated through molecular biology, epigenetic, and electrophysiological analyses. Finally, rescue experiments were conducted in *Klf9*-deficient mice by restoring the expression of downstream gene, confirming the mechanistic role of the *Klf9* signaling in modulating sleep.

Results: *Klf9* knockout mice exhibited a significantly reduced total wake duration, increased frequency of microarousals, and shortened average wake episode length, indicative of a fragmented sleep phenotype. In contrast, overexpression of *Klf9* in whole-brain neurons led to opposing effects on sleep architecture, suggesting a regulatory role for *Klf9* in maintaining stable sleep-wake states. In situ protein tracing revealed that KLF9 is highly expressed in the subthalamic nucleus (STN), substantia nigra (SN), and ventral tegmental area (VTA). Region- and cell-type-specific genetic manipulation further demonstrated that KLF9 is essential for wake maintenance and sleep structure stability

specifically in dopaminergic neurons of the VTA. Integrated multi-omics analysis identified B as a direct downstream transcriptional target of KLF9. Loss of *Klf9* resulted in markedly altered B expression and decreased excitability of dopaminergic neurons. Notably, in situ restoration of B expression in *Klf9*-deficient mice effectively rescued the observed sleep abnormalities, confirming the functional relevance of the KLF9-B regulatory axis in sleep regulation.

Conclusions:

This study is the first to demonstrate the critical role of KLF9 in maintaining wakefulness and stabilizing sleep architecture.

Living with OSA & CPAP: Preliminary Report of a Multicenter Italian Study (Apulia Region)

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent chronic respiratory disorder, associated with significant cardiovascular and metabolic complications. Although CPAP represents the first-line treatment, suboptimal adherence and the persistence of daytime symptoms often limit its clinical effectiveness. This multicentre study involved all Sleep Centres in the Apulia Region and aimed to describe the clinical characteristics of patients with OSA, as well as their self-reported symptoms, adherence to CPAP therapy, and residual complaints despite treatment, in a real-world setting.

Materials and methods: A shared regional database was created, including 1,396 consecutive patients diagnosed with OSA, enrolled from all specialized centres in Apulia. Clinical, demographic, and polysomnographic data were collected. In addition, patients underwent a comprehensive assessment on subjective sleep quality and disturbances cognitive symptoms, depression, anxiety, and quality of life. Adherence to CPAP therapy was evaluated, with adequate adherence defined as a minimum of 4 hours of use per night on at least 70% of nights.

Results: Preliminary analysis of the data showed a mean age of 60.4 ± 12.6 years, with a male predominance. The mean BMI was 34.04 kg/m^2 , indicative of class I obesity. The mean apnea-hypopnea index (AHI) was 39.3 events/hour, and the mean oxygen desaturation index (ODI) was 38.6/h. The average ESS score was 9.5 ± 5.3 , suggesting moderate sleepiness. A good adherence to CPAP was observed in 72% of patients. However, approximately 44% reported persistent cognitive symptoms and attention difficulties despite treatment.

Conclusions: Preliminary findings from this multicenter study reveal that, despite generally good adherence to CPAP therapy, a substantial proportion of patients continue to report residual symptoms such as cognitive difficulties, sleep disturbances, and daytime fatigue. These results underscore the need for more personalized follow-up and targeted therapeutic strategies that go beyond respiratory parameters alone. Moreover, this study highlights the importance of regional cooperation among Sleep Centers in generating a comprehensive, real-world understanding of OSA management and patient-reported outcomes.

LncRNA NONMMUT009018 drives tumorigenesis and progression by modulating the miR-8100/Col1a2/Thbs1 axis under intermittent hypoxia

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Introduction: This study aims to investigate the mechanism by which LncRNA NONMMUT009018/miR-8100/Col1a2/Thbs1 in promoting tumor proliferation, invasion, metastasis mediated by obstructive sleep apnea hypopnea syndrome (OSAHS)-related intermittent hypoxia (IH). To provide a theoretical foundation and potential therapeutic targets for the clinical prevention and treatment of OSAHS-associated tumors.

Materials and methods: Affymetrix Clariom D microarray and bioinformatics analysis, RIP, and dual-luciferase reporter assays were used to confirm binding interactions within the ceRNA network. DMOG was used to stabilize HIF-1 α expression in tumor cells, and C57BL/6J mouse tumor-bearing models were subjected to IH mimicking OSAHS for 28 days in vivo. Lentiviral and mimic transfection techniques were applied to modulate LncRNA NONMMUT009018 and miR-8100 expression in LLC and B16F10 melanoma cells, influencing downstream target genes *Col1a2* and *Thbs1*. CCK-8, transwell chamber, scratch wound healing assays, in vivo imaging, tumor weight/volume measurements, HE staining, RT-qPCR, and western blot were conducted to explore the role of the LncRNA NONMMUT009018/miR-8100/*Col1a2*/*Thbs1* regulatory axis in tumor growth, invasion and metastasis.

Results: Compared to the normoxic group, IH significantly upregulated the expression of LncRNA NONMMUT009018, *Col1a2*, and *Thbs1* in tumor tissues ($P < 0.05$), while miR-8100 expression was markedly downregulated ($P < 0.01$). RIP, MS2/AGO2-RIP and dual-luciferase reporter assays demonstrated direct binding of HIF-1 α to LncRNA NONMMUT009018, LncRNA NONMMUT009018 to miR-8100, and miR-8100 to *Col1a2* and *Thbs1*. Knockdown of LncRNA NONMMUT009018 and overexpression of miR-8100 significantly reduced *Col1a2* and *Thbs1* mRNA expression by RT-qPCR ($P < 0.01$). CCK-8 assays, transwell invasion and migration assays, scratch wound healing experiment, and EMT-related marker proteins E-cadherin, N-cadherin and MMP9 revealed that knockdown of LncRNA NONMMUT009018 or overexpression of miR-8100 can significantly inhibit HIF-1 α -mediated proliferation, invasion and metastasis of LLC and B16F10 tumor cells. However, overexpressing LncRNA NONMMUT009018 or inhibiting miR-8100 restored proliferation, invasion, migration of tumor cells. Similar phenotypic characteristics were found in IH-mediated tumor tissues.

Conclusions: This study established the LncRNA NONMMUT009018/miR-8100/*Col1a2*/*Thbs1* ceRNA network driving IH-associated tumor progression. HIF-1 α activation upregulated LncRNA NONMMUT009018, which sponged miR-8100 to derepress *Col1a2*/*Thbs1*, promoting tumor proliferation, invasion, migration, and EMT. Targeting this axis may offer novel strategies for OSAHS-related cancer prevention and therapy.

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Massai sleep in high altitude, kenya

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Introduction: The massai tribe live in the south part of kenya and the north part of tanzania around the mt kilemanjaro. This tribe of 2 million people live as nomads on a strong social order. They eat and drink water, tea, milk, worm blood, and meat. Fruits only from forest small fields.

Materials and methods: we interviewed 62 persons in a manyata about the sleep duration, sleep disturbances in the village. the questionnaire was adapted on PSQI, We talked with 24 female and 38 male persons. All persons are wake up with sunrise and go to sleep at 8:30 pm. the teenagers dance often in moonshine much longer. the range was between 24-76 years. But no worrier was in the study. The massai are tall mean value 190 cm for men and 175 for female. The BMI of all members was under 24. We measured sleep with the Apple watch, O2 saturation, heart beat, Snoring, breathing/ min.

Results: We interviewed 62 persons, sleep disturbances are reported like crying animals, kids, cold temperature, but no snoring in this village. not one O2- desaturation during sleep.

Conclusions: To live in the massai tribe is combined with a sportive living. a massai walk every day 10-20 km a day. women are used for cooking, water fetching. man as cattleman and worriers. To be a massai in kenya protects you from breathing disorders in sleep.

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Maternal sleep disordered breathing impacts cortisol regulation in pregnancy

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Introduction: Maternal sleep disordered breathing (SDB) is arguably the most common respiratory condition in pregnancy, and is an independent risk factor for adverse perinatal outcomes. While epidemiologic data link the condition to various adverse outcomes in pregnancy, mechanistic data examining the association are scarce. Therefore, in this study we examined if de-novo maternal SDB impacts maternal cortisol secretion and fetal cortisol exposure via placental gene methylation in pregnant women at risk.

Materials and methods: Pregnant women at risk for SDB who screened negative for SDB by in-home sleep apnea testing in early pregnancy, were enrolled and had repeat sleep apnea testing in the third trimester of pregnancy. Women had wake, 30 minutes post wake, and bedtime salivary cortisol collected at the two time points in pregnancy. A subset of consecutive women who agreed to have placental tissue collected at the time of delivery had quantitative pyrosequencing performed to assess DNA methylation of 11 β -hydroxysteroid dehydrogenase-1 (11 β HSD-1) and 11 β HSD-2.

Results: Seventy-five women with average BMI 35 ± 5 Kg/m², and 43% developed SDB by third trimester. 29% were primigravida, self-reported race/ethnicity was as follows: 26% Hispanic, 67% White, 11% Black, 3% Asian, 1% Native American, and 11% multiracial. After adjusting for maternal age, BMI, and stress symptoms (symptoms of depression and perceived stress as measured by the Patient Health Questionnaire-9 and Perceived Stress Scale), third trimester apnea hypopnea index (AHI) and oxygen desaturation index (ODI) were significantly associated with cortisol area-under-the-curve, (B= -2.69, p= 0.010) and (B= -0.32, p= 0.035), respectively. One-way ANOVA revealed that women with SDB displayed a significantly lower cortisol area-under-the-curve in third trimester (F= 4.41, p=0.040). Third trimester AHI was significantly associated with placental 11 β HSD1 methylation (B= -2.80, p= 0.019). A convenience sample of cord blood cortisol showed higher -but non-statistically significant- cord blood cortisol levels in women with SDB in third trimester compared to women without SDB.

Conclusions: This study demonstrates that SDB is associated with significant alterations in cortisol regulation in pregnancy to include reduced maternal cortisol output and reduced DNA methylation of 11 β HSD1. Our limited sample suggests overexposure of the fetus to cortisol; however, this finding needs to be confirmed in larger studies.

Modelling Amyloid-beta clearance dynamics across sleep-wake cycles in healthy conditions

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Introduction: Understanding the fundamental mechanism of brain waste clearance is essential to elucidate physiological neurometabolite dynamics in healthy individuals. Sleep, particularly slow-wave sleep, is critical for the clearance of neurometabolites that accumulate in the brain during wakefulness. One of these neurometabolites is amyloid beta (A β), whose clearance increases approximately twofold

during sleep compared to wakefulness, and whose accumulation has been linked to Alzheimer's Disease. Clearance of neurometabolites is proposed to take place via complex interaction between the brain, cerebrospinal fluid and plasma, including the glymphatic system and the blood-brain barrier. Mathematical modelling is a useful tool to quantify and to better understand this complex system, especially since some of its dynamics are hard to measure experimentally. Successful models include microglial phagocytosis, glymphatic flow, and blood-brain barrier transport in rodents or in pathological states. However, they have not yet accounted for the effects of the sleep-wake cycles on the clearance dynamics. The objective of this study was to (i) develop a multi-compartment model of A β clearance dynamics across the brain, CSF, and plasma along the sleep-wake cycles in healthy individuals, and (ii) apply this model to explain experimental data.

Materials and methods: A three-compartment model, employing ordinary differential equations (ODEs), was developed to simulate A β dynamics across the brain, CSF and plasma, integrating production, and sleep-enhanced glymphatic clearance modulated by the sleep-wake cycle. The model was calibrated with human CSF and plasma data from studies of healthy individuals under normal sleep conditions. Model parameters were identified from experimental data where possible. The remaining parameters were found by fitting the model to data using the normalised root mean square error (NRMSE).

Results: Our three-compartment model predicts 24-hour A β oscillations during healthy sleep-wake cycles and achieves good agreement with experimental values for CSF and plasma A β concentration (NRMSE: 0.156–0.217). The default parameter set thus corresponds to a group average normal sleep-wake cycle in healthy people. With CSF A β concentration in the model ranging from 650 to 800 pg/ml, and plasma A β concentration from 15 to 19 pg/ml, the model predicts brain concentration of A β to range between 320 and 390 pg/ml. These CSF and plasma ranges align closely with experimental measurements, while concentration in the brain is yet to be measured experimentally. Application of the model to CSF data obtained with invasive CSF sampling over a 36-hour protocol predicts that such a procedure disrupts brain-to-CSF clearance dynamics with brain-to-CSF flux increasing by 1.25–25% during wake, while sleep-related glymphatic clearance decreases by 14.29–89.55%.

Conclusions: Our three-compartment model successfully reproduced the sleep-wake dynamics of A β concentration in CSF and plasma, and predicted A β dynamics in the brain. By applying the model to data, we were able to predict the potential mechanisms behind experimental observations of elevated CSF A β levels during normal sleep-wake cycles. Further model validation should be done against sleep disruption experiments.

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mPFC activation drives phasic REM population dynamics in the pons

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Introduction: Rapid eye movement (REM) sleep is a heterogeneous state consisting of tonic and phasic substates. Phasic REM sleep is characterized by rapid eye movements and pontine waves (p-waves), which are brief events generated in the pons. P-waves are linked to coordinated activity across many brain areas and may play a role in memory and plasticity. However, much about the neural expression of p-waves and how p-waves are triggered or regulated remains poorly understood. In this study, we tested whether the medial prefrontal cortex (mPFC) may regulate p-waves during REM sleep. We then used Neuropixels recordings and dynamical systems analysis to examine how mPFC activation drives neural population dynamics in the pons.

Materials and methods: We used chronic EEG/EMG recordings for sleep staging in mice, combined with fiber photometry and optogenetics to measure and manipulate mPFC activity. Pupil movements were tracked during REM sleep using video oculography in head-fixed animals. To assess downstream responses in the brainstem, we recorded single-unit activity using Neuropixels probes.

Results: Our results show that mPFC activity increases around the time of spontaneous p-waves, as measured by fiber photometry, suggesting that cortical activation may contribute to their occurrence. To test this, we optogenetically stimulated the mPFC using brief pulses delivered across sleep and wake states and found that mPFC activation triggered p-waves reliably only during REM sleep.

Stimulation induced additional phasic REM features, such as rapid eye movements and muscle twitches. To examine downstream effects of cortical input, we recorded population activity in the brainstem. In the pons, spontaneous activity showed a biphasic pattern, with periods of coordinated high firing followed by relative quiescence. During mPFC stimulation, we observed broad activation of brainstem neurons during laser-triggered p-waves, but not when stimulation failed to evoke a p-wave. **Conclusions:** Our findings show that activity in the pons is biphasic, alternating between tonic and phasic substates. mPFC stimulation shifts this local activity from the tonic to the phasic state, promoting the generation of p-waves and other features of phasic REM sleep. This suggests that the mPFC may contribute to initiating or coordinating phasic REM events through top-down modulation of brainstem circuits, offering a new perspective on cortical involvement in REM sleep regulation.

Multi-Person Sleep Monitoring Based on mmWave Radar

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Introduction: The 60GHz mmWave radar enables non-contact detection of subtle thoracic respiratory movements, facilitating the estimation of sleep stages. In this study, we extend the application of this technology from single-subject monitoring to multi-person environments by developing a real-time sleep monitoring system capable of simultaneously assessing multiple individuals. The proposed multi-person sleep staging algorithm achieved a classification accuracy of 76% (Cohen's kappa: 0.61), comparable to the 78% accuracy (Cohen's kappa: 0.64) of our previously validated single-subject model. These results demonstrate the system's ability to overcome the limitations of single-user monitoring, highlighting its feasibility for real-world deployment in shared living environments.

Materials and methods: In this study, we implemented a real-time multi-person sleep monitoring system using a 60GHz mmWave radar. The radar captures reflected signals from transmitted waves to extract distance, velocity, and angle information, which is then mapped into a three-dimensional coordinate system to generate a point cloud.

The sequentially acquired point cloud data were processed using the DBSCAN (Density-Based Spatial Clustering of Applications with Noise) algorithm, a density-based clustering method. This approach enabled the formation of distinct clusters based on spatial density, allowing for independent identification and tracking of multiple individuals within the radar's sensing range by assigning unique IDs to each cluster.

Once individuals were detected to have entered a stable posture with minimal movement, spatial zones were defined based on their positions. Sleep stages were then independently estimated for each person, enabling simultaneous multi-subject sleep analysis.

Results: In our previous study (presented at *Sleep* 2024), we achieved a sleep stage classification accuracy of 78% (Cohen's kappa: 0.64) using a CNN and Transformer-based model in a single-subject setting, validated through a clinical trial involving 340 participants (200 for training and 140 for validation).

To evaluate the performance of the newly developed multi-person algorithm, we conducted a clinical trial in an environment where two individuals slept simultaneously. The system performed real-time tracking and spatial separation, allowing for individual sleep stage estimation. Due to limitations of the PSG device, sleep stage accuracy could only be validated for one participant at a time. A total of 20 subjects participated in the trial.

The results showed that the multi-person system achieved a classification accuracy of 76% with a Cohen's kappa of 0.61, indicating a slight decrease in accuracy compared to the single-subject model, yet maintaining comparable performance under multi-occupant conditions.

Conclusions: This study extends conventional single-person sleep analysis to a multi-person setting using point cloud-based techniques. The results demonstrate that mmWave radar-based sleep monitoring can maintain a comparable level of accuracy in estimating sleep stages for multiple individuals, similar to that observed in single-subject scenarios. These findings validate the feasibility of applying mmWave radar for real-world, non-contact sleep monitoring in environments with multiple occupants.

The significance of this work lies in its demonstration of the practical potential of non-contact sensor

technologies for multi-person sleep monitoring, marking a step forward in scalable, unobtrusive sleep assessment systems.

Neural Adaptations Across Daily Torpor and Sleep: Ultrastructural, Molecular, and Behavioural Changes in Djungarian Hamsters (*Phodopus sungorus*)

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Introduction: Torpor is a controlled and reversible state characterised by a lowered metabolic rate and body temperature. In golden-mantled ground squirrels (*Spermophilus lateralis*), torpor induces dendritic spine retraction and the re-localisation of synaptic proteins, which are restored within two hours upon arousal (von der Ohe et al., 2007). Emergence from torpor is followed by increased slow-wave activity (SWA), a well-established marker of sleep pressure. Our study aims to elucidate the structural, molecular, and behavioural effects of torpor and subsequent sleep in Djungarian hamsters (*Phodopus sungorus*), a species that exhibits daily torpor in response to a shortened photoperiod.

Materials and methods: Animals (n = 5–6 per group; sex-balanced) were sampled at various stages: euthermia, mid-torpor, arousal, two hours post-torpor, and two hours of sleep deprivation after torpor. The occurrence of torpor was confirmed using continuous, non-invasive thermal imaging.

To examine neural changes across states, three approaches were employed. First, serial block-face scanning electron microscopy (SBEM) was used to assess changes in the synaptic ultrastructure of layer 2 pyramidal neurons in the primary motor cortex. Second, novel object recognition (NOR) testing was conducted to evaluate novelty detection in animals that underwent daily torpor compared to non-torpor controls. Third, Western blotting and immunohistochemistry were used to quantify and localise synaptic and cytoskeletal protein markers across the torpor–euthermia cycle.

Ultrastructural and behavioural data were analysed using linear mixed-effects models to account for inter-individual and stage-related variability.

Results: Our preliminary SBEM data revealed that the area of the axon-spine interface (ASI), an indicator of synaptic strength, did not differ significantly between the mid-torpor and euthermia groups (t = 0.277, P = 0.785; linear mixed-effects model), suggesting that daily torpor does not compromise synaptic strength. However, a significantly lower proportion of synapses containing presynaptic mitochondria was observed in the mid-torpor group compared to the euthermia group (p = 0.0389; generalised linear mixed model).

In our behavioural experiments (n = 12), novel object recognition performance did not differ significantly between torpor and non-torpor groups (p = 0.61; linear mixed-effects model), indicating that torpor does not impair this form of learning immediately after arousal.

Our pilot Western blot data (n = 2) revealed synapse-specific differences in the localisation of plasticity-related proteins, such as NMDAR1 and CaMKII α , between the mid-torpor and euthermic states. These differences may reflect molecular mechanisms underlying the rapid synaptic recovery observed after torpor.

Conclusions: Our preliminary findings suggest that daily torpor in Djungarian hamsters preserves synaptic strength and cognitive function, as evidenced by comparable axon-spine interface size and novel object recognition performance between torpor and euthermic states. However, changes in mitochondrial distribution at synapses and the localisation of plasticity-related proteins indicate that torpor induces specific molecular and structural adaptations. These results highlight the brain's resilience and dynamic plasticity during naturally occurring hypometabolic states.

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Neural correlates of sleep depth and sleep-wake perception during NREM sleep

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Introduction: How do we perceive sleep? Serial awakenings in humans – our best proxy of sleep-wake perception during sleep – have shown that we frequently perceive sleep as wake. But is this “misperception”? And how does perception relate to objective sleep depth? The primary aim of this study was to explore neural correlates of sleep depth and sleep-wake perception during NREM sleep in healthy sleep. In addition, we included patients with insomnia disorder as a potential model of altered sleep depth and perception.

Materials and methods: Thirty healthy participants (21 female, 9 male, 36±13 years) and 30 patients with insomnia disorder (21 female, 9 male, 39±15 years) were tested across three nights in the sleep laboratory with high density EEG. After an adaptation and baseline night, up to 12 successful awakenings per participant were performed out of non-rapid eye movement (NREM) sleep in night three. A gentle awakening protocol was used through a vibrating bracelet. Waking response was used as an index of sleep depth. Upon successful awakening, participants reported on their sleep-wake perception through an automatized interview.

Results: We performed a total of 750 awakening attempts out of NREM sleep (405 in controls, 346 in patients), of which both controls and patients showed around one third no awakenings, sleep reports upon awakening and wake reports upon awakening, respectively. There were no significant differences in the percentages of these events between controls and patients (small effect sizes). Analyzing high density EEG in the 2 minutes prior to the awakening signal, no-awakenings were mainly predicted by increased slow wave activity (SWA), while wake as compared to sleep reports were predicted by increased fast spindle and beta activity. No differences between groups were observed.

Conclusions: Our results suggest general mechanisms of sleep depth and its perception, with slow wave activity predicting sleep depth and high frequency activity wake perception, in line with concepts of fluid sleep-wake dynamics (sleep-wake continuum). Our results also indicate that fundamentals of sleep-wake regulation and direct sleep-wake perception are intact in patients with insomnia disorder. This suggests that the clinical symptomatology emerges post-sleep, from “downstream” cognitive, emotional and behavioral mechanisms.

Nighttime Administration of 0.25-Hz Binaural Beats Reduce Stage 1 Sleep in Individuals with Self-Reported Difficulty Initiating Sleep

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Introduction: Pharmacological and cognitive behavioral therapies are effective for insomnia, but occasionally involve side effects, tolerance, dependence, and limited accessibility. This study investigated a non-pharmacological and non-invasive approach using binaural beats (BB). BB are auditory stimuli generated by presenting two slightly different frequencies to each ear. A previous daytime nap study reported that 0.25-Hz BB significantly reduced the latency of N2 and slow-wave sleep compared to silence (Fan et al., 2024). This study examined whether similar effects occur during nocturnal sleep in individuals with difficulty initiating sleep.

Materials and methods: Fourteen adults (mean age: 36.9 ± 14.0 years; 10 women) with self-reported difficulty initiating sleep and who could perceive BB participated in a randomized, counterbalanced, within-participant crossover study. To minimize the first-night effects, participants completed an

adaptation night in a sleep laboratory. Subsequently, participants underwent two overnight sessions (8 hours in bed): one with 0.25-Hz BB and one sham (silence), both delivered continuously via earphones. Sleep was recorded via polysomnography and scored into stages W, N1, N2, N3, and REM according to the AASM criteria. To investigate whether BB effects varied across the night, sleep cycles were identified using the “SleepCycles” R package (Blume & Cajochen, 2021) and visually confirmed. The analysis focused on the first four cycles. To detect EEG changes during sleep onset that were not reflected in the AASM staging, data were segmented into 5-second epochs and scored into nine stages based on Hori’s stages (Hori et al., 1994).

Results: In contrast to previous nap studies, BB did not significantly affect the latency to any sleep stage. However, it significantly decreased the proportion of N1 and increased the proportion of N2 (both $p < 0.05$). Arousal and the arousal index showed non-significant reductions (both $p < 0.1$). No other parameters differed significantly (all $p > 0.05$). These results suggest that BB may reduce light sleep without affecting latency. The sleep cycle analysis showed that BB increased the proportion of N2 across cycles ($p < 0.05$), with no condition $\times$ cycle interaction, suggesting a consistent effect. The proportions of W and N1 did not differ (both $p > 0.05$). The proportions of N2, N3, and REM varied by cycle (all $p < 0.05$), reflecting typical sleep architecture. In the Hori’s stages analysis, latency, mean duration, proportional duration, and total transitions showed no between-condition differences (all $p > 0.05$). However, a significant condition $\times$ Hori stage interaction was observed in stage-specific transition counts ($p < 0.05$); BB increased transitions in H1 and H2 and decreased them in H4 (all $p < 0.05$).

Conclusions: The 0.25-Hz BB did not facilitate sleep onset, but consistently reduced N1 and increased N2 without inducing arousal. The increase in N2 persisted across sleep cycles, suggesting the potential of BB for continuous nocturnal use. Although BB induced instability during the early phase of sleep onset, this did not persist in the mid phase. These findings suggest that 0.25-Hz BB is a potentially simple, non-pharmacological, and non-invasive approach for improving sleep.

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Night-Time Internet Use and Its Association with Poor Sleep Quality and Autonomic Dysregulation in Medical Students

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Introduction: High-quality sleep supports cognitive performance, emotional resilience, and cardiovascular health—critical for young adults in demanding academic settings. However, prevalent night-time internet use among medical students challenges sleep health. Beyond discomfort, poor sleep quality is linked to autonomic dysregulation marked by increased sympathetic activity and reduced parasympathetic tone, early indicators of cardiovascular risk. This study assessed the prevalence of poor sleep quality in undergraduate medical students and its association with internet addiction and cardiovascular autonomic modulation.

Materials and methods: In this cross-sectional analytical study, 148 undergraduate medical students aged 18–24 years were assessed. Sleep quality over the past month was measured using the Pittsburgh Sleep Quality Index (PSQI), with scores ≥ 5 indicating poor sleep. Internet addiction was evaluated using Young’s Internet Addiction Test (YIAT-20), categorizing participants as normal, mild, moderate, or severe users. Baseline cardiovascular parameters - heart rate (HR) and blood pressure (BP) were recorded. Autonomic function was assessed by heart rate response to deep breathing (E:I ratio, reflecting parasympathetic tone) and diastolic BP rise during isometric handgrip (Δ DBPiHg, indicating sympathetic reactivity). Statistical analyses included t-tests, ANOVA, Pearson’s correlation, and logistic regression; significance was set at $p < 0.05$.

Results: A concerning 66.9% of students reported poor sleep quality (mean PSQI score 5.6 ± 2.5). Internet addiction was prevalent in 87.2% of participants, with 73.6% classified as mildly addicted and 13.5% as moderate to severe. Notably, 82.4% preferred internet use at night. Students with poor sleep quality had significantly higher PSQI component scores—including sleep latency, duration, efficiency, disturbances, and daytime dysfunction—compared to good sleepers

($p < 0.001$). Logistic regression showed internet addiction independently tripled the odds of poor sleep (OR: 3.29; $p = 0.018$), even after adjusting for BMI and waist-hip ratio. Furthermore, total PSQI scores positively correlated with internet addiction severity ($r = 0.224$; $p < 0.05$), suggesting a dose-response relationship.

In physiological measures, students with poor sleep quality exhibited greater sympathetic reactivity, as indicated by a higher diastolic BP rise during handgrip (21.5 ± 8.7 vs. 17.3 ± 4.1 mmHg; $p < 0.001$). Internet-addicted students also showed elevated resting heart rates (86.7 ± 11.0 vs. 79.4 ± 12.9 bpm; $p = 0.019$), suggesting autonomic imbalance.

Conclusions: This study highlights poor sleep quality as a widespread issue among medical students, closely linked to excessive, predominantly night-time internet use. Importantly, poor sleep quality was associated with objective signs of heightened sympathetic activity—an established risk factor for future cardiovascular disease. These findings underscore the need to promote healthy digital habits and prioritize sleep health in medical education to safeguard both immediate well-being and long-term autonomic and cardiovascular health.

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Noninvasive Sleep Metrics Provide Early Diagnosis of Traumatic Brain Injury in Mice

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Introduction: Accurately diagnosing traumatic brain injury (TBI), particularly in the acute phase, remains a major clinical challenge, with current tools often lacking sensitivity to functional brain disruption. Sleep-wake disturbances are among the most common and persistent consequences of TBI yet are rarely leveraged for diagnostic purposes. Because sleep regulation depends on widespread and highly integrated neural networks, early post-injury changes may offer a sensitive window into diffuse neurophysiological dysfunction. Advances in noninvasive sleep monitoring now enable real-time, scalable assessment of sleep behavior, presenting new opportunities to incorporate functional biomarkers into clinical TBI workflows. In this study, we evaluated whether acute sleep metrics could distinguish TBI from sham injury and differentiate among injury mechanisms in a mouse model, with direct relevance to scalable diagnostic applications.

Materials and methods: Adult male and female C57BL/6J mice ($n = 111$) were randomized to receive one of three injuries: midline fluid percussion injury (mFPI), closed-head impact (CHI), or controlled cortical impact (CCI), or respective sham surgeries. Noninvasive piezoelectric sensors recorded physiological parameters used to determine sleep for 72 hours post-injury. Key sleep metrics included total minutes slept and number of sleep-wake transitions. Data were modeled using generalized linear mixed models (GLMMs) with fixed effects of injury model, sex, and time. Righting reflex was used to standardize injury severity. Random forest classifiers were trained on summary sleep features (mean, SD, range) to predict injury. Model performance was assessed by ROC curve analysis and principal component analysis (PCA).

Results: Acute post-injury sleep behavior served as a highly accurate behavioral biomarker for TBI diagnosis. Within the first 24 hours, injured mice exhibited significantly increased total sleep and more frequent sleep-wake transitions compared to sham controls ($p < 0.01$). These sleep disruptions varied by injury type and sex: diffuse injuries (mFPI, CHI) produced earlier and more fragmented sleep than focal injury (CCI), and males showed greater disruption than females. Righting reflex time, a proxy for acute injury severity, also significantly predicted the extent of post-injury sleep disturbances, particularly in male and MFPI-injured mice, indicating that early neurological suppression is coupled to both increased sleep need and altered sleep architecture. Using only noninvasive sleep data collected

over 72 hours, a random forest classifier identified TBI with 94.4% accuracy (AUC = 0.944, 95% CI: 0.89–0.99), supporting the diagnostic potential of early sleep profiles. Sleep metrics also enabled classification of injury mechanism with 83.3% accuracy (AUCs: CHI = 0.93, CCI = 0.81, mFPI = 0.80). PCA revealed distinct clustering by injury type, particularly among females (PC1 ANOVA, $p < 0.01$). Among all features tested, the frequency and variability of sleep-wake transitions were the strongest contributors to model performance, reinforcing their value as functional, noninvasive biomarkers of brain injury.

Conclusions: Noninvasive measures of sleep quantity and quality reliably detect early TBI-induced changes and accurately classify injury type in mice. These results support the use of sleep-wake metrics as behavioral biomarkers of brain injury and demonstrate their promise as scalable, translational tools for early diagnosis in both research and clinical settings.

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Non-noxious cooling stimulation of trunk skin inhibits melatonin secretion from the pineal gland in urethane-anesthetized rats

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Introduction: Melatonin, secreted from the pineal gland primarily under sympathetic control, plays key roles in regulating the sleep-wake cycle and other physiological functions. Thermal stimulation of the skin can elicit reflexive autonomic nerve responses and thereby influence visceral and endocrine functions. Although photostimulation is a well-known regulator of melatonin secretion, the effect of skin thermal stimulation remains unclear. In this study, we investigated whether non-noxious cooling stimulation of the skin alters melatonin secretion from the pineal gland.

Materials and methods: The experiments were conducted on Fischer rats (5-8 months of age) that were housed with a 12-h light-dark cycle (lights on at 8:00 h). Animals were anesthetized with urethane, artificially ventilated, and maintained at a constant rectal temperature using heating pad and lamp during experiment. Using *in vivo* microdialysis, pineal perfusate was collected every 20 min and melatonin concentrations were measured using ELISA. Perfusate collection was completed during the light phase. Intermittent cooling stimulation was applied to the trunk skin using a Peltier-based contact thermode by alternating the temperature between 30 °C and 15 °C (15 °C/s) for 20 min. To assess the involvement of the cervical sympathetic nerves in the effect of skin stimulation, bilateral cervical sympathetic trunks were surgically transected.

Results: Without cooling stimulation, melatonin concentrations in the pineal perfusate remained stable over 100 min. Cooling stimulation had no effect on melatonin concentrations during application, however, reduced melatonin for 40 min after the stimulation ended. This suppression was abolished in rats with bilateral cervical sympathetic nerve transection.

Conclusions: These findings suggest that non-noxious cooling stimulation of the skin suppresses pineal melatonin secretion via cervical sympathetic nerves. This transient suppression may offer novel insights into non-photoc modulation of melatonin secretion.

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Pilot Study: Severity of Cyclical Intermittent Hypoxia Varies Lung Adenocarcinoma Progression via Different Mechanisms

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Introduction: Background

Systemic cyclical intermittent hypoxia (CIH) is a major underlying pathological consequence of OSA, and severe CIH is associated with increased cancer incidence and mortality. However, the mechanisms of how mild, moderate and severe CIH might affect natural cancer progression is not known.

Objective

To determine whether CIH reduces the "killing" immune response or increases the "suppression" immune response in the setting of cancer, compared to Local Tumor Hypoxia (LTH).

To determine whether CIH increases angiogenesis in potential metastatic sites such as the brain.

Materials and methods: Mouse model of CIH: The Hycon system (Figure 1) was developed with the engineer to mirror patients with OSA (Figure 2A) specifically the SpO₂ (Figure 2B) desaturation-resaturation time.

Importance of studying mild, moderate and severe CIH: We analyzed data from 4 public databases (Figure 2C) and most patients have mild OSA, so it is important to study all severities.

Mice with lung adenocarcinoma exposed to mild, moderate and severe CIH underwent uCT scans to calculate tumor rate increase/day (Figure 2D) as well as survival compared to Sham (room air, which represents LTH).

Mice without cancer exposed to moderate (CIH10) and severe (CIH5) CIH to calculate angiogenesis in the hippocampus (Figure 3B-D) and genes including TIE2, VEGFA, HIF1 α , and GLUT1 (Figure 3E).

Mice with lung adenocarcinoma exposed to severe CIH (CIH6) compared to Sham were harvested at early-stage cancer and evaluated for immune cells (Figure 4) in left lung (primary tumor), right lung (no sign of metastases yet), bone marrow, thymus, spleen and mediastinal lymph nodes.

Results: 1. In the setting of lung cancer, severe (CIH6) decreases survival and mice have larger metastatic tumors; moderate (CIH10) increases survival and mice have larger primary tumors; mild (CIH15) has no effect on survival, has the lowest combined tumor volume; LTH increases "Suppression" immune cells.

2. In the setting of no lung cancer, CIH (1) increases angiogenesis and increases VEGFA and GLUT1 transporters; there is no increase in HIF1 α ; (2) decreases "Killing" immune cells.

Conclusions: 1. CIH is a likely underlying pathophysiology that effects cancer progression in a mouse model of lung adenocarcinoma.

2. Implication for the sleep field: More attention should be placed on evaluating systemic intermittent hypoxia in the setting of lung cancer.

Preliminary analysis of intestinal flora characteristics in children with obstructive sleep apnea hypopnea syndrome

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Introduction: Obstructive sleep apnea-hypopnea syndrome (OSAHS) has attracted increasing attention due to its high prevalence and serious long-term complications. A growing number of studies demonstrate a link between OSAHS and gut microbiota. We speculate that OSAHS can probably lead to changes in the abundance and composition of gut microbiota.

Materials and methods: Children diagnosed with primary snoring and OSAHS by PSG were enrolled in the study group. Nonsnoring children undergoing elective surgery were selected as the control group. Stool, sleep monitoring data and medical history data were collected. 16S rRNA high-throughput sequencing technology was used to analyze the composition of the intestinal flora.

Results: A total of 62 OSAHS patients (42 mild OSAHS and 20 moderate to severe OSAHS), 16 primary snoring patients and 46 controls were enrolled in this study. There were differences in some intestinal flora at the phylum, class, order, family, genus and species levels between the control group and OSAHS group. The predictive model for OSAHS diagnosis established by the receiver operating characteristic (ROC) curve showed that the area under the curve (AUC) of Firmicutes and the abundance ratio between Firmicutes and Bacteroidetes (F/B) were more than 50%. At the genus level, Akkermansia, Dialister, Escherichia-Shigella and Faecalibacterium was correlated with some PSG indicators.

Conclusions: The intestinal flora of children with OSAHS is slightly different at the phylum, class, order, family, genus and species levels. The F/B and Firmicutes abundance detection have auxiliary value for the diagnosis of OSAHS. At the genus level, some gut microbiota were correlated with PSG indicators.

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Reducing complement activation during sleep deprivation yields cognitive improvement by dexmedetomidine

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Introduction: Sleep loss and its associated conditions (e.g. cognitive deficits) represent a large societal burden, but the underlying mechanisms of these cognitive deficits remain unknown.

Neuronal synapse formation and pruning, which are critical for cognitive function, are regulated by glia during sleep. Microglia were reported to modulate synaptic connectivity in the healthy and diseased brain. Complement activation was reported to aberrantly stimulate synapse loss in demyelinating disease. Recent studies have revealed that synaptic function is enhanced during sleep, and microglia appear to selectively eliminate opsonised synapses through phagocytosis during each sleep phase. However, the causal relationship between the complement system and synaptic function during sleep deprivation and the underlying molecular mechanisms remain unknown.

Dexmedetomidine (DEX) is a highly selective agonist of α_2 adrenoceptors located both presynaptically and postsynaptically in the brain and peripheral tissues. It is commonly used clinically for sedation in the intensive care unit and as an adjunct to general anaesthesia in the operating room. DEX was found to induce a state mimicking natural sleep, and modestly improve subjective sleep quality in patients with chronic intractable insomnia. Previous studies have indicated that sleep loss can reduce spine density and attenuate synaptic efficacy, reduce the synthesis of proteins associated with neuroplasticity in the hippocampus, and impair hippocampal neurogenesis. Although DEX was reported to ameliorate the incidence of delirium and postoperative cognitive dysfunction, the effect of DEX on cognitive deficits induced by sleep deprivation remains unknown.

In this study, we aimed to explore whether DEX ameliorates cognitive deficits in mice subjected to chronic sleep restriction (CSR) and to explore the underlying mechanisms with a focus on complement proteins (C1q, C3, and C3aR), microglial activation, and associated synaptic and molecular changes.

Materials and methods: C57BL/6 mice were subjected to chronic sleep restriction (CSR) for 20 h (5 pm-1 pm the next day) daily for 7 days, and cognitive tests were subsequently carried out. The neuromolecular and cellular changes that occurred in the presence and absence of DEX (100 $\mu\text{g kg}^{-1}$, i.v., at 1 pm and 3 pm every day) were also investigated.

Results: CSR mice displayed a decline in learning and memory by 12% ($P<0.05$) in the Y-maze and by 18% ($P<0.01$) in the novel object recognition test; these changes were associated with increases in microglial activation, CD68+ microglial phagosome counts, astrocyte-derived complement C3 secretion, and microglial C3a receptor expression (all $P<0.05$). Synapse elimination, as indicated by a 66% decrease in synaptophysin expression ($P=0.0004$) and a 45% decrease in postsynaptic density protein-95 expression ($P=0.0003$), was associated with the occurrence of cognitive deficits. DEX activated astrocytic α_{2A} adrenoceptors and inhibited astrocytic complement C3 release to attenuate synapse elimination through microglial phagocytosis. DEX restored synaptic connections and reversed cognitive deficits induced by CSR.

Conclusions: The results demonstrate that complement pathway activation associated with synapse elimination contributes to sleep loss-related cognitive deficits and that dexmedetomidine protects against sleep deprivation-induced complement activation. Dexmedetomidine holds potential for preventing cognitive deficits associated with sleep loss, which warrants further study.

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Relationship between circadian sleep parameters and self-perceived quality of life in patients on the liver transplant waiting list

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Introduction: Sleep should be one of the health factors studied in patients on the waiting list for liver transplantation, but it is not usually given much attention. On the other hand, there are different ways of assessing sleep; on the one hand, self-perceived quality questionnaires such as the Pittsburgh or Epworth scales, and on the other hand, objective methods such as actigraphy or polysomnography. In this study, we compared self-perceived quality using the aforementioned questionnaires with the parameters obtained through actigraphy.

Materials and methods: Fifty patients on the waiting list for liver transplantation at the Virgen de la Arrixaca University Hospital (Murcia, Spain) completed the Pittsburgh questionnaire, which ultimately provide an index called PSQI, which reaches 21 points for poor sleep quality; the Epworth questionnaire (EI), which provides an indication of daytime sleepiness, and the Munich questionnaire. On the other hand, the parameters were monitored using a Kronowise K6 device and the data were analysed using Kronowise 100 software (both from Kronohealth, Murcia, Spain). The patients wore the device on their non-dominant wrist for at least 7 days before the transplant. Forty-two parameters of sleep quality or circadian rhythm were calculated.

Results: Correlations have been found between the PSQI and various parameters such as WASO ($r=0.396$; $P=0.006$), sleep efficiency ($r=-0.417$; $P=0.004$), total time in bed ($r=0.438$; $P=0.002$), average activity during sleep ($r=0.415$; $P=0.004$), total light ($r=0.357$; $P=0.014$) and blue light ($r=0.376$; $P=0.009$) received during sleep, nap frequency ($r=0.440$; $P=0.002$) and nap duration ($r=0.355$; $P=0.014$). The overall score on the Epworth questionnaire correlated with light received during sleep ($r=0.431$, $P=0.002$), blue light received during sleep ($r=0.425$; $P=0.003$), total light ($r=0.463$; $P=0.001$) and blue light received 2 hours before sleep ($r=0.377$; $P=0.009$). The Munich questionnaire correlated the time of waking during the week with blue light received 2 hours before sleep ($r=0.325$; $P=0.034$), the time of waking with total light received during the 2 hours before sleep, and the reported latency with the objective onset of sleep ($r=0.443$; $P=0.008$) and with the average temperature 2 hours before sleep ($r=0.349$; $P=0.043$).

Conclusions: It seems clear that self-perception of sleep correlates significantly with numerous objective sleep parameters, especially the PSQI, which correlates with up to 14 objective sleep parameters. Interestingly, the Epworth daytime sleepiness index is significantly related to the amount of light the patient receives two hours before bedtime and during sleep, which marks a point of intervention for sleep quality in these patients to reduce such sleepiness. These data corroborate that initial assessment of patients using self-perception questionnaires, in the absence of objective data such as actigraphy or polysomnography, is useful in evaluating sleep health in patients on the waiting list for liver transplantation.

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Restoring proteostasis rescues cognitive performance and improves sleep in Alzheimer's disease and Down syndrome mouse models

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Introduction: Cognitive impairment and sleep disruption are hallmark features of both Alzheimer's disease (AD) and Down syndrome (DS). A shared molecular contributor is the amyloid precursor protein (APP), implicated in familial AD and triplicated in DS. APP overexpression leads to elevated amyloid- β ($A\beta$) production and proteotoxic stress, which contribute to early AD pathology, particularly in individuals with DS. Given that AD pathology involves misfolded protein aggregates, proteostasis pathways—including the unfolded protein response (UPR)—are key modulators of disease progression. Impaired proteostasis and aberrant UPR activation are observed in AD, sleep disruption, and DS. Previous work has shown that alleviating proteostatic stress with chaperones improves cognition and sleep in aged *Drosophila* and mice. Based on these findings, we hypothesized that restoring proteostasis through chaperone therapy would improve cognitive and sleep outcomes in mouse models of AD and DS.

Materials and methods: AD models used in this study included transgenic 3xTg and knock-in APP^{NLGF} mice. DS models included Ts65Dn and TsY66ah mice. Mice received either intraperitoneal (I.P.) injections of the chemical chaperone 4-phenylbutyrate (PBA) weekly for 10–12 weeks or hippocampal

injections of AAV-mediated BiP (an endogenous ER chaperone). Control groups received saline or AAV-mCherry. Cognitive function was assessed using the Spatial Object Recognition (SOR), Y-maze, and Novel Object Recognition (NOR) tasks. A subset of mice were instrumented for EEG recordings and sleep assessment. Brain tissues were collected post-perfusion for immunohistochemistry and biochemical analysis.

Results: PBA treatment improved both short- and long-term memory in hippocampal-dependent tasks in TsY66ah and Ts65Dn mice. In the NOR test, PBA-treated TsY66ah mice significantly outperformed vehicle-treated controls. Similar cognitive benefits were observed in both AD models. AAV-mediated BiP expression in the hippocampus led to significant improvements in spatial memory across both male and female AD model mice. However, only female 3xTg mice showed enhanced working memory following BiP overexpression. Preliminary sleep analyses revealed that PBA treatment in APP_{NLGF} mice increased NREM sleep and improved sleep and wake consolidation. Ongoing analysis of sleep data from 3xTg and Ts65Dn mice will further elucidate these effects. Molecular analyses demonstrated that both PBA and BiP attenuate PERK activation and enhance protein synthesis, processes critical for learning and memory.

Conclusions: Pharmacological and genetic restoration of proteostasis via chaperone administration significantly improves cognitive performance in AD and DS mouse models. Early findings also suggest beneficial effects on sleep architecture. These results highlight the therapeutic potential of targeting proteostasis mechanisms to alleviate cognitive and sleep dysfunction in neurodegenerative and neurodevelopmental disorders such as AD and DS.

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Roll, Pitch and Yawn: When Rotational Vestibular Stimulation Modulates Sleep Macroarchitecture

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Introduction: Rocking devices are receiving increasing attention as a non-pharmacological modulator of sleep. In rodent models, changes in sleep architecture were attributed primarily to vestibular input, rather than proprioceptive or visual cues. While these findings suggest a key role for vestibular stimulation, studies in humans yielded contradictory results, particularly concerning sleep microarchitecture. To date, most human studies focused on manipulating motion frequency or stimulation duration, with little attention given to the motion pattern itself. Despite the vestibular system's sensitivity to rotational (angular) and translational (linear) acceleration, prior work primarily focused on translational stimulation. To extend this work, we examined whether passive rotational vestibular stimulation could modulate human sleep macro- and microarchitecture.

Materials and methods: Forty-one healthy participants (mean age = 23.2, range 18-36) completed four consecutive overnight sleep sessions in a within-subject, randomized design: one adaptation night and one stationary baseline night and two motion nights with rotational vestibular stimulation on a motion platform that generated sinusoidal movements at 12.34°/s² - above the perception threshold - to ensure vestibular engagement, switching between yaw, pitch, and roll every 3 minutes. Sleep was recorded using a 256-channel EEG over an 8-hour 10-minute period each night.

Results: Condition effects were assessed using linear mixed-effects models (LMMs), with significant results followed by post-hoc *t*-tests. For N2, the LMM revealed a significant main effect of motion ($F(2, 75.766) = 5.985, p = .004, R^2 = .43$), with post-hoc comparisons confirming significantly higher proportion of N2 sleep during both the first ($t(74.5) = 2.943, p = .012$) and the second motion night ($t(75.9) = 2.995, p = .01$), compared to the stationary night. We found no main effect for sleep onset latency, but a significantly lower arousal index in the second motion compared to the stationary night ($t(74.9) = 2.48, p = .04$). Furthermore, a post-hoc comparison indicated significantly higher REM in the stationary night compared to the second motion night ($t(77) = 3.501, p = .002$). Proportions of wake, N1, and N3 did not significantly differ between the stationary and the second motion night.

Conclusions: Rotational passive vestibular stimulation increased N2 sleep without impairing sleep continuity. Effects were most consistent after a night of adapting to the motion. The observed gain in N2 may reflect engagement of thalamocortical circuits involved in sensory processing and sleep spindle

generation, potentially at the cost of REM. The ongoing analyses will examine microarchitectural markers such as sleep spindles and slow oscillations. These findings highlight the potential of rotational vestibular stimulation as a novel, non-invasive method to support sleep quality.

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Shared genetic architecture between sleep apnea related sleep traits and cardiometabolic diseases

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Introduction: Sleep apnea related sleep traits show high comorbidities with cardiometabolic diseases (CMDs). Although genetic relationships between them have been widely reported, it is still unknown whether a small number of loci or the whole genome would be responsible for the overall genetic association. Genome-wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) associated with either sleep apnea or cardiometabolic diseases. These findings provide a foundation for subsequent analysis of pleiotropic SNPs exhibiting cross-traits associations, which might aid in the understanding of potential shared genetic architectures underlying these comorbid conditions. The purpose of this study was to find shared genomic regions, genes, and pathways between sleep apnea and associated sleep traits (insomnia, sleepiness and snoring) and seven cardiometabolic diseases (atrial fibrillation, coronary artery disease, heart failure, hypertension, stroke, type 2 diabetes and venous thromboembolism).

Materials and methods: Using GWAS summary statistics from publicly available data sources, we calculated genetic correlation between two traits using linkage disequilibrium (LD) score regression (LDSC) and high-definition likelihood (HDL) analysis. Furthermore, PLACO, a pleiotropic analysis under a composite null hypothesis, was used to identify genetic variants that influence risk of two traits. And causal variants were identified by FM-summary, a Bayesian fine-mapping method. Colocalized association signals between trait pairs or among multiple traits were determined by the R packages coloc or HyprColoc. ANNOVAR program were used to identify nearest genes of causal variants and MAGMA was used to detect potential pleiotropic genes. Phenotype enrichment analysis and over-representation enrichment analysis were performed to characterize the phenotype and pathway specificity of these pleiotropic genes. Two-sample and multivariable mendelian randomization (MR) were used to identify causal associations between these traits and potential factors mediating causal relationships.

Results: Among 28 trait pairs between four sleep traits and seven cardiometabolic traits, 23 showed significant genetic connections. Pleiotropic analysis identified 720 (678 unique) pleiotropic causal SNPs in 23 trait pairs, with 92 (85 unique) colocalized loci. 73 nearest genes of colocalized loci were annotated with ANNOVAR program and gene-based analysis verified 48 of them. Shared genes were highly enriched in aging, liver/biliary system, muscle and endocrine/exocrine gland phenotypes. Furthermore, pathway enrichment analysis highlighted biological pathways including Cushing syndrome, an endocrine and metabolic disease characterized by too much cortisol in the body, and signal transduction like cAMP, Rap1 and cGMP-PKG signaling pathway. Vertical pleiotropy was further demonstrated across 14 trait pairs using MR analysis. Adjusting triglyceride, total cholesterol and glycemic traits, genetically predicted snoring was associated with higher risk of atrial fibrillation and heart failure. And genetically predicted sleep apnea was independently related with heart failure and type 2 diabetes, after adjusting blood pressure. Particularly, some pleiotropic loci were identified to be shared among multiple traits, such as 3q27.1 (ECE2), 4p12 (GNPDA2) and 17q21.31 (ACBD4).

Conclusions: This study not only supported the observed comorbidity of sleep apnea related sleep traits and CMDs, but also indicated shared genetic determinants underlying these trait pairs, might facilitating treatment and management of comorbid sleep apnea and CMDs.

SIMILARITIES AND DIFFERENCES BETWEEN FATIGUE AND DROWSINESS

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Introduction: In addressing the issue of human fatigue and reduced work capacity, particularly with the aim of reducing the number of accidents in specific application areas, new uncertainties arise regarding concepts such as fatigue and drowsiness. These states are not sufficiently studied, and there is no answer to the question of whether they are identical. If not, what characteristics are different and which are similar? It is clear only that drowsiness is much more dangerous than fatigue, as its end state is falling asleep, which leads to accidents. The aim of the study is to develop a monitoring system to determine the severity of these states.

Materials and methods: To solve this problem, in addition to physiological experiments in laboratory conditions, it is proposed to analyze the topological functional models (TFM) of these states, developed by scientists at Riga Technical University and used in computerized disease diagnostics tasks. TFM is a directed graph consisting of cause-effect chains, which in turn consist of vertices and directed arcs. The vertices represent functional parameters, and the arcs represent the links between them.

Results: The TFM created by the expert team, with 69 vertices and 74 arcs for the mental component of fatigue and drowsiness, provides several significant results. Mental fatigue is associated with energy imbalance parameters, while drowsiness is related to changes in nervous system functions. The sets of parameters that cause and maintain fatigue or drowsiness are also different. Drowsiness can depend on fatigue, but not vice versa. Drowsiness can occur without fatigue and fatigue without drowsiness. Severe fatigue can even lead to insomnia.

Conclusions: Fatigue, including its mental component, and drowsiness are not identical concepts, but their parameters and links can overlap. It has been confirmed that drowsiness is more dangerous than fatigue in many application areas. The parameters of drowsiness are easier to determine than those of fatigue, especially for determining the extreme state of drowsiness, i.e., falling asleep. Fatigue does not have such a clearly defined extreme state. The results of the study have made it possible to develop a monitoring system that not only determines the level of drowsiness during work but also, with a preemptive alert system, prevents the final state of drowsiness – falling asleep.

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Sleep architectural changes during recurrent cycles of sleep restriction: comparing stable and variable short sleep schedules

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Introduction: While several studies have investigated the effects of sleep restriction on sleep architecture, they have largely been limited to a single cycle of sleep loss and recovery and do not address the effects of re-exposure to subsequent cycles of sleep restriction. Sleep restriction implemented in previous studies are typically also evenly distributed across nights, limiting the generalisability of their findings to short sleep schedules with more night-to-night variability in sleep duration. To address these limitations, we tracked sleep architecture changes over recurrent cycles of “weekday” sleep restriction and “weekend” recovery in young adults, and investigated whether short sleep schedules with differing sleep duration variability on weekdays would lead to different sleep architectural responses.

Materials and methods: Fifty-two healthy young adults (25 males, age: 21-28) participated in this 15-night laboratory-based study. They were randomly assigned to three sleep schedules: stable short sleep, variable short sleep, or control. The participants started with two baseline nights of 8-h time-in-bed (TIB), followed by two cycles of “weekday” sleep opportunity manipulation and “weekend” recovery (8-h TIB). For each manipulation period, the control group received 8-h TIBs nightly, the stable short sleep group received 6-h TIBs nightly, while the variable short sleep group received 8-h, 4-h, 8-h, 4-h, and 6-h TIBs from the first to the fifth night (thereby receiving the same total TIB of 30 h as the stable short sleep group across the five nights). Participants kept to the same wake times throughout the protocol. Polysomnography was conducted every night. Group and night effects on sleep parameters (TIB, total sleep time [TST], N1, N2, slow wave sleep [SWS], rapid eye movement

[REM], sleep efficiency, wake after sleep onset [WASO], N2 latency and mean slow wave activity [SWA]) were analysed using mixed models. Average values across each period of sleep manipulation and recovery were also derived and compared using mixed models.

Results: Significant group x night interactions were found for all sleep parameters ($p < .03$). For both short sleep schedules, changes in sleep architecture resulting from sleep restriction returned to baseline levels by the first or second recovery night, and were mostly similar between corresponding nights of the first and second sleep restriction periods. There were no significant differences observed between the two short sleep groups for any of the sleep parameters averaged across each sleep restriction or recovery period ($p > .25$).

Conclusions: The similar sleep architectural responses observed in the two sleep restriction periods suggest that in young adults, sleep architecture does not adapt to recurrent weeks of moderate partial sleep loss. Furthermore, unlike with some neurobehavioural functions, such sleep patterns did not have compounding effects on sleep architecture. Additionally, overall, increasing night-to-night variability in sleep duration did not have much additional impact on sleep physiological responses relative to a stable short sleep schedule, suggesting that sleep duration variability may be a negligible factor for human sleep physiology as compared to overall sleep duration.

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Sleep depth is reflected in the spectral characteristics of the human wrist actigraphy

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Introduction: Previous studies have demonstrated that the spectral characteristics of human activity show a power-law ($1/f^\alpha$) trend both during wakefulness (with $\alpha \sim 1$) and sleep (with α below 1) with different spectral exponents. However, a recent finding proposes that preprocessing methods of the acceleration signal and deterministic measurement errors can substantially influence the results of such analyses. Furthermore, to our best knowledge, there is no study on whether analysing human activity provides an insight about sleep pressure. The present study aims to fill this gap by comparing the slope (α exponents) of the power spectral density (PSD) derived from calibrated triaxial raw acceleration, unfiltered magnitude of acceleration (UFM), magnitude of acceleration after separating the gravitational component (UFNM, and ENMO), and minutely activity data derived from them using traditional methods (e.g., PIM). These comparisons are made between sleep and wakefulness on both weekdays and weekends, as well as between habitual and sleep-deprived sleep.

Materials and methods: The sample consists of two datasets with $N=35$ (D1 dataset) and $N=65$ (D2 dataset) healthy participants, both containing raw triaxial acceleration signals derived from the wrist. D1 is a 35-hour long sleep deprivation dataset including acceleration signals during the participants' baseline and recovery sleep periods. D2 contains 4-7-day wrist actigraphy recordings collected during habitual sleep and wake periods including at least one weekend sleep period. The PSD is calculated using the Discrete Fourier Transform, and spectral slope (α exponent) is estimated by applying least squares linear regression to log-transformed spectra in the 10^{-4} to 10^{-2} Hz frequency range.

Results: Our results show that the spectral exponent of calibrated wrist data derived from the three axes (UFX, UFY, UFZ) significantly differed between sleep and wakefulness, with a steeper slope observed during sleep (e.g. UFY: $t=29.8$, $p<10^{-6}$). Furthermore, increased sleep depth due to sleep deprivation has a significant effect on UFM-derived spectral slope resulting in steeper slope in recovery sleep. However, there is no significant difference between weekend and weekday sleep slope.

Conclusions: These preliminary results suggest that sleep depth may be inferred from the spectral characteristics of acceleration signals, particularly the slope of the power spectral density. While the spectral slope derived from triaxial raw acceleration shows a clear distinction between sleep and wakefulness, the spectral slope derived from calibrated UFM reliably reflects changes in sleep depth due to sleep deprivation. However, further investigation is needed to validate and refine this approach, as both calibration and the actigraphic methodology used largely influence the PSD slope during sleep. Furthermore, this metric responded only to substantial interventions, like sleep deprivation, and did not capture differences between weekday and weekend sleep.

Sleep fragmentation and mental health: understanding anxiety and depression upon experimental sleep modulation

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Introduction: Sleep is essential for mental health and disruption of sleep quality are related to mental health, emotional status, cognitive performances, as well as somatic health status. Obstructive sleep apnea (OSA), a prevalent sleep breathing disorder, is accompanied intermittent hypoxia and sleep fragmentation. Depression and anxiety has been more prevalent in OSA patients comparing to general population. The specific impact of sleep fragmentation, without reduced total sleep time, remains under-explored in this context related on mental health. Therefore, the aim of our study was to investigate the effects of sleep fragmentation mimicking OSA on depression- and anxiety like behavior, as well as on redox status and hippocampal plasticity in a rat model.

Materials and methods: Experiments were performed using adult male Wistar albino rats and were approved by relevant ethical committees. Rats were randomized into three groups (n=8 in each): sleep fragmentation (SF), activity control (AC) and treadmill control (TC). SF was induced via treadmill protocol (30sON/90sOFF) during the first 6h of the light phase for 14 consecutive days. Behavioral assessments were performed on days 1, 7 and 14 using Forced Swimming Test (FST) to explore depression – like behavior; Elevated Plus Maze (EPM) and Light Dark Box (LDB) tests to evaluate anxiety – like behavior. Redox status via oxidative stress markers and anti-oxidative enzyme activity were determined in the hippocampus via ELISA. Immunohistochemically analysis of hippocampal neurogenesis (DCX, Ki67) and astrocyte activity (GFAP) was performed.

Results: Sleep fragmentation significantly ($p<0.05$) increased malondialdehyde level (MDA), while reducing ($p<0.05$) the activity of superoxide dismutase and glutathione peroxidase in the hippocampus compared to controls. In the FST, SF rats showed increased floating and reduced swimming and struggling time, indicating depression –like behavior which was duration dependent and correlated with indicators of oxidative stress in the hippocampus. In the EPM and LD test, significantly decreased ($p<0.05$) number of transitions and time in the open arms and light compartment, respectively, were recorded in rats from SF group comparing to controls. Despite behavioral and redox status changes, immunohistochemistry did not reveal any significant difference in DCX, Ki67 or GFAP expression in the dentate gyrus among the groups ($p>0.05$).

Conclusions: Sleep fragmentation, mimicking severe OSA without reducing sleep duration, induced behavioral changes in rats which pattern is consistent with depressive-like and anxiety-like states. These effects are probably mediated by oxidative stress, rather than changes in hippocampal neurogenesis and astrocyte activation. Our findings indicate mechanistic link between sleep fragmentation and mental health and support the hypothesis that disrupted sleep architecture alone may contribute to psychiatric comorbidities in OSA.

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Sleep in South African ambulance emergency care personnel

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Introduction: Ambulance emergency care personnel (ECPs) are a vital frontline workforce who operate in rotating shifts and are subjected to long and challenging working hours with high levels of trauma and stress. Shiftwork can cause both mental and physical health problems with sleep disturbances being especially prevalent. Those disturbances include circadian misalignment, poor sleep quality, increased sleepiness, daytime dysfunction, burnout and fatigue. Very limited research has investigated ECP sleep in settings where resources are limited and trauma exposure is above average, like that within South Africa. In this study, we investigated sleep quality in ECPs, and examined the effects of sex and shift (night vs day vs nonwork) on sleep.

Materials and methods: We collected the Patient Health Questionnaire-2 (PHQ-2), Pittsburgh Sleep Quality Index (PSQI), and Shift Work Disorder Questionnaire (SWDQ). Participants were given sleep and work diaries that included daily stress and sleepiness scores, as well as an actigraphy device (Actigraph wGT3X-BT). Two shift structures were investigated including the '4on4off' and 'long/short week' shift, both typical within South Africa and frontline professions globally.

Results: A total of 60 ambulance ECPs (33.6 ± 8.4 years; 58.5% male; 8.7 ± 6.8 years of shift work experience; 57% 'long/short week' shift) participated in the questionnaire component of the study, of which 43 (66%) also completed the actigraphy component. Mean PHQ-2 score was 1.50 ± 1.4 , with 21.5% ($n=14$) at risk for major depressive disorder. Mean PSQI total score was 7.8 ± 3.7 , with 70.8% ($n=46$) classified as poor sleepers ($PSQI > 5$). Poor sleepers had higher PHQ-2 depression risk scores ($p < 0.05$). Risk for SWD was present in 40% ($n=24$) and was associated with higher PHQ-2 depression risk scores and PSQI poor sleep scores ($p < 0.05$). Female ECPs had significantly higher global PSQI scores than males ($p < 0.05$) and were more likely to be poor sleepers (92.6 vs 55.3%, $p = 0.001$) even when adjusting for age and shift type (β (SE) = 1.92 (0.89); $p = 0.036$). Female ECPs had higher odds of reporting a high risk for developing SWD compared to males (OR = 3.69, 95% Wald CI 1.09-12.49). No significant differences were found between shift structures for all questionnaire variables. Using actigraphy, we found longer total sleep time on nonwork days (7.4 ± 1.9 hours), compared to post-day shifts (6.9 ± 1.8), and post-night shifts (4.2 ± 2.0). Additionally, wake after sleep onset (WASO) was high overall: nonwork, 71 ± 46 mins; post-day shift, 61 ± 39 ; post-night shift, 37 ± 36 . WASO was significantly higher for participants working the 'long/short week' compared to the '4on4off' shift for sleep on nonwork days and post-day shifts ($p < 0.05$).

Conclusions: Sleep quality, measured both objectively and through self-reported sleep questionnaires, is poor in South African ambulance ECPs. Sleep quality was poorer in females and after night shifts and was associated with higher depression symptoms. This study also suggests that the 'long/short week' shift structure may be more detrimental than the '4on4off'. Further investigation and potential intervention are required to reduce the effects on such a critical, yet vulnerable group of frontline workers.

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Sleep pressure causes birds to trade asymmetric for symmetric sleep

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Introduction: Sleep is a dangerous part of an animal's life. Nonetheless, following sleep loss, mammals and birds sleep longer and deeper, as reflected by increased EEG slow-wave activity during NREM sleep. Stimulating a brain region during wakefulness also causes that region to sleep deeper afterwards, indicating that NREM sleep is a local, use-dependent, homeostatically-regulated process. Birds and some marine mammals can keep one eye open during NREM sleep. Unilateral eye closure is associated with lighter sleep or wakefulness in the hemisphere opposite the open eye – states called asymmetric and unihemispheric NREM sleep, respectively. Closure of both eyes is associated with symmetric NREM or REM sleep. Birds sleep with one eye open to mitigate the simultaneous need for sleep and ecological demands for wakefulness. However, as sleeping with one hemisphere at a time doubles the time required for both hemispheres to fulfill their need for NREM sleep, increased sleep pressure might cause birds to engage in symmetric sleep at the expense of asymmetric sleep. Using high-density EEG recordings of European jackdaws, we investigated intra- and inter-hemispheric asymmetries during normal sleep and following sleep deprivation.

Materials and methods: Epidural electroencephalogram electrodes were surgically implanted in hand-raised, 10-month-old jackdaws ($N=9$). The 28 electrodes spanned the dorsal surface of both cerebral hemispheres. A head-mounted data logger recorded the signals at 250 Hz. A 3-axis accelerometer recorded changes in head position related to wakefulness (frequent, rapid movements) and REM sleep

(head still or dropping). The 3 days recordings (12:12 photoperiod, 21°C, food and water *ad libitum*) consisted of a baseline day, 4-or 8-h sleep deprivation starting at lights out, and an additional recovery day. The recordings were scored in 4-s epochs using standard criteria. A state was scored when the majority of the signals exhibited that state for the majority of the epoch. Aside from occasional periods of asymmetrical NREM sleep, switches between states were largely synchronous.

Results: Jackdaws exhibited little (<0.1%) unihemispheric sleep, but over 20–30% of NREM sleep was classified as asymmetric. The proportion of asymmetric sleep was lower early in the sleep period and following sleep deprivation – periods of increased sleep pressure.

Conclusions: Our findings demonstrate a trade-off between the benefits of sleep and vigilance, and indicate that a bird's utilization of asymmetric sleep is constrained by temporal dynamics in their need for sleep.

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Slow oscillatory responses to 300 ms closed-loop auditory stimuli during sleep: effects of timing and stimulus type

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Introduction: Closed-loop targeted memory reactivation (CL-TMR) is a novel method for precise targeting and reactivation of selective memories consolidated during sleep. The method has also been shown to enhance slow oscillations (SOs) and is currently being investigated as a tool to improve sleep quality. However, the impact of stimulation parameters—including timing, duration, and type of the sound stimulus—remains poorly understood. This study investigated the effect of 300 ms auditory stimuli on SOs characteristics, with the aim to determine: 1) whether the timing of stimulus phase of stimulation (upstate vs. downstate) modulates the evoked SO, 2) whether the topographic properties of evoked and spontaneous SOs differ, 3) and whether different types of sounds elicit distinct spectral EEG responses.

Materials and methods: Data were collected from 25 healthy adults (aged 20–29 years) during full-night polysomnography using a CL-TMR protocol. Auditory stimuli were delivered 330 ms after detection of a SO trough at the AFz electrode referenced to the pooled mastoids with a minimum interval of 2.5 seconds between two successive stimuli; one-third of the stimulation tags represented a sham condition (no sounds played). Prior to the analyses, trials were categorized into upstate and downstate. EEG responses were analyzed using event-related potentials (ERPs), topographical mapping, Hjorth parameters (activity, mobility, complexity), and spectral entropy. Data-driven analyses were used to evaluate brain responses to different sounds.

Results: Auditory stimuli of 300 ms duration reliably evoked slow oscillations during both upstate and downstate phases of endogenous SOs. Stimuli delivered during the upstate phase were associated with stronger ERP components, especially around the P300 latency, and more pronounced differences in frontal and occipital topography, suggesting increased cortical engagement. At 300 ms following stimulus onset, upstate stimulation produced larger scalp topography differences than downstate stimulation (compared to sham). There were no differences in EEG response to distinct sounds.

Conclusions: These findings suggest that both upstate and downstate phase stimulation with long (300 ms) auditory stimuli successfully elicits slow oscillatory activity during NREM 3 sleep. Although upstate stimulation may enhance certain aspects of cortical response (e.g., frontal amplitude, cognitive processing components), the consistent EEG responses observed for both timing conditions indicate a high level of robustness. Importantly, the brain's response remained stable across a variety of naturalistic sounds. These findings suggest that longer auditory stimuli may tolerate less precise timing while maintaining efficacy—an important prerequisite for real-world, home-based CLAS applications targeting sleep improvement in individuals with insomnia.

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Spectral and network investigation reveals distinct power and connectivity patterns between phasic and tonic REM sleep

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Introduction: Although rapid eye movement (REM) sleep is often thought of as a singular state, it consists of two substates, phasic and tonic REM, defined by the presence (respectively absence) of bursts of rapid eye movements. These two substates have distinct EEG signatures and functional properties. However, whether they exhibit regional specificities remains unknown.

Materials and methods: Using intracranial EEG recordings from 31 patients, we analyzed expert labeled segments from tonic and phasic REM and contrasted them with wakefulness segments. We assessed the spectral and connectivity content of these segments using Welch's method to estimate power spectral density and the phase locking value to assess functional connectivity.

Results: We found a widespread power gradient between low and high frequencies ($p < 0.05$, Cohen's $d = 0.17 \pm 0.20$), with tonic REM being dominated by lower frequencies ($p < 0.01$, $d = 0.18 \pm 0.08$), and phasic REM by higher frequencies ($p < 0.01$, $d = 0.18 \pm 0.19$). However, some regions such as the occipito-temporal areas as well as medial frontal regions exhibit opposite trends. Connectivity was overall higher in all bands except in the low and high ripple frequency band in most networks during tonic REM ($p < 0.01$, $d = 0.08 \pm 0.09$) compared to phasic REM. Yet, functional connections involving the visual network were always stronger during phasic REM when compared to tonic REM.

Conclusions: Phasic and tonic REM sleep display distinct and heterogeneous activation patterns depending on the region, network, and frequency band examined. Consistent with findings that sleep and wakefulness are local phenomena, we demonstrate that phasic and tonic REM also show region-specific electroencephalographic properties

Subcortical connectivity patterns during the introduction of NREMS and isoflurane-induced loss of responsiveness are partly different along the sleep/wake promoting pathway in mice

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Introduction: NREMS and general anesthesia (GA) are often seen as two separate states, however, they share some neurophysiological similarities. Identifying common mechanisms may increase our understanding of these states and may help to develop even safer anesthetic regimes. This study focused on functional connectivity between the ventrolateral preoptic nucleus (VLPO) and locus coeruleus (LC) – two major nuclei along the sleep/wake-promoting pathway. Transitions between NREMS and wakefulness (WAKE), as well as loss (LOR) and return (ROR) of responsiveness during GA were recorded electrophysiologically *in vivo* and analyzed. Similar patterns in functional connectivity during natural NREMS/WAKE transitions and GA-induced transitions would point to a possible involvement of the sleep/wake-promoting pathway in isoflurane-induced GA.

Materials and methods: Twelve male C57Bl6/N mice were implanted with local field potential (LFP) electrodes in the VLPO and LC to record their activity, as well as with EEG electrodes to monitor vigilance states. Chronic recordings included two baseline days and LFP/EEG recordings during GA. Functional connectivity was calculated using coherence, inter-site phase clustering (ISPC), and Granger

causality (GC) analyses for frequencies between 0.5–40 Hz. Significance was set at 95% (Wilcoxon signed rank test). Parallel, we trained a support vector machine (SVM) using the consensus of 8 experts on WAKE/NREMS and LOR/ROR transitions to automatically identify all transitions detected manually.

Results: Coherence analysis revealed an increase at WAKE/NREMS transitions and a decrease at NREMS/WAKE transitions. During GA, coherence decreased after LOR; no significant changes at ROR could be detected. ISPC showed a similar trend with an increase during NREMS and a decrease during WAKE; no significant changes during LOR and ROR could be found. GC index from VLPO to LC increased during NREMS and decreased during WAKE. Also, it increased after LOR, with no significant changes at ROR. GC from LC to VLPO decreased during NREMS; there were no significant changes upon transition to WAKE. GC did not change significantly during LOR, but increased after ROR. The trained SVM model could predict transitions with high precision within the expert range and was used to pinpoint transitions between WAKE, NREM and ROR. In contrast, LOR showed very low consensus among experts. Therefore, an anomaly detection approach (semi-supervised) was used to identify the time point at which the EEG exhibited sharp changes after LOR.

Conclusions: This study supports findings from literature about functional connectivity between VLPO and LC during WAKE/NREMS/WAKE transitions. Their functional connectivity pattern at GA transitions suggests at least a less prominent role during LOR and ROR. However, their involvement in LOR and ROR is still not fully understood. Current research in our lab uses targeted inhibition of VLPO and LC to gain a deeper understanding of their role in GA. For these experiments, the newly developed SVM model will be applied to automatically detect WAKE/NREMS and LOR/ROR transitions.

Temporal effects of chronic intermittent hypoxia on genioglossus electromyography and ultrastructure in a rat OSA model

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Introduction: This study established a chronic intermittent hypoxia (CIH) rat model simulating obstructive sleep apnea (OSA) to evaluate the temporal impact of CIH on genioglossus (GG) electromyography (EMG), mitochondrial morphology, and neuromuscular junction (NMJ) integrity.

Materials and methods: Forty healthy male Sprague-Dawley rats (7-week-old) were randomized into three groups: normal control (NC, n=10), CIH (4-week hypoxia, n=15), and prolonged CIH (8-week hypoxia, n=15). CIH groups underwent daily 8-hour cycles of alternating hypoxia (90s at 7% O₂) and normoxia (90s at 21% O₂). Serial measurements of GG-EMG activity were performed at baseline and weekly intervals, complemented by repetitive nerve stimulation (RNS) assessments during weeks 4-8. Histopathological evaluation through H&E staining and transmission electron microscopy (TEM) quantified myofibrillar architecture and subcellular organelle integrity.

Results: In the CIH group, the GG-EMG showed a gradually increasing trend from the first week of CIH to the end of the fourth week ($P < 0.05$). And the multiple comparisons of GG-EMG between the groups during 1-4 weeks of CIH were statistically significant ($P < 0.05$). Meanwhile, the GG-EMG in most CIH prolonged groups showed a decreasing trend around 6 weeks of CIH. At 4 weeks of CIH, 15% of the rats showed decreased RNS high-frequency (20Hz) stimulation, and with the extension of hypoxia time, up to 8 weeks of CIH, 60% of the rats showed decreased RNS high-frequency stimulation ($P < 0.05$). Compared with the NC group, the CIH group had disordered arrangement of GG fibers, irregular and swollen fibers. TEM showed that the damage of GG muscle fibers and mitochondria was not obvious two weeks before CIH, and the damage of GG mitochondria was earlier than that of GG muscle fibers. With the prolongation of CIH exposure, the damage of GG muscle fibers and mitochondria was further aggravated.

Conclusions: CIH induces time-dependent GG neuromuscular dysfunction: Early compensatory EMG enhancement (≤ 4 weeks) transitions to decompensation (≥ 6 weeks). Mitochondrial vulnerability manifests earlier than myofibril damage. Progressive NMJ impairment correlates with RNS-detected abnormalities. These findings highlight critical phases of hypoxic adaptation in OSA-related upper airway dysfunction.

THC and CBD in insomnia associated to neuropathic pain: effect on sleep architecture and descending anti-nociceptive pathways

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Introduction: Neuropathic pain (NP) is a chronic pain condition caused by a lesion on the somatosensory system and affects 7-10% of the population. Additionally, up to 48 % of the patients who suffer from NP experience sleep disturbances. Preclinical and clinical studies indicate that delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) possess both analgesic and hypnotic effects; however, the mechanisms of action in models of NP are not fully understood. Here, we examined the effects of THC and CBD on the sleep-wake cycle (EEG/EMG) in NP condition and explored their possible mechanism of action, examining the neurons of the descending anti-nociceptive pathway.

Materials and methods: We induced NP in Wistar rats; 14 days later, rats were evaluated for allodynia using von-Frey filament. To assess mechanical allodynia, NP animals were treated with THC (1, 1.5, 2, 2.5 and 5 mg/kg, i.p.) or CBD (5, 10 and 20 mg/kg, i.p.) or respective vehicle, and allodynia was measured during 7 h. Next, to evaluate the effect on sleep, NP rats were implanted with six stainless-steel wire electrodes in the skull and EEG/EMG was recorded for a period of 6 h (from 6 AM to 12 PM) with a single injection of THC (5 mg/kg, i.p.) or CBD (20 mg/kg, i.p.). To investigate the involvement of CB1 and 5-HT1A receptors in the pro-hypnotic effect of THC and CBD, rimonabant (1 mg/kg) and WAY 100635 (2 mg/kg) were injected 10 min before an effective dose of THC (5 mg/kg) and CBD (20 mg/kg), respectively. Next, the effects of microinjection of CBD (1 µg) and THC (10 µg) into the ventrolateral periaqueductal gray (PAG) were assessed by recordings of ON (pro-nociceptive) and OFF (antinociceptive) cells in the rostral ventral medulla (RVM) in NP rats.

Results: CBD (10 and 20 mg/kg, i.p.) and THC (2.5 and 5 mg/kg, i.p.) decreased mechanical allodynia in rats with NP vs VEH treated rats ($p < 0.001$) 1h after administration, reaching an antiallodynic peak of 7 (CBD) and 6 (THC) grams. NP rats developed insomnia characterized by decreased duration of NREM (-41.2%) and REM (-73.3%) during the inactive phase. CBD (20 mg/kg, i.p.) and THC (5 mg/kg, i.p.) were able to increase NREM ($p < 0.01$) and REM sleep ($p < 0.001$) in NP rats. Additionally, the pre-administration of rimonabant (1 mg/kg) was able to block the effect on sleep of THC (5 mg/kg) and WAY 100635 (2 mg/kg) the effect of CBD (20 mg/kg). On the other hand, microinjection of THC (10 µg) decreased the firing activity of ON cells and activated the firing of OFF cells in the RVM. Unlike THC, CBD reduced the activity of both ON and OFF neurons in NP rats.

Conclusions: The findings suggest that THC and CBD have a moderate acute analgesic effect, but significantly recovered the sleep disruption in NP rats by modulating the neural nociceptive pathway. Therefore, THC and CBD have potential in the treatment of neuropathic pain and comorbid insomnia.

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The Association among the Sleep Spindle and Category-Induced False Recognition

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Introduction: Research investigating sleep and memory suggests clear benefits of sleep on true memories; however, sleep's role in false memories is still unclear. Electrophysiological activities of the sleeping brain have been linked with information processing and memory management. One such electrophysiological marker is spindle activity in the 12-15 Hz range, which is believed to be generated by thermocortical activity occurring during memory processing in sleep. False memories belong to the larger umbrella of memory, distinguishing only in terms of content from true memories. The present study is an attempt to investigate the link between sleep spindle activity and false memories induced through category associates.

Materials and methods: The study involved eleven healthy participants (all male; mean age 19.07 ± 1.07 years) without any known medical issues. Participants performed category-associated tasks before engaging in sleep or deprivation in the sleep laboratory. On a later old/new recognition test, participants performed a recognition on lists containing targets and distractors. Spindle activity was extracted using the standard protocol mentioned elsewhere (Verma, Pandey & Kashyap, 2025). The Pearson correlation coefficient (r) was used to determine the relationship between sleep spindles and false memory formation.

Results: Significant positive correlation between sensitivity of critical lures and spindles on central [(C₃: $r_{(11)} = .711$, $p = .01$); (C₄: $r_{(11)} = .652$, $p = .03$)], and occipital [(O₁: $r_{(11)} = .645$, $p = .03$); (O₂: $r_{(11)} = .598$, $p = .05$)] channels were found. All other results were non-significant.

Conclusions: These results emphasise a strong positive relation between the sensitivity of high-frequency category-associated critical lures and spindle activity, indicating that sleep spindle activity may contribute to the retrieval mechanisms of high-frequency category-associated false memory formation. These findings highlight the relevance of studying the connection between sleep spindle activity and memory sensitivity to examine the cognitive process underlying memory consolidation and distortion.

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The Effect of L-alanine on Sleep in *Drosophila melanogaster*

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Introduction: Sleep and nutrition are vital for survival. In fruit flies (*Drosophila melanogaster*), sweetness alone can promote sleep. Amino acids are essential nutrients involved in diverse physiological functions. The L- form of amino acids are the prominent form, and they are involved in sleep regulation. However, their sleep regulation mechanisms have been less explored by their taste. L-ala was shown to be attractive to flies and promotes feeding (Aryal et al., 2022; Yang et al., 2018) Yang we examined how its taste affects sleep by comparing sucrose-based (sweet) and sorbitol-based (non-sweet) foods.

Materials and methods: Wild type (w^{1118}) male flies were fed with food based on either 5% sucrose (sweet, nutritive) or 5% sorbitol (non-sweet, nutritive) supplemented with amino acids. Sleep was measured using DAM5 (single-beam) and DAM5H (multi-beam) *Drosophila* Activity Monitoring systems. Feeding behavior was assessed by food intake assays using blue dye and attractiveness was assessed by proboscis extension response (PER) tests. We examined both young and aged flies.

Results: We examined how amino acids, specifically L-alanine (L-ala), influence sleep via taste mechanisms, comparing sweet (sucrose) and non-sweet (sorbitol) base diets. We found that L-ala supplementation significantly enhanced sleep when given in sorbitol (non-sweet), but not in sucrose (sweet) food, indicating a taste-dependent effect. The sleep-promoting effects of L-ala in sorbitol were comparable to those of sucralose, an artificial sweetener. Furthermore, combining L-ala with low-dose sorbitol significantly extended lifespan, highlighting its role as a feeding promoter under nutrient-limited conditions. The concentration-dependent effects of L-ala supplemented in sorbitol was more prominent than in sucrose. By performing proboscis extension response (PER) assays, we confirmed that L-ala was attractive to flies. Importantly, aged flies supplemented with L-ala in sorbitol food doubled sleep duration compared to sorbitol alone. In addition, L-ala supplementation increased survival, with fewer flies dying (22/32 survived sorbitol alone; 30/32 with L-ala).

Conclusions: Our study demonstrates that L-alanine modulates sleep and survival in *Drosophila melanogaster* depending on sugar context and sweetness. Behavioral assays showed flies found L-ala attractive, increasing consumption of sorbitol food containing L-ala. However, higher L-ala concentrations reduced proboscis extension responses, possibly due to aversion. Nonetheless, flies still consumed L-ala food, suggesting a feeding-promoting effect. L-ala increased sleep even under nutrient restriction, but it only enhanced longevity when paired with minimal dietary sugars. Therefore, we show that sorbitol is an effective base sugar to examine taste-driven effects. L-ala addition to sorbitol food extends both sleep amount and lifespan suggesting its potential use for promoting lifespan.

The effects of environmental factor-related alterations on post-arousal hypersynchrony

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Introduction: Post-arousal hypersynchrony (PAH) denotes a delta burst followed by arousal, hypothetically functioning to antagonize arousal, because it shares similar characteristics with K-complexes and correlates with arousal numbers (Suzuki et al., 2021). Meanwhile, external environmental factors including sound and first-night effects (FNE), can induce sleep-related changes. Closed-loop auditory stimulation (CLAS) has been used to enhance slow oscillations (Ngo et al., 2013) via a mechanism that could involve auditory evoked potentials, such as the K-complex. Using 0.25-Hz binaural beats (BB), sleep structure-related alterations have been described in healthy adults with insomnia symptoms, characterized by a %N1 decrease and a %N2 increase, suggesting sleep stabilization (Hirayama et al., 2024). FNE promote wakefulness, including an increment in the number of arousals (Boulos et al., 2019). We hypothesized that external factors may increase the occurrence of PAHs, and examining PAH-related changes during sleep altered by these factors may help clarify the function of PAHs.

Materials and methods: In Experiment 1, 16 healthy adults with high anxiety (State-Trait Anxiety Inventory trait scores of 45-80) participated in the CLAS study (23.9±3.7 [mean±standard deviation] years, six females) (Suzuki et al., 2024). In Experiment 2, 14 healthy adults (36.9±14.0 years, 10 females) with insomnia symptoms (Insomnia Severity Index score >7) who could discriminate 0.25-Hz BB were enrolled in the study using 0.25-Hz BB (Hirayama et al., 2024). Both experiments were crossover study designs, with and without sound conditions. In Experiment 3, we examined four non-consecutive nights of PSG in 15 healthy adults (21.7±1.6 years, five females) who had not undergone PSG previously (Suzuki et al., 2025). In each experiment, PAH and sleep variables were assessed by a scorer and compared across conditions.

Results: In Experiments 1 and 2, the occurrence of PAHs remained unchanged between conditions (sound vs. no sound: 2.4±2.0 vs. 2.8±2.7 times and 0.5±0.7 vs. 0.4±0.8 times, respectively). In Experiment 3, the increase was observed during the first night (5.1±3.3 times) compared to the fourth night (2.7±1.8 times), while sleep variables showed no change in measurement number. As PAH was unexpectedly low in Experiment 2, we additionally compared it and sleep variables with three groups for Experiments 1 and 2 under no sound conditions and Experiment 3 on the second night, all recorded in the same sleep lab. PAH decreased in participants with insomnia symptoms compared with the other groups. Compared with healthy adults in Experiment 3, %N1 increased in the other groups and %N3 decreased in those with insomnia symptoms.

Conclusions: PAH was unaffected by CLAS and 0.25-Hz BB. It was acutely affected by FNE and could potentially contribute to sleep stabilization. Surprisingly, in those with insomnia symptoms, PAH incidence and %N3 were lower, and %N1 was higher. PAH might be influenced not only by the external environmental factor FNE, but also by insomnia symptoms with decreased objective sleep quality.

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The Effects of Latitude on Sleep and Blood Pressure at an Altitude of 4300 m

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Introduction: Over 140 million people live above 2400 m worldwide. Additionally, even more visit high altitudes (HA) every year for recreation, military and religious reasons. Exposure to HA is associated with hypoxia-related cognitive impairments and sleep disruptions and can cause negative impacts on physiology such as an increase in blood pressure. Additionally, latitude could cause additional negative impacts. Because of the Earth's rotation, there is a slight bulge at the equator, which causes both barometric pressure and the partial pressure of oxygen to be greater at the equator than at the poles. The additive effects of latitude and high altitude have yet to be studied. Thus, the aim of the current study was to determine if latitude has an impact on sleep and blood pressure at ~4,300 m.

Materials and methods: Similar testing protocols were utilized at ~4,300m at "Camp 14" on Denali at a latitude of ~63° (Alaska, USA) and at 4,300 m along the Everest Basecamp Route (Dingboche, Nepal) at a latitude of ~28°. 31 climbers (3 females) participated in the Denali study (age 34.0±9.7 mean±SD) and twenty-five climbers (6 females) participated in the Everest study (age 28.0±9.7). Participants were instructed to go to bed and wake up at their habitual bedtimes and wake times. Sleep architecture was recorded with a wireless sleep recording device and blood pressure was measured either with the auscultatory method or a blood pressure machine.

Results: Independent t-tests revealed a statistically significant decrease in total sleep on Denali when compared to Mt. Everest. There were nonsignificant trends for a decrease in rapid eye movement (REM) sleep and sleep onset latency on Denali. Other sleep stages appear relatively unaffected by latitude. Systolic blood pressure was significantly higher ($p<0.05$) on Denali (143.39±2.66 mmHg mean±SEM) vs Everest (127.54±3.16 mmHg), whereas there was no significant difference in diastolic blood pressure (Denali: 88.89±3.14 mmHg, Everest: 85.36±2.18 mmHg) between latitudes.

Conclusions: Our findings indicate that there is an increase in systolic blood pressure and a decrease in total sleep time at higher latitude with comparable altitude. Prior research has linked a decrease in total sleep time to decreased cognitive impairments and other physiologic disruptions. Additionally, systolic blood pressure has been reported to be an indicator of heart disease. Based on our findings of systolic blood pressure increasing with a higher latitude, latitude could have an impact on cardiac health since the participants were in the hypertensive range on Denali but not Everest. Our findings suggest that latitude should be considered when venturing into HA environments, designing research protocols, analyzing results, and for clinical applications and military operations.

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The first night effect on sleep in school-age children

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Introduction: Sleep is often altered in the first night of polysomnography (PSG) due to discomfort from sensors and unfamiliar lab environments – a phenomenon known as the first-night effect. In adults, this typically manifests as longer sleep latency, longer wake after sleep onset (WASO), reduced REM sleep, and lower sleep efficiency on the first night of PSG recordings compared to subsequent recordings. Two recent studies in healthy children show inconsistent results: one found significant first-night changes in sleep stages in a lab setting, while another, using at-home recordings, observed stable sleep architecture across nights. To further evaluate the first night effect in this population, this study compared both macrostructural and microstructural (EEG spectral power) measures between two non-consecutive nights of at-home PSG in healthy 7- to 12-year-olds.

Materials and methods: 41 Singaporean children (mean age ± SD = 9.77 ± 1.29 years; 22 males) underwent two unattended at-home PSG recordings one week apart. They were instructed to follow their sleep-wake timing on school nights for both nights. PSG records were first automatically scored (Neurobit PSG with FASST) and then visually validated against AASM criteria to derive sleep macrostructural metrics. For sleep microstructure, artifact-free NREM epochs (0.5–40 Hz, notch at 50 Hz harmonics) were segmented into 30-second epochs and analysed via Welch's method (5-second Tukey windows, 1-second overlap) to compute power for the following frequency bands: Delta (δ): 0.5–4 Hz, Theta (θ): 4–7 Hz, Alpha (α): 8–13 Hz, Sigma (σ): 11–16 Hz, Beta (β): 13–30 Hz., For each

participant and frequency band, total power, mean power and hourly average power were computed. Paired t-tests compared macro- and microstructural parameters between nights of recordings.

Results: Relative to the second night of PSG recording, in the first night, children had 15.97 ± 12.20 min (mean $\pm$ SD) longer time in bed ($p = 0.04$, $dz = 0.33$), but there was no difference in total sleep time ($p = 0.87$), resulting in higher WASO (10.63 ± 7.47 min, $p = 0.02$, $dz = 0.37$) and lower sleep efficiency (-2.28 ± 3.37 %, $p = 0.02$, $dz = 0.38$). REM latency was also slightly delayed by 19.39 ± 15.92 min in the first night ($p = 0.02$, $dz = 0.37$). Durations of the sleep stages, as well as, N2 and N3 latency did not differ between nights ($ps > 0.11$). Spectral power showed no night-to-night differences in mean, total, or hourly power ($ps > 0.05$).

Conclusions: In healthy school-age children sleeping at home, first night effect is small and limited primarily to delayed REM onset, with stable overall sleep architecture and spectral measures, especially if time-in-bed is kept constant. Hence, a single night of at-home PSG may suffice for this population for most sleep parameters.

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The immune mechanisms study of dihydroartemisinin in alleviating airway inflammation of chronic intermittent hypoxic obese asthmatic mice model by inhibiting TLR4

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Introduction: To explore the immune mechanisms of dihydroartemisinin (DHA) in alleviating airway inflammation of chronic intermittent hypoxic(CIH) obese asthmatic mice model by inhibiting toll like receptor 4 (TLR4).

Materials and methods: Thirty 3-week-old female CD-1 (Swiss) mice were randomly divided into 5 groups: Control group; Model group; DHA treatment group, Model group were given DHA treatment; Lenti-TLR4-OE+DHA treatment group, mice of the Model group were given DHA combined with lentivirus-mediated overexpression of TLR4 treatment; Lenti-vector+DHA treatment group. A chronic CIH obese asthmatic mouse model was established. The lung function of mice was measured. The inflammatory cytokines IFN- γ , IL-6 and IL-10 in mouse lung homogenates were determined by ELISA. Flow cytometry was used to determine the percentage (%) of neutrophils infiltrated in lung tissues. The activation levels of TLR4/NF- κ B/PI3K/AKT signaling pathway in mice lung were determined by Western blot.

Results: Compared with Control group, in Model group and DHA treatment group, the body weight/tibia length of mice were increased ($P < 0.05$); FEV0.1/FVC decreased ($P < 0.05$); the levels of IFN- γ , IL-6 and IL-10 were increased ($P < 0.05$); the levels of TLR4, p-P65, p65, p-PI3K and p-Akt were increased ($P < 0.05$); the percentage (%) of neutrophil infiltration in lung tissues were increased ($P < 0.05$). Compared with Model group, in DHA treatment group there was no significant difference in body mass/tibia length ($P > 0.05$); FEV0.1/FVC increased ($P < 0.05$); IFN- γ and IL-6 levels were decreased ($P < 0.05$), and IL-10 levels were increased ($P < 0.05$); the levels of TLR4, p-P65, p65, p-PI3K and p-AKT were decreased ($P < 0.05$); the percentage (%) of neutrophil infiltration in lung tissues were decreased ($P < 0.05$). Compared with DHA treatment group, in Lenti-TLR4-OE+DHA treatment group, the levels of TLR4, p-P65, p65, p-PI3K and p-AKT levels were increased ($P < 0.05$); the percentage (%) of neutrophil infiltration in lung tissues were increased ($P < 0.05$).

Conclusions: Dihydroartemisinin could inhibit TLR4, reduce the activation level of NF- κ B/PI3K/AKT signaling pathway, enhance lung function and inhibit airway inflammation in CIH obese asthmatic mouse models.

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The Impact of Early Morning Training on Subjective and Objective Sleep Indices Among Male Collegiate Rowers in Japan

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Introduction: Sleep deprivation is a well-known factor that can impair cognitive, physical, and technical aspects of athletic performance. Despite increasing awareness, many athletes-especially those with early morning training schedules-are unable to secure sufficient and high-quality sleep. Although sleep patterns in athletes have been studied, little research exists on Japanese collegiate rowing athletes. Moreover, few studies have combined both subjective and objective methods to assess sleep. This study aimed to clarify the sleep characteristics and lifestyle habits of male collegiate rowing athletes in Japan, focusing on the impact of early morning training on sleep.

Materials and methods: This study included 11 male collegiate rowers from University A, observed over 7 consecutive days in June 2025. Participant characteristics were as follows: height 172.8 ± 5.1 cm, age 20.3 ± 0.9 years, weight 71.0 ± 4.3 kg, and BMI 23.8 ± 0.9 . Collected data included demographic factors (e.g., caffeine and alcohol consumption, nap habits), subjective sleep quality using the Japanese version Pittsburgh Sleep Quality Index (PSQI-J) and sleep diaries, objective sleep data from wrist-worn actigraphy, dietary records, and training schedules.

Results: During the 7-day observation period, participants had morning training starting at 5:00 a.m. on three weekdays, 6:30 a.m. on two weekend days, and two weekdays without morning training. 63.6% of athletes were classified as having poor subjective sleep quality ($5.5 < \text{PSQI-J score}$; mean $\text{PSQI-J} = 6.9 \pm 2.6$).

Actigraphy data showed that Total Sleep Time (TST) was significantly shorter on nights before weekday morning training compared to nights before weekdays without morning training and nights before weekend ($p < 0.01$). Furthermore, bedtime on nights before weekday morning training was more than two hours earlier than that on nights before weekday without morning training.

One-way ANOVA revealed significant differences across training categories in some objective sleep indices. TST and total minutes in bed on nights before weekday morning training were significantly shorter than those on nights before weekdays without morning training ($p < 0.01$) and on weekend nights ($p < 0.01$). The number of awakenings was also significantly smaller on nights before weekday morning training than that on nights before weekend training ($p = 0.014$). Subjective TST from sleep diaries showed similar results: significantly shorter on nights before weekday morning training than on the other nights ($p < 0.01$). TST was significantly shorter in objective data than in subjective sleep diary data ($p < 0.001$, 0.013 , and < 0.001 for weekday with morning practice, weekday without morning practice, and weekend, respectively). On the other hand, subjective sleep latency was significantly longer ($p = 0.003$), and sleep efficiency was significantly higher ($p = 0.017$) than those in objective measures respectively.

Conclusions: This study found that early morning training reduced TST and caused earlier bedtime among Japanese male collegiate rowers. Many athletes reported poor subjective sleep quality and discrepancies were observed between subjective and objective sleep assessments. These findings highlight the importance of using both types of measures when evaluating sleep and suggest that training schedules should be reviewed to support adequate sleep and recovery.

The Impact of Obstructive Sleep Apnea on Patients with Ischemic Stroke

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Introduction: Obstructive sleep apnea (OSA) is a widespread but often overlooked condition that contributes to cardiovascular diseases, including ischemic stroke (IS). While its role in increasing stroke risk is well documented, its influence on stroke severity and recovery remains an area requiring further exploration. Additionally, there is ongoing debate regarding the extent to which continuous positive airway pressure (CPAP) therapy improves stroke outcomes. This study examines how OSA affects IS severity and prognosis while evaluating the therapeutic value of CPAP.

Materials and methods: This retrospective cohort study analyzed 200 patients diagnosed with both IS and OSA. Participants were divided into two groups: those who did not receive CPAP therapy or were non-compliant with treatment (Group A, n=119) and those who adhered to and consistently used CPAP therapy (Group B, n=81). A control group of 104 IS patients without OSA was also assessed. Stroke severity was measured using the National Institutes of Health Stroke Scale (NIHSS), and functional independence was evaluated using the modified Rankin Scale (mRS). OSA was diagnosed through respiratory polygraphy or full polysomnography. Statistical analyses included chi-square tests, Mann-Whitney U tests, and multivariate logistic regression, with significance set at $p < 0.05$.

Results: Patients with IS and OSA experienced significantly greater stroke severity compared to those without OSA ($p < 0.05$). Within the OSA cohort, individuals in the CPAP group demonstrated improved functional outcomes compared to non-CPAP users when analyzed as a continuous variable (Mann-Whitney U test, $p = 0.003$). However, when assessing functional independence as an endpoint (mRS 0-2), the difference did not reach statistical significance ($p = 0.17$). The most frequently observed comorbidities among OSA patients were hypertension (92.6%), smoking (55.5%), dyslipidemia (55.5%), type 2 diabetes (40.7%), and atrial fibrillation (33.3%), all of which correlated with increased stroke severity. Multivariate analysis confirmed that the presence of OSA, especially when combined with multiple cardiovascular risk factors, more than doubled the likelihood of experiencing a more severe stroke, with an odds ratio (OR) of 2.68 (95% CI, $p < 0.05$).

Conclusions: OSA is a key contributor to increased stroke severity and poorer recovery outcomes, particularly in patients with multiple cardiovascular risk factors. CPAP therapy demonstrated measurable improvements in overall functional recovery, yet this benefit did not reach statistical significance in terms of full functional independence within three months. These findings underscore the importance of early OSA detection and intervention in stroke patients. Given its potential role in rehabilitation, CPAP therapy should be further explored as a targeted intervention to enhance post-stroke recovery and reduce recurrent cerebrovascular events.

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The Impact of Obstructive Sleep Apnea on the Temporal Coupling of NREM Sleep Oscillations in Schizophrenia

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Introduction: Dysfunctional connectivity between and within brain regions is a proposed mechanism underlying schizophrenia. Electroencephalographic (EEG) abnormalities during Non-Rapid Eye Movement (NREM) sleep such as reduced and dysmorphic sleep spindles and slow oscillations (SO) have been described in schizophrenia. The temporal coupling between these oscillations is thought to reflect the coordination and integrity of the thalamocortical circuitry and has been associated with functions of memory with uncoupling being associated with aspects of ageing and cognitive decline. We investigated 1) whether a reduction in the temporal relationship between SO and spindles are observed in the schizophrenia group reflecting thalamocortical dysfunction. Individuals with schizophrenia are often given obesogenic medication, increasing the likelihood of developing obstructive sleep apnea (OSA). We further explored 2) whether this oscillatory coupling would be further impaired in those with OSA and 3) the association of coupling with cognitive performance.

Materials and methods: We measured high-density EEG overnight polysomnography in two groups 1) people with schizophrenia (n=31) and 2) without schizophrenia (n=31) across a range of OSA severity, defined by the Apnea Hypopnea Index (AHI), matched for age and sex. Participants completed a cognitive test battery before and after sleep. Sleep spindles and SO events were automatically detected using previously reported algorithms across 256 High-density EEG. The mean phase angles (phase preference), the resultant vector length (coupling strength) and coupling density of each co-

occurring event between SO and sleep spindles were measured. To reduce bias of phase angle concentration, participants with >10 events were included in the analyses. General linear models were used to test the association between coupling metrics and the effects of group and AHI and the interaction between the two and the association of cognition in the form of a procedural memory task (finger tapping) with the main effect of the coupling strength, group and AHI.

Results: We observed group differences in the schizophrenia group showing reduced coupling density compared to controls ($b = -0.06$, $p < 0.01$) this was not further impaired if they had comorbid OSA ($b = 0.00$, $p = 0.65$). Across both groups, we did not see a difference in coupling strength (resultant vector length) (Group $\times$ AHI $b = 0.00$, $p = 0.82$). No significant differences were observed in overnight improvement on the procedural memory motor task and AHI ($b = -0.11$, $p = 0.31$). Worse task performance was observed in the schizophrenia group ($b = -22.37$, $p = 0.01$) but not significant if these patients had OSA ($p = 0.05$).

Conclusions: Our results show that the coupling of SO and sleep spindles in schizophrenia may be preserved and is not impacted by the presence of OSA. The schizophrenia group show additional activation in the centroparietal regions which may possibly reflect a compensatory mechanism. This interpretation might suggest that recruitment of function with adjacent areas could be due to local network dysfunction in the frontal brain regions in schizophrenia. Future work will aim to understand the effects on these dynamics following CPAP treatment in schizophrenia and explore the potential of SO-spindle coupling reflecting functional connectivity and its interaction with other brain regions.

The Impact of Sleep Perception on Cognitive Functions in Adults with Objectively Sufficient Sleep Duration

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Introduction: Misperception of sleep is characterized by significant discrepancy between objective and subjective sleep measurement (SOSD). Most of the previous studies primarily focus on clinical insomniac population and suggested that individual with greater SOSD tend to perform poor in cognitive performance. However, this relationship remains understudied in healthy community samples, especially those with normal sleep duration. It is unclear whether subjectively perceived shorter sleep could have influential effect on their cognitive performance. This study aim to investigate the association between SOSD and cognitive functioning in community-dwelling adults with objectively sufficient sleep (6–8 hours per night). Additionally, we examine whether this association extends beyond elderly populations, thereby exploring potential age-independent effects of sleep misperception on cognition.

Materials and methods: This is a cross-sectional study of 196 participants (mean age: 50.3 ± 14.5 years; 71.9% female) recruited from the community. They were invited to complete a set of sleep-related questionnaires, 7-day sleep diary and actigraph. Participants with at least three valid days of actigraphy data and obtained an average of objectively measured TST between 6–8 hours were included. The subjective-objective sleep discrepancy (SOSD) was calculated by subtracting objective TST (actigraphy-derived) from subjective TST (self-reported from sleep diaries). Cognitive function was assessed using the Hong Kong Montreal Cognitive Assessment (HK-MoCA) for global cognition and n-back tasks for working memory. The n-back tasks measured accuracy (percentage of correct responses), discriminability (d' prime, reflecting participants' sensitivity to distinguish items presented n trials back), and reaction time for correct responses. Multiple linear regression models examined associations between SOSD and cognitive parameters, controlling for age and sex.

Results: There are significant positive associations observed between SOSD and multiple cognitive parameters. For those who underestimated their sleep duration, they tend to have poor cognitive performance across several domains including lower global cognition measured by HK-MoCA ($\beta = 0.006$, 95% CI: 0.001–0.011, $P = 0.018$), poor working memory demonstrated by lower accuracy on both 1-back ($\beta = 0.028$, 95% CI: 0.008–0.046, $P = 0.005$) and 2-back tasks ($\beta = 0.03$, 95% CI: 0.001–0.058, $P = 0.04$), slower mean reaction time of correct responses during 1-back task ($\beta = -0.0003$, 95% CI: -0.0005–0.000007, $P = 0.012$), and impaired working memory as indicated by greater d' prime

values for both 1-back ($\beta=0.001$, 95% CI: 0.0001–0.002, $P=0.037$) and 2-back tasks ($\beta = 0.002$, 95% CI: 0.001–0.004, $P=0.001$).

Conclusions: Our findings suggest that underestimation of sleep duration (shorter self-reported than objectively measured TST) is associated with poorer global cognition and working memory performance in community-dwelling adults who have objectively sufficient sleep. SOSD may be an important factor in understanding sleep-cognition relationships. Future research should explore the bidirectional causal mechanisms underlying this association—whether cognitive dysfunction leads to sleep perception discrepancies or if reducing sleep discrepancies could enhance cognitive function. Understanding this relationship may provide new avenues for cognitive interventions and improved sleep assessment strategies.

The Impact of Sleep Quality on Suicidal Ideation One Year Later: The Mediating Role of Emotional Distress and the Moderating Effect of Social Support in Korean Adults

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Introduction: Sleep disturbances are a well-established risk factor for suicidal ideation, yet longitudinal evidence on the psychological mechanisms and protective moderators involved in this association remains limited, particularly among Asian populations. This study aimed to investigate whether emotional distress variables—hopelessness, depression, anger, and loneliness—mediate the longitudinal relationship between sleep quality and suicidal ideation, and whether perceived social support moderates this pathway.

Materials and methods: A total of 941 Korean adults (mean age = 45.0, range = 19–84) participated in a two-wave panel survey conducted during the COVID-19 pandemic, with baseline data collected in 2020 and follow-up in 2021. At Time 1 (T1), participants completed the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality, the Beck Hopelessness Scale (BHS), the Center for Epidemiologic Studies Depression Scale (CES-D), the Dimensions of Anger Reactions-5 (DAR-5), and the UCLA Loneliness Scale (ULS) to measure emotional distress, and the Multidimensional Scale of Perceived Social Support (MSPSS) to assess perceived social support. Suicidal ideation was measured at Time 2 (T2) using the Depressive Symptom Inventory–Suicidality Subscale (DSI-SS). Parallel mediation and moderation analyses were performed using standardized regression models with 5,000 bootstrap resamples.

Results: Poor sleep quality at T1 significantly predicted greater suicidal ideation at T2 ($\beta = .24$, $p < .001$). This relationship was partially mediated by increased levels of hopelessness (indirect effect $\beta = .10$, $p < .001$), anger ($\beta = .05$, $p = .003$), and loneliness ($\beta = .06$, $p = .002$), while depression did not show a significant mediating effect ($\beta = .03$, $p = .098$). Furthermore, perceived social support moderated the direct association between sleep quality and suicidal ideation (interaction $\beta = -.11$, $p = .004$), such that the relationship was strongest among individuals with low social support (slope $\beta = .38$, $R^2 = .13$) and weakest in the mid-range support group ($\beta = .18$, $R^2 = .03$).

Conclusions: These findings indicate that poor sleep quality increases suicidal ideation over time through elevated emotional distress, particularly hopelessness and loneliness. Moreover, social support serves as a protective factor that buffers this effect. Suicide prevention efforts should incorporate both sleep-focused interventions and strategies to enhance emotional regulation and social connectedness.

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The influence of Obstructive Sleep Apnea on the peripheral blood supply of wound Healing: Microscopic and Macroscopic findings. Insights from a Murine Model. Preliminary results

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Introduction: Obstructive Sleep Apnea (OSA) is associated with chronic inflammation, intermittent hypoxia, and oxidative stress, all of which may impair wound healing. Wound healing is a complex biological process that occurs in four overlapping but distinct stages: hemostasis, inflammation, proliferation, and remodeling. The study is about wound healing under the condition of OSA.

Objectives: To assess macroscopic wound healing progression (wound size reduction over time). and to evaluate microscopic histological differences (inflammation, fibrosis, epidermal thickness, and angiogenesis).

Materials and methods: Our model is a combination of two validated models. An osa model, in which mice were exposed to chronic intermittent hypoxia (60 events/hour: 20 sec at 5% O₂ followed by 40 sec of room air) for 6 hours/day over a period of 2 weeks. And a control group who kept in normal air conditions. Wound healing model, we created a two full-thickness wounds on mouse dorsum. Silicone splints are then centered and fixed with immediate-bonding adhesive and nylon sutures. 10 mice randomly assigned into two groups: OSA group who kept in IH for a period of 4 week in total and a healthy group. On day 14, we created 2 wounds on mice dorsum. We observed and studied wound healing process for another 2 weeks until total closure. Wounds were photographed every 2-3 days from day 0 till day 14 and wound closure rates were measured. Histological samples collected at day 0 and day 14. H&E staining were performed to assess fibrosis and inflammation. Quantitative evaluation of: Mononuclear inflammatory cell count, Fibroblast count, Capillary count and Epidermal thickness have been done. All mice were held the same conditions.

Results: Macroscopic findings, percentage of closure rate over time indicates a slower healing rate in OSA group especially at the first week. The mean total closure time was at day 12 for healthy and 14 for OSA mice. Half closure time was at day 6 for healthy and 8 for OSA mice. We also calculated the area under curve which reflect the total wound burden over time. Higher AUC values indicate delayed healing, reflecting wounds that remain open for longer durations. Microscopic evaluation on day 0, there was no notable differences between the two samples. The epidermis was significantly thicker on day 14. The count of mononuclear cells, fibroblast and capillaries were significantly higher in OSA.

Conclusions: OSA negatively affects both the macroscopic and microscopic aspects of wound healing. The delayed closure and altered histological profile in OSA-exposed mice suggest that patients with OSA may be at higher risk for impaired or prolonged wound healing. These findings highlight the importance of screening for and managing OSA in patients undergoing surgery or those with chronic wounds. Further research focus on the molecular pathways underlying IH-induced immune dysregulation to identify potential therapeutic intervention that may mitigate the negative impact of intermittent hypoxia on tissue repair.

The Intraslow Fluctuation of Sigma Power During Sleep in Young Individuals with Schizophrenia

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Introduction: Reductions in sleep spindles—brief oscillatory events characteristic of Non-Rapid Eye Movement sleep—have been proposed as a biomarker of schizophrenia. While prior research has largely emphasized spindle quantity, emerging work has begun to examine their temporal dynamics

across the night. In healthy individuals, spindles fluctuate on an infraslow timescale of approximately 50 seconds, alternating between periods of elevated and reduced spindle activity. This rhythm, termed the infraslow fluctuation of sigma power (ISFS), is modulated by noradrenergic input from the locus coeruleus and has been implicated in the temporal coordination of markers of arousal and memory reactivation during sleep. Given the well-documented spindle deficits, altered noradrenergic function, and disruptions in sleep continuity and memory in schizophrenia, the ISFS represents a promising target for investigation in this clinical population. Additionally, childhood and adolescence, periods characterized by brain maturation and increasing vulnerability to psychiatric illness, may offer a critical window for detecting early circuit-level disruptions in rhythms like the ISFS, with potential implications for earlier diagnosis and intervention.

Materials and methods: Sleep electroencephalographic data were analyzed from individuals with either Childhood-Onset Schizophrenia (N = 17) or Early-Onset Schizophrenia (N = 11), aged 9 to 21 years, alongside age- and sex-matched healthy controls (N = 56). Features of the ISFS, including its presence and strength, sleep spindle density, and clinical characteristics were examined.

Results: This study found that the ISFS is present in young individuals with Childhood-Onset Schizophrenia and Early-Onset Schizophrenia. Both the presence and strength of the ISFS were reduced in central-parietal regions in individuals with schizophrenia compared to healthy controls. These ISFS alterations were observed in both the groups with schizophrenia despite differences in sleep spindle density and clinical characteristics.

Conclusions: These findings suggest that the ISFS is present but attenuated in young individuals with schizophrenia, reflecting reduced infraslow clustering of sleep spindles. Moreover, they underscore the potential relevance of spindle timing—in addition to quantity alone—for advancing pathophysiological models of schizophrenia, and highlight its promise as a target for early detection and intervention.

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The Infraslow Fluctuation of Sigma Power During Sleep: Links to Markers of Arousal and Memory Reactivation Across Development

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Introduction: Sleep poses considerable evolutionary challenges—reduced responsiveness and increased vulnerability to external threats. A growing hypothesis emerging from rodent studies suggests that sleep is not solely a vulnerable state, but rather orchestrates a balance between environmental awareness and critical protected periods for memory reactivation. One candidate mechanism underlying this balance is the infraslow fluctuation of sigma power (ISFS), a rhythm reflecting the periodic clustering of sleep spindles over 10–100 seconds. In rodents, the ISFS segments non-rapid eye movement sleep into alternating fragile periods, characterized by heightened responsiveness to external input, and protected periods, during which sensitivity to the environment seems to be reduced and memory reactivation processes seem to be enhanced. However, how arousal and memory reactivation markers are organized within the human ISFS—and whether this rhythm is conserved during development—remains unclear.

Materials and methods: The ISFS was characterized in a sample of healthy individuals aged 8 to 26 years (N = 154) using high-density sleep electroencephalography. Two complementary approaches were applied. First, spectral analysis confirmed the presence of the ISFS and quantified key parameters, including peak frequency, variability, and strength across development. Second, electrophysiological markers of arousal and memory reactivation were examined to determine whether they were temporally organized within the ISFS from childhood to young adulthood.

Results: Findings demonstrate that sigma power fluctuates on an infraslow time scale from childhood to young adulthood. The peak frequency, variability, and strength of the ISFS increase from childhood and early adolescence to late adolescence and young adulthood. Notably, across all age groups, markers of arousal and memory reactivation are consistently organized within the ISFS, occurring most frequently during the spindle-rich peak.

Conclusions: The consistent presence and organization of the ISFS from childhood to young adulthood suggest that this rhythm is intrinsic to human sleep. Developmental increases in its frequency, variability, and strength highlight adolescence as a dynamic window of change. By elucidating how arousal and memory-related processes are temporally organized within the ISFS in humans, this study provides a foundation for future research into how sleep supports cognitive development and arousal regulation. These insights may inform interventions aimed at promoting healthy sleep trajectories and understanding disruptions across childhood and adolescence.

Acknowledgments: We would like to thank the participants for their time and data contributions, as well as their families for their support. We also appreciate the invaluable advice and support from everyone in Reto Huber's lab and Miriam Gerstenberg's research group throughout this project.

The Intersection of EEG and Oculometry: Insights from 5-MeO-DMT-Induced Effects on Sleep and Brain States

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Introduction: Understanding the intricate dynamics between sleep and wakefulness is crucial for advancing our knowledge of sleep and brain function. Psychedelics, particularly 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), offer a unique lens through which to explore these dynamics by inducing a state of "paradoxical wakefulness." This phenomenon is characterised by the coexistence of cortical slow-wave activity (SWA), typically associated with non-rapid eye movement (NREM) sleep, alongside behavioral wakefulness and heightened autonomic arousal. By integrating electroencephalography (EEG) with oculometry, we aim to investigate the neurophysiological underpinnings of this state and its implications for understanding sleep-wake regulation.

Materials and methods: Our study employed freely moving mice (C57BL6, n=27) to investigate the effects of 5-MeO-DMT on brain states. We conducted chronic frontal and occipital EEG and electromyography (EMG) recordings in n=21 mice. In subsets of these animals, local field potentials were recorded in the visual cortex with multiunit activity (n=4), or 4-hour sleep deprivation was performed (n=8). Additionally, pupil dilation and eye movement were recorded in freely moving animals following 5-MeO-DMT injection (n=11), with a subset also undergoing chronic EEG and EMG recordings (n=5). Each animal received an intraperitoneal injection of 5-MeO-DMT (5mg/kg) or saline at either the beginning of the light period or after sleep deprivation. Vigilance states were manually scored in 4-second epochs using SleepSign, and electrophysiology data were analysed with Matlab.

Results: Administration of 5-MeO-DMT induced a dissociated state of arousal characterised by increased cortical SWA, resembling NREM sleep, co-occurring with behavioral wakefulness and pronounced pupil dilation. EEG spectral analysis revealed significant regional differences, with increased SWA and steepened spectral slopes in frontal regions, contrasting with decreased theta power in occipital regions. These findings suggest a hybrid brain state regulated globally yet exhibiting localised dynamics. Pupillometric data confirmed heightened sympathetic activation, highlighting the decoupling of cortical slow-wave generation from traditional autonomic regulation. Notably, sleep deprivation did not significantly impact the power of 5-MeO-DMT-induced slow waves, suggesting these effects are not entirely reliant on sleep regulatory pathways. Further analysis of sleep showed no alteration of SWA in the sleep episodes following the injection, and 24 to 48-hours monitoring suggest potential long-term alteration of REM sleep homeostasis.

Conclusions: Our study demonstrates that 5-MeO-DMT induces a novel state of paradoxical wakefulness, offering a unique window into the mechanisms underlying the regulation of sleep-wake processes. By integrating EEG and oculometry, we reveal complex brain-behavior relationships that challenge traditional frameworks of vigilance states. These findings not only advance our understanding

of how psychedelics modulate brain states but also provide a translational framework for exploring their therapeutic potential in sleep disorders and depression. Moreover, the innovative use of EEG-oculometry integration highlights its potential for advancing both basic science and clinical applications. **Acknowledgments:** This work was funded by BBSRC UKRI DPhil Scholarship and the 2020 *In Vivo* skills award, and supported by Beckley Psytech

The neural network involved in torpor maintenance and arousal in mice

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Introduction: Torpor is an energy-saving strategy characterized by a reduction in metabolism and body temperature (T_b) that allows many species to survive harsh winters. While our understanding of the neural network involved in torpor onset has recently advanced in mice, a species that exhibits daily torpor, little is known about the network underlying the arousal from torpor. Since arousal entails a steep rise in T_b and the Raphe Pallidus (RPa) is a key brain area in the central control of thermogenesis, the present study aimed at investigating the neural network which is active during the arousal from torpor in mice, focusing on its projections to the RPa.

Materials and methods: Female C57BL/6J mice (18–23g), acclimated to T_a 21°C, underwent surgery under general anesthesia for the injection of a monosynaptic retrograde tracer (Cholera Toxin B, CTb) into the RPa and the implantation of a wireless T_b monitoring device. After a 7-day recovery, mice were acutely food-deprived to induce torpor. The three following experimental conditions were studied: i) Torpor (n=7): mice were euthanized during stable torpor, at least three hours after its onset; ii) Arousal (n=6): mice were euthanized 90 min. after the onset of the arousal from stable torpor; iii) Torpor-resistant (n=4): normothermic mice, in which torpor did not occur despite fasting, were euthanized at least three hours after fasting onset (fasted controls). At the end of the experiment, the brain was harvested for immunohistochemical quantification of cFos, and CTb expression.

Results: The results showed widespread cFos expression in the brain across the different experimental conditions. Notably, within the thermoregulatory network, in the Dorsomedial Hypothalamus (DMH) overall activity was significantly increased in “Torpor” compared to “Torpor-resistant” animals, and significantly decreased in “Arousal” compared to “Torpor” ones. However, no significant changes in the activity of neurons projecting from the DMH to the RPa was observed among the three conditions. Moreover, the number of active cells projecting from the Preoptic Area (POA) to the RPa was significantly lower in “Torpor” compared to “Torpor-resistant” animals, and further significantly decreased in “Arousal” compared to “Torpor” ones. The analysis of the brainstem and hypothalamic structures involved in wake promotion showed that overall activity was increased in both “Torpor” and “Arousal” animals compared to “Torpor-resistant” ones in both Dorsal Raphe and Locus Coeruleus, but no differences between “Torpor” and “Arousal” animals were observed.

Conclusions: These findings highlight the role of the central thermoregulatory network in torpor regulation, with distinct levels of activity during its maintenance and the subsequent arousal. In particular a specific role in the process of arousal from torpor seems to be played by the DMH, as previously observed for torpor induction, and by the POA, with a specific reference to its functional relationship with the RPa.

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The relationship between rest-activity rhythms and Mild Cognitive Impairment in elderly community dwellers in a hyper-aged society

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Introduction: As the aging population increases worldwide, the number of people with dementia and MCI has surged over the past decade. Recent studies have highlighted the association between disruption of daily resting activity rhythms (RAR) and cognitive decline and the development of dementia in the elderly. This study aimed to determine the relationship between RAR and MCI among elderly individuals living in a highly aged community.

Materials and methods: We analyzed the data from 177 participants aged 65 and over (77.4 ± 5.8), classified into MCI group ($n=62$) and Non-MCI group ($n=115$). Demographic data for each participant included age, gender, education, height, weight, usual walking speed, grip strength, Kihon checklist and cognitive function (Word list memory, Trail making test version A & B, and symbol digit substitution task). During the collection period, participants wore a triaxial accelerometer (Active Style Pro; Omron) on their waist for up to seven days to assess the following RAR parameters. These included interdaily stability (IS), which quantifies the stability of the 24-hour rhythm between different days; intradaily variability (IV), describing the fragmentation of the rhythm; and relative amplitude (RA), representing the robustness of a 24-hour rest-activity cycle. Additionally, the activity counts during the least active 5-hour period of the 24-hour cycle (L5) - likely representing hours during sleep - and during the most active 10-hour period (M10) were calculated. In the statistical analysis, independent t-tests were performed to compare demographic data, psychosomatic function tests, and RAR parameters between groups. Next, to examine the factors associated with MCI, a binomial logistic regression analysis was performed. The presence or absence of MCI was used as the dependent variable, with various assessment results serving as independent variables. Finally, activity plots for each group were created and compared using the independent t-tests. Statistical analyses were performed using SPSS Version 27.0 for Windows (SPSS Inc., IL, USA), with a significance level set at $p = 0.05$. This study was approved by the Ethics Committee of the Akita University Graduate School of Medicine (approval No. 3050).

Results: Results of the between-group comparison showed that the Non-MCI group performed significantly better in terms of age ($p < 0.01$), usual walking speed ($p < 0.01$), and the Kihon Checklist ($p < 0.05$). Similarly, the Non-MCI group performed significantly better in IV for RAR parameters ($p < 0.01$). Next, as a result of binomial logistic regression analysis, the Non-MCI group had a significant association with usual walking speed (Odds ratio, 0.142; 95% Confidence Interval [95%CI], 0.046-0.505; $p = 0.001$), IV (Odds ratio, 7.372; 95 % CI, 0.042-0.473, $p = 0.012$). Finally, the comparison of the 24-hour activity profiles for each group revealed significant differences in the mean activity at times 5 ($p < 0.05$), 6 ($p < 0.05$), 13 ($p < 0.01$), and 14 ($p < 0.01$).

Conclusions: In conclusion, this study suggested that older adults with MCI generally exhibit reduced walking speed and impaired rhythmic fragmentation. The study further indicated that periods of inactivity during early morning hours and post-noon may be indicative of an increased risk for developing MCI.

The Role of Endothelin Receptor Antagonist on Pulmonary and Systemic Hemodynamic Alteration in Chronic Intermittent Hypoxic Animal Model

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Introduction: Obstructive sleep apnea (OSA) has contributed critical risk factor for unfavorable cardiovascular outcome. On the basis of published evidence made the patients with OSA have potential to develop systemic and pulmonary vascular consequences, on the pathological basis of

chronic intermittent hypoxia (CIH) is found to be major responsible. CIH is associated with the alteration of sympathetic nervous system activation and cardiovascular variability. Furthermore, the involvement of endothelin in CIH animal model was previously demonstrated and provide the rationale to examine the crucial effect of bosentan (endothelin receptor antagonist) on hemodynamic alteration in CIH animal model (OSA model).

Materials and methods: Eighteen Wistar rats were randomly divided into three groups (six rats in each group), including one control group and two CIH-groups. Rats in both CIH-groups were exposed to alternating cycles of normoxia (30 seconds at 21% O₂) and hypoxia (30 seconds at 10% O₂), repeated continuously for 8 h/day during the light phase for 14 days. Bosentan 100 mg/kg/day was given to one CIH-group throughout the study. At the end of study, hemodynamic and histopathological studies were completely performed.

Results: Hemodynamic assessment revealed a significant reduction in mean right ventricular systolic pressure (RVSP) in the bosentan-treated CIH group compared with both the control and untreated CIH groups ($p < 0.001$). In the untreated CIH group, mean heart rate (HR) was significantly higher than in the control and bosentan-treated CIH groups ($p = 0.011$). Bosentan treatment significantly reduced mean HR and increased heart rate variability compared with the other groups. Histopathology showed no significant difference in percent wall thickness of pulmonary arterioles among groups. However, neomuscularization of small pulmonary arterioles was significantly greater in the CIH group (muscularized arterioles per 50 total vessels; $p = 0.042$). Right ventricular hypertrophy (RVH), expressed as the RV-to-(LV + septum) weight ratio, was also significantly higher in the CIH group compared with the other groups ($p = 0.015$).

Conclusions: Chronic intermittent hypoxia has been demonstrated to induce pulmonary and systemic hemodynamic alteration, recognized complication of OSA. The beneficial effect of endothelin receptor antagonist on systemic vascular parameters (heart rate and heart rate variability) and pulmonary vascular parameters (pulmonary arterial pressure, right ventricular hypertrophy and pulmonary vascular remodeling) suggest their potential as a therapeutic option for the cardiopulmonary consequences associated with OSA.

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The Role of the Orexin System in Modulating Human Energy Metabolism

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Introduction: There is a crosstalk between regulators of energy metabolism and control of sleep / wakefulness. A molecule, such as orexin, acts on regulation of energy metabolism and sleep. Sleeping energy metabolism is related to sleep architecture, and orexin receptor antagonist may affect energy metabolism as well as sleep. Suvorexant, an approved orexin receptor antagonist, targets the orexin-mediated wake-promoting system and offers an alternative mechanistic approach to treating insomnia by promote NREM and REM sleep. Effect of suvorexant on sleeping energy metabolism in human is not known, while stimulating effects of orexin system on energy expenditure was reported in animal studies. However, effect of suvorexant on oxidized substrate is inconsistent among the animal studies.

Materials and methods: In this placebo-controlled, double-blind, crossover intervention study, metabolic rate of 14 healthy young male without sleep problems was measured using whole-room indirect calorimetry, during which polysomnographic recording of sleep was made. The participants consumed suvorexant (20 mg) or placebo 10 minute before bedtime.

Results: Fat oxidation was significantly increased while protein catabolism was suppressed without changes in energy expenditure by suvorexant during sleep although energy expenditure and carbohydrate oxidation remained unchanged. In semi-parametric regression analysis, suvorexant revealed lower energy expenditure during WASO than placebo. Interestingly, sleep architecture was not notably affected by suvorexant. The only difference in sleep architecture between 2 trials was observed in REM sleep and NREM stage 1. Both trials indicated changes in the dominant sleep stage, beginning with SWS followed by a transition to REM sleep.

Conclusions: The present study suggests that the effect of suvorexant on energy metabolism was not mediated by major changes in sleep architecture. The orexin system may affect fat oxidation independent of its roles in sleep regulation in humans [*iScience* 27: 110212, 2024]. We also conducted an on-going study with a narcoleptic patient, who has no detectable levels of orexin. We observed that patients with narcolepsy appeared to have a lower energy expenditure both during the daytime (awake state, assessed by polysomnographic) and at bedtime compared to healthy individual. It is probably due to the activation of the orexin system in healthy subject during daytime.

Toward an animal model for stress-related sleep bruxism

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Introduction: In sleep medicine, sleep bruxism (SB) is considered one of the sleep-related movement disorders. It is characterized by excessive masticatory muscle activity (MMA) during sleep. However, it is hard to diagnose or treat SB effectively because the definitive pathological process has not been clarified. An animal model of SB is still lacking. Stress is known as a risk factor of SB. Inescapable foot-shock (IFS) is a well-known stressor in rats, resulting in sleep alteration and sympathetic activation. This study aimed to investigate the effects of acute IFS on sleep architecture, sympathetic activity, and MMA during the sleep-wake cycle.

Materials and methods: Experiment 1: Twelve male SD rats were evenly divided into sham and IFS groups. Rats in the sham group were placed in the IFS box from 10:00 to 10:30 without electrical stimulation, while rats in the IFS group received stimulation at 1.0 mA for 0.5 s with 30 s intervals. After that, the open field test was conducted for 15 min. Then, rats were perfused at 12:00, and immunohistochemistry staining was performed to quantify cfos-positive cells in stress-related areas, including the locus coeruleus and nuclei in the limbic system (i.e., prelimbic cortex, bed nucleus of the stria terminalis, paraventricular hypothalamic nucleus, and central nucleus of amygdala) between groups.

Experiment 2: In ten rats, electrodes were implanted for electroencephalogram (EEG), electromyogram (EMG) of the neck and masseter muscles, and electrocardiogram (ECG) to monitor sleep, MMA, and heart rate (HR). Sleep recordings were performed over 2 consecutive days during the dark phase (10:00 – 22:00). On day 1, rats were placed in the IFS box from 10:00 to 10:30 without stimulation, and recording was conducted from 11:00 to 18:00. On day 2, IFS was delivered before recording. All signals were analyzed in 10-s epochs. Vigilance states (wakefulness [W], non-rapid eye movement [NREM], and rapid eye movement [REM] sleep) were manually scored. Transient arousals during NREM were defined as no more than 3 consecutive epochs of W. Delta EEG power during NREM was calculated using Fast-Fourier transformation. HR was determined by R-wave counts. MMA was assessed by normalizing integrated EMG activity during chewing after artifact subtraction. EMG data of masseter muscle were log-transformed for Gaussian Mixture Model analysis, identifying two components: muscle contraction and muscle tone.

Results: Experiment 1: Time in the central zone was significantly less in the IFS group than in the sham group, confirming the stress condition. cfos-positive cells in stress-related areas were significantly increased after acute IFS.

Experiment 2: W significantly increased after acute IFS, while NREM and REM sleep decreased. Delta power ratio during NREM sleep also significantly decreased. HR during W and NREM sleep significantly increased. EMG activity of masseter muscle significantly increased during W, NREM sleep, especially within transient arousals. Furthermore, the mean value of muscle contraction and muscle tone during W and NREM sleep increased significantly after acute IFS.

Conclusions: IFS stress induced the elevation of MMA during the sleep-wake cycle, associated with cortical and sympathetic activation.

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Transient effect of a short recovery sleep after total sleep deprivation on attention network test (ANT) and driving performance

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Introduction: Sleep debt is a common constraint in professional environments such as the military, flight crew, or emergency responders. This phenomenon impacts cognitive performance, particularly attention, with an increased risk of accidents at work or during commutes. Sleep opportunities are sometimes available during work, but they are often limited in duration, and their effectiveness is still debated. The aim of our study is to objectify the impact of a short night of recovery sleep (3h TIB) after a 40h total sleep deprivation on attentional performance and driving.

Materials and methods: 41 healthy subjects (20 females, 32 +/- 7 years) participated in a 4-day / 4-night protocol, after eliminating a pre-existing sleep debt by actimetry. D1 corresponded to the day after a baseline night (BS, 8h TIB from 23:00 to 07:00), D2 the day after total sleep deprivation (TSD), D3 the day after a short recovery night (R1, 3h TIB from 23:00 to 02:00) and D4 the day after a longer recovery night (R2, 8h TIB from 23:00 to 07:00). Subjects performed an Attention Network Test (ANT) every day at 10:00 (sessions M1, M2, M3 and M4), as well as at 04:00 on TSD and R1 nights (sessions N1 and N2), allowing the assessment of reaction time (RT), reaction time variability (SD-RT), accuracy, as well as alerting, orienting and executive index. They then performed a 45-min session on a basic monotonous driving simulator, during which the number and duration of line crossings were measured, as well as the standard deviation of lateral position (SDLP). All parameters were analyzed using a mixed linear model, with a Bonferroni corrected post-hoc analysis. Simple linear regression assessed the prediction properties of each ANT parameters on driving performance.

Results: A significant session effect was noted on global ANT parameters (RT, SD-RT, accuracy) and driving performance ($p < 0.001$ for all). Post-hoc analyses confirmed the improvement in accuracy ($p = 0.01$), RT ($p < 0.001$), and SD-RT ($p < 0.001$) after the 3-hour sleep opportunity (N2 session) compared to the day after TSD (M2 session), even during a less favorable circadian phase. However, this improvement did not persist over time, with further deterioration during the M3 session. Similar results were observed for the number of line crossings and SDLP ($p = 0.003$), with no effect in the duration of line crossings ($p = 0.999$). Regarding the ANT indexes, only the executive index demonstrated a session effect ($p = 0.014$), without post-hoc analyses being conclusive. SD-RT emerged as the ANT parameter most predictive of driving outcomes. Performance returned to baseline after the 8-hour recovery night.

Conclusions: A 3-hour night of recovery after total sleep deprivation demonstrated short-term benefits for attentional performance and driving, thus confirming the value of these short sleep opportunities after a shift, for example. However, this benefit did not last over time. SD-RT, which reflects the instability of vigilance, appeared to be the most predictive parameter of driving performance, highlighting the notable interest of this parameter in ecological studies.

Urethane as an unparalleled anesthetic model for sleep cycling

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Introduction: Urethane (ethyl carbamate), unlike other common veterinary anesthetics, allows for sleep-like spontaneous alternations between NREM-like and REM-like forebrain activity states which makes it a powerful model for sleep cycles, and for sleep itself. The similarity across sleep and urethane anesthesia was shown for electrographic elements, physiological correlates, timing, pharmacology, brain correlates, as well as dependence on both ambient temperature and oxygen. The implication is that urethane anesthesia, unlike any other anesthetic studied to date, is the most complete model for the full spectrum of natural sleep. Furthermore, it suggests that the pharmacological mechanisms by which urethane acts to produce unconsciousness likely has broad similarities with the physiological regulation of sleep itself. If this is true, then drugs known to affect the sleep cycle should affect state alternations under urethane.

Materials and methods: Male Sprague-Dawley rats were anesthetized with i.v. urethane and local field potential recordings were made from frontal cortex and the hippocampus. Stable rhythmic alternations

with consistent proportions of activated (REM-like) and deactivated (non-REM-like) activity were recorded before i.v. or intra-cerebro-ventricular administrations of adenosine, caffeine, N6-cyclopentyladenosine (CPA), or CGS 21680. We characterized the effects by tracking any changes in the spectral features of both states and their alternations in the local field potential recordings.

Results: Adenosine, whether administered peripherally or centrally, promoted the deactivated (NREM-like) state. In contrast, caffeine (again either peripherally or centrally) decreased the NREM-like state. Interestingly, the A2A agonist CGS 21680 promoted the NREM-like state in a fashion similar to adenosine itself, but the A1 agonist CPA appeared to abolish state alternations altogether by promoting a highly deactivated state characterized by prominent and dense slow-waves.

Conclusions: Adenosine and both its agonists and antagonists have parallel effects across urethane anesthesia and natural sleep. This is further evidence supporting the validity of the urethane model of sleep itself.

Validation of a new patch-based polysomnography by Onera for patients with obstructive sleep apnea syndrome - an equivalence study

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Introduction: This study investigates the equivalence of a novel patch-based polysomnography system, the Onera STS-PSG, for the analysis of obstructive sleep apnea syndrome. OSAS is a major health problem worldwide, affecting an estimated one billion people and causing various cardiovascular and metabolic complications. Traditional polysomnography, while effective, is costly and requires a hospital setting, which limits its accessibility. The Onera STS-PSG offers a more user-friendly and accessible alternative and could revolutionize sleep diagnostics by enabling at-home monitoring.

Materials and methods: The study was conducted with a patient cohort of 74 individuals, with STS-PSG and inpatient PSG measurements performed simultaneously, during the initial diagnostic night. The main characteristics to be investigated in the study are AHI, ODI and PLM. The secondary characteristics are N1, N2, N3 and REM sleep. Due to technical reasons, the awake stage could not be measured. The results were presented graphically using boxplots and distribution diagrams. The correlation was determined using Pearson's R and the equivalence was determined using a two one-sided tests (TOST) procedure.

Results: Pearson correlation analysis revealed correlations for AHI (0.92), ODI (0.7), PLM (0.76), N1(0.7), N2 (0.49), N3 (0.76) and REM (0.72), indicating strong agreement between the measurement results. The TOST procedure showed that the STS-PSG measures the parameters AHI, PLM, N1, N2, N3 and REM equivalently to the PSG system based on a) the given sample, b) the TOST procedure, c) the predefined equivalence limits and d) the alpha level (Bonferroni-corrected $\alpha=0.00714286$). The only parameter whose equivalence was rejected is the ODI, but this can be attributed to the fact that the transcutaneous oxygen measurement is not performed via the fingers, as in conventional PSG, but via the forehead.

Conclusions: This study found equivalence of the Onera-STS-PSG compared to traditional polysomnography. Particularly for the values AHI, PLM, N1, N2, N3, and REM, it was found that the STS-PSG measures were equivalent to in-lab PSG. For the value ODI, it was shown that the measurement was not equivalent, but this could be attributed to measurement differences. Any potential complications were easy to solve during application, as the system is user-friendly and logic-based. In future patients, especially technical barriers can be avoided as reading and configuring the pods will continue to be under the responsibility of specialized personnel. This is another step towards comfort and practicality for those affected.

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What Influences Sleep Study Completion Among People with HIV in Care?

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Introduction: People with HIV (PWH) face a substantially higher prevalence of obstructive sleep apnea (OSA) than the general population, with rates ranging from 20% to 70% in PWH compared to 9% to 38% in the general population. Fatigue, also highly prevalent in PWH, can be caused by OSA. Despite its high prevalence and potential impact on quality of life, OSA is underdiagnosed in PWH and sleep studies to diagnose OSA are underutilized. We investigated characteristics associated with sleep study performance among PWH engaged in care.

Materials and methods: Demographic and clinical characteristics, comorbidities, and patient-reported outcomes (e.g., fatigue) were compared between PWH at Madison Clinic at the University of Washington who underwent sleep studies between 2008 and 2023 and those who did not. We used relative risk regression models to estimate associations between HIV factors (CD4 count and viral load) and fatigue and having received a sleep study, adjusted for demographic and clinical characteristics and comorbidities.

Results: Among 3,977 PWH, 165 (4%) completed a sleep study. Compared to those who did not receive sleep studies, PWH who underwent sleep studies were slightly older (mean age 50 vs. 48), had higher BMI, and better immunity, with higher mean CD4 cell counts (635 vs. 568) and greater HIV viral suppression (97% suppressed vs. 85%). PWH who received a sleep study had a greater prevalence of comorbidities such as diabetes (16% vs. 11%), dyslipidemia (41% vs. 27%), and hypertension (47% vs. 32%), as well as self-reported bothersome fatigue (79% vs. 55%). In adjusted models, we observed a 2.90-times (95% CI: 1.90-4.43) greater likelihood of having received a sleep study among PWH with bothersome fatigue, compared to those without.

Conclusions: We observed that PWH who received a sleep study had better HIV control (higher CD4 count and viral suppression), and a greater burden of fatigue and comorbidities often associated with OSA, than PWH who did not receive a sleep study. This suggests that healthcare providers and patients are more likely to prioritize evaluation of OSA in this context.

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Behavior, Cognition and Dreaming

A 365 nights: a yearlong electroencephalography investigation into human sleep in natural conditions

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Introduction: We spend approximately one-third of our lives asleep, yet sleep quality and patterns vary significantly from day to day due to both external and internal factors. Despite this, our understanding of the multiday variations remains limited, primarily because of challenges in obtaining reliable, ultralong-term EEG data outside clinical settings. Recent advancements in subcutaneous electroencephalography (sqEEG) technology have now made ultralong-term home sleep recordings feasible. In this study, we explored multiday periodicities of sleep and examined the role of internal and external cues such as seasonal variation, day of the week, holidays, weather conditions and physical activity.

Materials and methods: Continuous sqEEG home recordings from 20 subjects (F=11) over a one-year period (349.95±28.69 days). We accurately determined the total sleep time (TST); durations and proportions of sleep stages (N1, N2, N3, REM); sleep onset and offset; sleep latency; REM latency; sleep efficiency; and wake after sleep onset (WASO). These parameters were evaluated longitudinally to identify seasonal variations, differences based on the day of the week, holidays, and birthdays using a permutation test. Additionally, sleep parameters were correlated with meteorological data, including

daily maximum and minimum temperatures, sunlight exposure, cloud coverage, humidity, and precipitation levels. Data from participants' smartwatches were also extracted to correlate daily step counts and exercise duration and timing with sleep characteristics. Differences between males and females were examined, with a secondary analysis conducted specifically among female participants to correlate sleep parameters with menstrual cycle phases. Beyond these external influences, we also assessed intrinsic multiday cyclic patterns within each subject over intervals of 10, 30, and 60 days.

Results: We found that 70-100% of subjects displayed individual patterns of multiday internal cyclicality in TST, sleep latency, REM latency and WASO over periods of 10, 30 and 60 days (average phase locking value = [0.09-0.22]), not influenced by external factors. We observed that sleep was affected by the season with a lower TST, and WASO during the summer ($p < 0.05$). During summer, the proportion of REM sleep decreased and the proportion of N3 sleep increased ($p < 0.05$). In addition, sleep onset time increased and sleep offset time decreased in these months ($p < 0.05$). The daily weather influenced certain sleep parameters, with temperature and sunlight displaying negative correlation with TST which was driven by a decrease in N2, N3 and REM ($r = [-0.2 -0.52]$), while cloud coverage was positively correlated with sleep onset, offset and WASO ($r = [0.2 0.37]$). Subjects went to sleep and woke up later during weekends ($p < 0.05$), and the sleep stage composition changed with more N2 sleep on the weekends as well as shorter sleep latencies ($p < 0.05$). In addition, sleep onset and offset time were shifted later during national holidays ($p < 0.05$), with significantly lower TST and REM duration during New Year's Eve ($p < 0.05$). Males and females displayed overall similar trends, however, their seasonal trends differ in timing.

Conclusions: Sleep is a complex phenomenon that is shaped by both internal mechanisms and external influences. Seasonal changes, daily weather patterns, and specific days of the week or year can temporarily alter its natural intrinsic multiday cycle.

Actigraphy-Estimated Sleep and Circadian Rhythms and the Risk of Delirium Following Traumatic Brain Injury during hospitalization

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Introduction: Delirium is a serious neuropsychiatric syndrome characterized by inattention, disorganized thinking, and fluctuations in alertness, commonly occurring in patients after head trauma. The role of disrupted circadian rhythms in the development of delirium following traumatic brain injury (TBI) remains unclear. This study aimed to evaluate sleep metrics and circadian rhythm disturbances as potential risk factors for TBI-related delirium.

Materials and methods: This is a secondary data analysis from our previous translation research, which validated the Traditional Chinese version of the Confusion Assessment Method (CAM-TC). Participants admitted to a neurosurgery ward wore actigraphy devices for up to 7 days to monitor sleep metrics and circadian rhythms. Cox regression hazard models were used to associate sleep and circadian rhythm metrics with the incidence of TBI-related delirium.

Results: The study included 100 participants, with a median age of 68.5 years, and 10 of them developed delirium during their hospitalization. Sleep parameters, such as total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset, sleep fragmentation index, and activity index, showed no significant differences between those with and without delirium ($p > 0.05$). However, significant differences were observed in circadian rhythm metrics between the non-delirium and delirium groups: relative amplitude (0.57 vs. 0.29, $p < 0.05$) and autocorrelation (0.20 vs. 0.08, $p < 0.05$). Adjusted Cox regression analysis indicated that none of the circadian rhythm metrics were significant risk factors for post-TBI delirium.

Conclusions: This study is the first to examine sleep parameters and circadian rhythms in TBI patients during the acute stage of hospitalization. Patients with TBI-related delirium exhibited more variability in circadian rhythms, suggesting a disruption in their regular rest-activity patterns. Further research should focus on delirium prevention strategies that maintain circadian stability through nursing interventions and ensure a stable clinical environment.

An experimental study on the effects of railway vibration on sleep and the blood metabolome

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Introduction: Environmental vibration, such as from freight railway lines, and its impact on the sleep and health of exposed populations remains poorly understood. The small number of existing epidemiological studies show associations between chronic railway vibration exposure at night and subjective sleep disturbance and increased prevalence of diabetes. However, the pathophysiological pathways in the vibration-sleep-disease relationship remain unclear. We here investigate the mechanisms that may link vibration-induced sleep disruption with the development of metabolic disease.

Materials and methods: N=22 young, healthy individuals (mean±SD 22.6±2.2 years; 9 women) spent five consecutive nights in acoustically isolated bedrooms. Following one acclimation night and one quiet control night for baseline measurements, nights three through five included synthesised railway vibration exposure at 0.5 mm/s, 0.7 mm/s or 0.9 mm/s each night. Vibration was accompanied by low level railway noise (35 dB $L_{AF,max}$). Sleep was measured with unattended ambulatory polysomnography and questionnaires. Questionnaires further included items on restoration and positive and negative affect. Sleep fragmentation was assessed using the Odds Ratio Product (ORP), a continuous measure of sleep depth and stability derived from EEG spectral power. To identify metabolic consequences of nocturnal vibration, we collected daily blood samples for NMR metabolomics analysis. We measured cognitive performance across multiple domains with a daily computerised test battery. All data were analysed in linear mixed models (random subject effect) adjusted for sex and time in study. Event-related analyses of vibration-induced sleep disturbance were further adjusted for time of night and sleep at train onset.

Results: Vibration induced event-related elevations ORP in a dose-dependent relationship (main effect $p<.0001$), ranging from a maximal change relative to pre-event baseline of $\Delta ORP=0.08$ at 0.5 mm/s to $\Delta ORP=0.20$ at 0.9 mm/s. In all vibration conditions there was a reduction in stage N3 sleep of 18-24 minutes relative to the control night ($p<.001$), although there was no significant difference between the three vibration nights ($p>.01$ for all post-hoc comparisons). Relative to Control, nights with railway vibration were associated with elevated concentrations of glucose (z-scores +0.51 to +1.03, $p=.020$), glutamine (z-scores +0.53 to +1.12; $p=.021$), and acetic acid (z-scores +0.05 to +0.80; $p=.005$); and lower concentrations of proline (z-scores -0.07 to -1.02; $p=.003$), and ornithine (z-scores -0.66 to -1.08; $p=.040$). However, these metabolic effects did not survive statistical correction for multiple hypotheses testing. Vibration nights were followed by reduced perceived sleep quality ($p=.023$), lower positive affect ($p=.007$) and increases in all measures of vibration-induced sleep disturbance compared to the quiet Control (all $p<.0001$). No significant effects of vibration were found for cognitive performance.

Conclusions: Railway vibration impaired physiological and subjective sleep. These novel findings extend beyond previous research, and may implicate metabolic upregulation or reduced metabolite uptake after vibration-induced sleep fragmentation in the exposure-sleep-disease relationship. Although a promising first step, these findings need to be reproduced in larger and more representative studies before firm conclusions can be drawn.

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Association of sleep trajectories and depressive symptoms among rural-dwelling older adults

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Introduction: The relationship between sleep duration trajectories and depressive symptoms in China remains inconclusive. We aimed to explore this relationship over 9 years among rural-dwelling older adults in China.

Materials and methods: We used prospective data from participants of the MIND-China study. Sleep durations were measured at 3 study visits between 2014 and 2021 using the Pittsburgh Sleep Quality Index. We used group-based trajectory modeling to identify four sleep trajectories: "Normal stable," "Short stable," "Decreasing," and "Extremely short stable." Depressive symptoms were measured using 15-item Geriatric Depression Scale in 2023. Linear regression was used to relate sleep trajectories with depressive symptoms, and stratified analysis was conducted by physical activity, and hypertension.

Results: The mean [SD] baseline age was 68.60 [3.49], and 59.8% were female. Compared with having "Normal stable," having "Decreasing" (95% CI=0.06, 1.14) or "Extremely short stable" (95% CI=0.03, 1.46) sleep trajectories were associated with an increased likelihood of depressive symptoms. Compared to those who do not participate in physical activity, having "Decreasing" (95% CI=0.45, 1.91) sleep trajectories among participants who engage in physical activity were associated with an increased likelihood of depressive symptoms. Compared to those without hypertension, having "Decreasing" (95% CI=0.17, 1.47) or "Extremely short stable" (95% CI=0.44, 2.20) sleep trajectories in participants with hypertension were associated with an increased likelihood of depressive symptoms.

Conclusions: Prolonged exposure to decreasing and extremely short sleep duration may result in worse depressive symptoms. This association differed by physical activity, and hypertension.

Associations Between Dream and Nightmare Frequency, Respiratory Parameters, and Psychiatric Symptoms in Obstructive Sleep Apnea Syndrome

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Introduction: This study investigated the frequency of dreams and nightmares in patients with obstructive sleep apnea syndrome (OSAS) and examined their associations with respiratory parameters and psychiatric symptoms.

Materials and methods: A total of 3512 patients (1021 women; mean age: 53.45 years) who underwent polysomnography for suspected sleep apnea were included. Each participant completed standardized questionnaires assessing nightmare severity (Disturbing Dream and Nightmare Severity Index, DDNSI) and nightmare impact (Nightmare Effect Survey, NES). Reported dream frequency was categorized as: none, infrequent (≤ 1 /week), sometimes (2–3/week), and frequent (> 3 /week).

Results: The frequent dreaming group demonstrated significantly lower apnea–hypopnea index (AHI) ($p < 0.001$) and oxygen desaturation index (ODI) ($p = 0.011$). In contrast, this group showed significantly higher scores on the Beck Depression Inventory (BDI, $p < 0.001$) and Beck Anxiety Inventory (BAI, $p < 0.001$). DDNSI and NES scores were positively correlated with BDI ($r = 0.430$ and $r = 0.419$, respectively; $p < 0.001$) and BAI ($r = 0.476$ and $r = 0.382$, respectively; $p < 0.001$). However, neither DDNSI nor NES scores were significantly associated with AHI or ODI.

Conclusions: Despite prior hypotheses linking oxygen desaturation to dream content, our findings suggest an inverse association between respiratory parameters and dream frequency. Increased dream and nightmare frequency were more strongly associated with depressive and anxiety symptoms, highlighting the potential role of psychiatric comorbidity in dream activity among patients with OSAS.

Associations between multidimensional sleep health and cognitive continuum among Chinese older adults: a population-based study

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Introduction: To explore the relationship between multidimensional sleep health (MDSH) and cognitive continuum.

Materials and methods: This population-based study included 5272 participants living in rural China. Sleep parameters were measured using the Pittsburgh Sleep Quality Index (PSQI). The multidimensional sleep health (MDSH) score (ranges 0-5) was generated based on satisfaction, alertness, timing, efficiency, and duration, with a higher score indicating healthier sleep. Subjective cognitive decline (SCD) was assessed using three questions regarding memory problems. Mild cognitive impairment (MCI) and dementia were diagnosed according to the internationally recognized criteria. Linear regression analysis examined the correlation between MDSH and cognitive domains. Logistic regression models examined the relationship between MDSH and SCD, MCI and its subtypes, all-cause dementia, and AD. We also conducted stratified analyses based on APOE genotype.

Results: Of all participants, 2913 (55.3%) were diagnosed with SCD, 1310 (24.8%) with MCI, and 181 (3.4%) with all-cause dementia, including 117 (2.2%) with Alzheimer's disease (AD). As a continuous variable, MDSH was positively associated with memory (multivariate-adjusted β coefficient = 0.05, 95% confidence interval [CI] = 0.03 to 0.07), language (0.03; 0.01 to 0.05), attention (0.04; 0.02 to 0.06), executive function (0.02; 0.004 to 0.04), and the global cognitive function (0.04; 0.02 to 0.05). Each unit increase in MDSH was associated with an decrease in SCD (multivariate-adjusted odds ratio = 0.75, 95% CI = 0.69 to 0.82), MCI ((0.90; 0.85 to 0.96), amnesic mild cognitive impairment (aMCI) (0.88; 0.83 to 0.94), all-cause dementia (0.81; 0.71-0.93), and AD (0.76; 0.64 to 0.89), and similar associations were observed when MDSH was used as a categorical variable (0-1/2-3/4-5). In addition, we found that MDSH (as a continuous variable) interacted with SCD, all-cause dementia, and AD in the APOE genotype (p for interactions = 0.018, <0.001, and 0.018, respectively).

Conclusions: MDSH was significantly associated with the cognitive continuum. And the effects vary by APOE genotype.

Awakenings as Mnemonic Gateways for Dream Memory: Traits or States

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Introduction: The arousal-retrieval model posits that nightly awakenings act as gateways for the consolidation of dream memories. Leveraging longitudinal and naturalistic sleep datasets, this study disentangles trait and state effects to identify awakening characteristics that predict dreaming awareness (DA), content reconstruction (CR), and overall dream recall frequency (DRF).

Materials and methods: We analyzed two datasets: All Recallers ($n = 711$) included ZMax EEG recordings from 8,010 nights and DRF questionnaires across three assessment waves over one year, and High Recallers ($n = 94$) included nightly Fitbit sleep data and next-morning DA and CR from 2,383 nights. Separate mixed-effects models were conducted for each dataset, controlling for age and gender. Model 1 included subjective and objective awakening frequencies as predictors. Model 2 included short (<1 min), medium (1–2 min), and long (>2 min) awakening frequencies. Model 3 adjusted Model 2 for sleep duration and final sleep stage. Fixed effects were decomposed into between-person means and within-person deviations (scaled). False discovery rate (FDR) correction was applied.

Results:

In All Recallers, 28% of DRF variance was within-person (wave-to-wave), but not explained by within-person predictors. Between-person objective ($\beta \approx 0.16$, $p = .01$) and subjective ($\beta \approx 0.28$, $p < .001$) awakening frequencies explained 7% of the variance. Specifically, between-person long awakening frequency predicted DRF ($\beta = 0.23$, $p = .013$), even after adjusting for sleep duration and final sleep stage. Age negatively predicted DRF ($\beta = -0.18$, $p = .008$), while female gender positively predicted it ($\beta = 0.25$, $p = .008$).

In High Recallers, most variance in DA (68%) and CR (83%) was within-person (night-to-night). Within-person objective (DA: OR ≈ 1.18 , $p = .01$; CR: OR ≈ 1.25 , $p < .001$) and subjective (DA: OR ≈ 1.32 , $p < .001$; CR: OR ≈ 1.21 , $p < .001$) awakening frequencies explained 5% of the variance. Short and medium frequencies predicted CR (ORs ≈ 1.12 – 1.14 , $p < .05$), with a marginal effect for long awakenings ($p = .07$). These effects were accounted for by sleep duration (CR: OR = 1.27, $p = .003$) and REM sleep

before final awakening (DA: OR = 1.64, $p = .006$; CR: OR = 1.68, $p < .001$). Between-person predictors did not explain the remaining variance. Female gender positively predicted DA (OR = 2.20, $p = .03$).

Conclusions: Individuals who habitually experience and remember longer awakenings tend to have higher dream recall frequency. High recallers are more likely to report a dream and its content after longer nights of sleep, when they wake up from REM sleep and experience and remember more awakenings. These findings support the arousal-retrieval model and clarify that awakenings function differently at the trait and state levels: long awakenings distinguish high from low recallers, and in high recallers, any length of awakening in a specific night increases the likelihood of remembering the dream content the next morning.

Balancing the specificity and generalisability of learning: roles of sleep and wakefulness

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Introduction: Training on a visual task can lead to significant improvements in visual performance, a phenomenon known as visual perceptual learning. Notably, these improvements are not fixed and may extend beyond the online phase, when individuals actively engage in training, and continue into the offline phase during sleep. The continued improvements during sleep, achieved without conscious effort or behavioural engagement, highlight the brain's ability to harness visual perceptual learning through neural plasticity. However, how wakefulness and sleep coordinate to optimise visual perceptual learning remains poorly understood. It is also unclear whether online learning during wakefulness and offline learning during sleep rely on the same or distinct neural circuits.

Materials and methods: Fifty healthy young adults (ages 18–31) participated in two sub-studies, with $N = 30$ in Study 1 and $N = 20$ in Study 2, examining the learning of visual features (orientation or luminance) in a backward masking task. Participants were randomly assigned to morning (8 AM) or evening (8 PM) learning sessions, followed by test sessions immediately after (0 hours), 12 hours, and 24 hours post-learning. In each sub-study, training occurred in the lower-left visual field, and test sessions included ten tasks probing cross-location, cross-feature, and cross-task generalisation. The temporal spacing between sessions allowed us to isolate the effects of sleep versus wake on learning. Visual stimuli were presented on a high-refresh-rate monitor under controlled lighting; eye position was monitored, and task accuracy was adaptively thresholded.

Results: Here, we found that during wakefulness, visual improvements were confined to the specific visual feature and visual field location being trained. By contrast, during sleep, these improvements generalized to other visual features and visual field locations. Both local and generalised improvements persisted for weeks after training had ended.

Conclusions: Our findings suggest that wakefulness and sleep jointly balance the specificity and generalisability of visual perceptual learning: wakefulness enhances specificity by prioritising training-related visual signals and driving targeted improvements in visual performance, while sleep fosters generalisability, making the learned visual skills more adaptable.

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Cardiovascular Risk Biomarkers Moderate the Associations Between Different Sleep Stage Durations and Global Cognition in Older Black Adults

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Introduction: Sleep disturbances increase the risks of cognitive impairment and dementia, but the underlying mechanisms to elucidate this remain elusive. Prior studies have shown that each distinctive sleep stage has unique health effects and impacts on cognitive function, but current literature has been mixed regarding which sleep stages affect overall cognition. Mixed findings may be in part due to prior work not testing potential moderating factors that are independently known to influence both sleep

disturbances and cognitive performance, such as cardiometabolic health. Therefore, we tested whether cardiometabolic biomarkers moderated the relationships between the proportions of the different stages of sleep (light (N1/N2) sleep, slow-wave sleep (SWS, or N3), and rapid eye movement (REM) sleep) and global cognition.

Materials and methods: Thirty-five older Black adults aged ≥ 55 years (77.1% female) who resided in New York and Florida were invited to participate in a two-phased, prospective, observational study. Participants continuously wore a Fitbit Inspire 2 HR wrist-worn device for seven consecutive days; the FitBit measured sleep and wake activity, including the total minutes of the light, SWS, and REM sleep nightly. Serum cardiovascular risk biomarkers (total cholesterol:high-density lipoproteins (TC:HDL-c) ratios, low-density lipoproteins (LDL) cholesterol, triglycerides, and high-sensitivity C-reactive protein) and insulin resistance markers (glucose, insulin, glycated hemoglobin) were quantified. Participants completed the Montreal Cognitive Assessment-BLIND (MoCA-BLIND) task. Hierarchical moderated regression analysis was utilized to test whether cardiometabolic biomarkers moderated the links between different sleep stage durations and global cognition.

Results: TC:HDL-c ratios moderated the links between the proportions of light ($\Delta R^2=0.22$, $\Delta F=9.95$, $p=0.004$) and REM ($\Delta R^2=0.26$, $\Delta F=12.55$, $p=0.002$) sleep stage durations and MoCA scores. Additionally, LDL and triglycerides values moderated the associations between the proportion of REM sleep duration and MoCA scores ($\Delta R^2=0.19$, $\Delta F=8.62$, $p=0.007$ and $\Delta R^2=0.21$, $\Delta F=9.64$, $p=0.005$, respectively). Insulin resistance did not moderate the relationships between the proportions of any sleep stage durations or total sleep duration and MoCA scores.

Conclusions: These data suggest that the associations between the proportions of light and REM sleep obtained, but not SWS, and global cognition differ by cholesterol levels in older Black adults. Future work should investigate these links longitudinally using larger, more representative samples.

Chronotype and time-of-day in inhibitory control performance among healthy adults – a randomised cross-over trial

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Introduction: Chronotype reflects stable individual differences in the preferred timing of behavioural activity, productivity, and sleep. Morning-types tend to function best earlier in the day, whereas evening-types perform better later. Prior research shows that cognitive performance – particularly executive functions such as working memory and attention – varies by chronotype and time-of-day; however, their effects on distinct components of inhibitory control remain unclear. Inhibitory control is widely studied using the Go/No-Go Task (GNG) and Stop-Signal Task (SST), which assess action restraint (withholding a prepotent response) and action cancellation (halting an ongoing response), respectively. This study investigated whether chronotype and time-of-day modulate GNG and SST performance in healthy adults.

Materials and methods: This randomised crossover study recruited adults aged 18-30 years from Melbourne, Australia, who self-identified as either morning- or evening-types. Participants completed demographic questionnaires including the Pittsburgh Sleep Quality Index and the Munich Chronotype Questionnaire. Sleep was monitored via actigraphy and sleep diaries prior to testing. Each participant completed two laboratory sessions in randomised counterbalanced order (stratified by chronotype and gender): one in the morning (08:00-10:00h) and one in the afternoon/evening (16:00-18:00h). At each session, participants completed subjective sleepiness ratings, the Psychomotor Vigilance Task (PVT), GNG and SST. Commission error rates and stop-signal reaction times were the primary outcomes. Linear mixed models assessed effects of chronotype, time-of-day and covariates (subjective sleepiness and objective vigilance), with Bayesian equivalents used to calculate likelihood ratios. This study was approved by the Human Research Ethics Committee (2022-333).

Results: The final sample included 59 healthy adults (55.9% female; mean age: 22.1 ± 3.77 years), with 29 identified as morning-types and 30 as evening-types. At baseline, groups differed significantly in sleep-corrected mid-sleep timing (mean $\pm$ SD: morning-types = 2.98 (0.96); evening-types = 5.76 (1.14); $p < .001$), but not in age, gender, or sleep quality. No significant effects of chronotype ($BF_{01} = 2.717$), time-of-day ($BF_{01} = 3.742$) or their interaction ($BF_{01} = 34.623$) were observed for GNG performance. In contrast, SST performance showed a significant main effect of chronotype ($BF_{10} = 1.645$), with

evening-types exhibiting longer SSRTs than morning-types, independent of time-of-day. No significant effects of time-of-day ($BF_{01} = 2.999$) or interaction ($BF_{01} = 6.078$) were found for SST performance. Subjective sleepiness and objective vigilance were not significant covariates for either task.

Conclusions: These findings highlight the importance of considering the multifaceted nature of inhibitory control, suggesting its subcomponents are differentially sensitive to chronotype. Evening-types may experience greater difficulty cancelling initiated responses, regardless of time-of-day. This work underscores the significance of accounting for subjective and objective alertness in contexts where inhibitory control is critical. Future work should integrate biological circadian markers and neurophysiological measures to provide a more comprehensive understanding of individual variability in inhibitory control across the day.

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Clinical significance criteria in the ICSD and DSM sleep disorder classifications: A content overlap analysis using the Jaccard index

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Introduction: Both the International Classification of Sleep Disorders (ICSD) and the Sleep-Wake disorders section of the Diagnostic and Statistical Manual (DSM) emphasize the importance of clinical judgment in distinguishing the normal from the pathological in sleep medicine. The DSM-IV (1994) introduced the Clinical Significance Criterion (CSC) to standardize this judgment and enhance diagnostic reliability.

Materials and methods: We conduct a theoretical and historical content analysis of CSC presence, frequency, and formulation in the diagnostic criteria of sleep disorders. Three steps were undertaken: i) selecting main sleep disorder classifications and main disorders within them, ii) systematically extracting CSC-related content, and iii) analyzing the evolution of CSC presence through quantification (Jaccard Index) and visualization (radar plots).

Results: The DSM-5-TR includes CSC in five of nine main sleep disorders, compared to two in the ICSD-3-TR (Circadian Rhythm Sleep-Wake Disorder and Nightmare Disorder). The overlap between DSM-5-TR and ICSD-3-TR is moderate (Jaccard Index = 0.40). The overlap between DSM versions is higher (0.53). Conversely, ICSD revisions exhibit minimal similarity (0.16). Radar plots reveal a gradual increase in CSC use within ICSD versions.

Conclusions: These results highlight the variable application of CSC in sleep disorder classifications. Universal CSC inclusion may not be essential, but systematic discussion of its potential use can help refine diagnostic criteria. This refinement is important for accurately diagnosing sleep disorders and better differentiating the normal from the pathological, a major challenge in sleep medicine.

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Cognitive Impairment and Its Impact on Gait Parameters and Physical Function in the Elderly

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Introduction: Cognitive impairment is a major issue in aging societies, as it significantly reduces quality of life and independence. It is closely associated with gait disturbances and an increased risk of falls. Subtle changes in gait patterns can serve as early indicators of cognitive decline, highlighting the importance of preventive approaches through physical function assessment. Therefore, this study aimed to analyze differences in gait characteristics and physical function according to cognitive status based on gait data.

Materials and methods: A total of 65 participants from the KLOSDOM Gangwon Living Lab at Yonsei University Wonju Severance Christian Hospital were included. Cognitive function was assessed using the Short Blessed Test (SBT), which evaluates memory, concentration, orientation, and ability to perform activities of daily living. Gait and physical performance were evaluated using the N Steps Walking Test (NSWT), Timed Up and Go Test (TUGT), Five Times Sit to Stand Test (FTSST), and Single Leg Stance Test (SLST). Participants were divided into two groups based on SBT scores: cognitively normal ($SBT \leq 8$; $n = 36$; mean age = 70.7 ± 5.7 years; male: 41.7%) and cognitively impaired ($SBT \geq 9$; $n = 19$; mean age = 74.4 ± 6.2 years; male: 47.4%).

Results: The analysis revealed that the cognitively normal group showed significantly higher values in L_Toe (%) from NSWT_L (left side), R_Final Score from NSWT_R (right side), and Total Score of the SPPB ($p < 0.05$). Conversely, they demonstrated significantly lower values in L_Mid (%) from NSWT_L, R_Heel (%) from NSWT_R, and time (seconds) required to complete the TUGT and FTSST ($p < 0.05$), indicating overall superior gait and physical performance.

Conclusions: These findings suggest that cognitive impairment is closely related to changes in gait characteristics. This study provides foundational evidence for the use of physical function and gait analysis as a potential tool for early detection and prevention of cognitive decline in older adults.

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Comparing home and laboratory morning dream reports

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Introduction: Serial awakenings in a laboratory setting are the gold standard for collecting multiple dream reports over a night. However, there is an ongoing debate about the ecological validity of dreams reported in sleep laboratories. Since serial awakenings sample different sleep stages and times of night, it is unclear how many differences between home and lab dreams are due to the setting or the different sampling methods. Therefore, in this study, we compare morning dream reports collected in the laboratory after an adaptation night (with no serial awakenings) with home dream reports from the same participants to examine how the sleep environment affects the characteristics of recalled dreams.

Materials and methods: A total of 107 healthy young adults ($M = 23.79$ years, $SD = 3.02$; 75 female) participated in the study. Each participant completed one adaptation night in a sleep laboratory with a morning dream report and completed a sleep diary at home over 4 weeks. 2,064 morning dream reports were analyzed ($n=121$ adaptation night, $n=1,943$ home). Each report was rated by the participant for different sensory modalities, lucidity, vividness, arousal, valence, as well as how accurate and complete they think their report is. We used linear mixed models and generalized linear mixed models for the analysis with participant as random effect.

Results: Home dreams were rated by participants to contain more visual, tactile, gustatory, and vestibular perceptions (all $p < 0.008$) than dreams in the laboratory, with no difference in auditory, olfactory, and somatosensory perceptions (all $p > 0.06$). Home dreams were rated by participants as having higher arousal and being more vivid (both $p < 0.004$), while there was no difference in dream valence and lucidity (both $p > 0.3$). Additionally, participants remembered the dreams with the same accuracy and completeness in both settings (both $p > 0.1$).

Conclusions: These findings suggest that the sleep environment impacts the phenomenology of recalled dreams. Dreams reported from home were rated as more vivid, emotionally arousing, and rich in sensory detail, pointing to a potential blunting of dream experiences in the laboratory setting.

However, other aspects of dreaming, such as lucidity and valence, seem to be unaffected by the setting. An alternative interpretation is that the lower dream recall frequency at home leads to a memory bias favoring more vivid or emotional dreams. This might be due to lower adherence to immediately reporting their dreams after waking up. In contrast, the higher recall rate in the laboratory may reflect priming or increased motivation. These results underscore the importance of considering the research setting when interpreting dream data.

Correlation between Cognitive Dysfunction and the Integrity of the Dopaminergic System in Neurodegeneration: A Narrative/Comprehensive Review

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Introduction: Dopaminergic dysfunction has been implicated in the cognitive impairment observed in neurodegenerative disorders, particularly in α -synucleinopathies such as Parkinson's disease (PD). Although positron emission tomography (PET) studies have suggested a link, findings remain inconsistent. In clinical settings, dopamine transporter (DAT) scans are more commonly used, assessing presynaptic dopaminergic integrity, particularly in the striatum. Given that nigrostriatal degeneration is central to Parkinsonian syndromes, it has been hypothesised that this may contribute to cognitive deficits. However, the specific role of dopaminergic dysfunction in cognitive decline remains uncertain, with evidence suggesting a multifactorial aetiology extending beyond the dopaminergic system.

This review aims to examine the relationship between DAT imaging and cognitive performance in individuals with α -synucleinopathies.

Materials and methods: A systematic review was conducted following PRISMA guidelines. Databases searched included Medline, Ovid, APA, and EMBASE, limited to English-language studies published since 2000. Eligible studies assessed the association between cognitive performance and dopaminergic imaging (DAT SPECT or PET) in neurodegenerative disorders. After screening, 22 studies met the inclusion criteria.

Results: In Parkinson's disease (17 studies), 8 reported a positive association between DAT binding and cognitive performance, particularly within the domains of attention and executive functioning. Four studies identified a relationship with memory performance, whereas five found no significant correlation. In the single available study of individuals with REM sleep behaviour disorder (RBD), no association was reported. Among the seven studies focusing on dementia with Lewy bodies (DLB), three observed correlations with specific cognitive domains (awareness, reaction time, and simultaneous processing speed), while four reported null findings. The two studies which compare alpha-synucleinopathies and Alzheimer's disease (AD) populations found the link between DAT binding and cognition only in the A-syn population. Notably, the majority of studies reporting no correlation relied solely on brief cognitive screening measures, whereas studies using more comprehensive neuropsychological assessments were more likely to identify significant associations.

Conclusions: This review highlights the heterogeneity of findings regarding dopaminergic dysfunction and cognitive impairment in α -synucleinopathies. Where significant associations were identified, they were typically observed in studies employing detailed neuropsychological testing, suggesting that cognitive deficits may, at least in part, reflect dopaminergic system dysfunction within the nigrostriatal pathway. However, the overall evidence base remains mixed, and the contribution of dopaminergic deficits should be viewed in the context of broader, multi-system involvement. Further longitudinal and multimodal studies are warranted to delineate the specific role of dopaminergic pathways in the cognitive decline observed across synucleinopathies.

Correlation between iron deposition and cognitive function in OSA patients of different severity levels based on quantitative susceptibility mapping

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Introduction: Excessive cerebral iron deposition has been implicated in cognitive dysfunction across various neurological disorders. This study investigates severity-dependent patterns of cerebral iron accumulation in OSA using quantitative susceptibility mapping (QSM) and examines their potential role in mediating cognitive impairment.

Materials and methods: The study cohort comprised 139 OSA patients stratified by severity (68 mild-moderate [OSA-M: apnea-hypopnea index (AHI) 5-30 events/hour]; 71 severe [OSA-S: AHI>30]) and 48 healthy controls (HC). All participants underwent polysomnography, neurocognitive assessment using the Montreal Cognitive Assessment (MoCA), and 3T MRI with multi-echo gradient echo sequences for QSM analysis. Whole-brain voxel-wise comparisons were conducted to characterize iron deposition patterns. Correlation analysis and mediation models evaluated associations between OSA severity, regional iron content, and cognitive performance.

Results: As the severity of OSA patients increases, iron content increased in the left central anterior gyrus, left medial superior frontal gyrus, right central anterior gyrus, right medial superior frontal gyrus, right putamen, and middle cingulate gyrus increases; while it decreased in the left superior temporal gyrus, left superior frontal gyrus, right parietal sulcus, and middle right frontal lobe. Critically, higher iron levels in the left precentral gyrus and right putamen negatively correlated with cognitive deficits (MoCA), particularly in visuospatial function ($P < 0.05$), whereas lower iron in the left superior temporal gyrus and right parietal sulcus correlated with poorer cognition ($P < 0.05$). Mediation effect analysis demonstrated that iron deposition in the right putamen partially mediated the relationship between AHI, BMI, N3 stage proportion, Pulse oxygen<90% and cognitive function, especially the visuospatial abilities.

Conclusions: Our findings suggest that cerebral iron overload may contribute to cognitive dysfunction in OSA patients across severity levels, with chronic intermittent hypoxia-induced iron metabolism dysregulation serving as a potential neuropathological mechanism.

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Dementia prediction tool based on accelerometry measures of circadian rhythm in older adults

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Introduction: Given the absence of a cure for dementia and the emergence of therapies targeting its preclinical stages, enhancing early detection of individuals at higher risk or in the earliest stages of dementia is crucial for better patients care and effective interventions. This study aimed to develop and validate a biobehavioral tool leveraging accelerometry measures to predict dementia risk in older adults.

Materials and methods: We analyzed the prognostic utility of 36 accelerometer-derived features in a population-based sample of 53,448 participants aged 60 years or more in the UK Biobank (54.2% women; mean [standard deviation] age= 67.5 [4.2] years; 758 (1.4%) dementia cases; mean follow-up= 8.2 [1.2] years). Using a machine-learning approach, we identified key features of rest-activity rhythm, daytime activity, sleep, and chronotype that better predict dementia risk, and derived composite scores. We evaluated the added predictive value of these scores compared to traditional dementia risk factors. We performed external validation in the Whitehall II accelerometer sub-study (N = 3,971; 25.8% women; mean age 69.4 [5.7] years; 329 (8.3%) dementia cases; mean follow-up 10.5 [2.4] years).

Results: We identified nine core features of daytime activity, sleep, and chronotype, combined in two composite scores, that predicted dementia risk. Composite score 1 was mainly related to daytime activity features, with a higher score representing shorter duration and less frequent bouts of moderate-to-vigorous physical activity, more time in low intensity activity, less well distributed activities of different intensities, and a higher probability to transition from activity to rest. In contrast, composite score 2 was primarily related to chronotype and sleep features, with a higher score representing earlier wake-up time, longer wake bouts during sleep, lower probability to transition from

wake to sleep, and more extreme sleep durations (either shorter or longer). Both composite scores were associated with higher risk of dementia (hazard ratio (HR)= 1.43, 95% confidence interval (CI)= 1.33–1.54 for score 1 and HR=1.10, 95% CI= 1.04–1.17 for score 2) and improved the predictive value of a model including sociodemographic, behavioral, and health-related dementia risk factors (increase in C-index = 0.018, 95% CI= 0.011–0.025 with both composite scores included). Results were confirmed in the validation cohort.

Conclusions: Our findings support the development of an accelerometer-based biobehavioral tool for early identification of older adults at increased risk of dementia. This approach could aid primary care providers in referring high-risk individuals for further evaluation and initiation of promising new early-stages therapies, such as anti-amyloid monoclonal antibodies. Future studies may examine the potential of early interventions to reinforce circadian rhythmicity (increase activity during the day, improve sleep, delay waking time) to help slow disease progression.

Dream and Its Interpretation- Scientific Perspective

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Introduction: Dream is a mental activity that occurs during sleep. It is an altered state of consciousness embraced with images, thoughts, and emotions widely ranging in nature from joyful to sad and sometimes make no sense at all during sleep. As a correlate of neural activity, dreams can only be experienced by the living and ceases with brain death. It occurs in all stages of sleep, though vivid dreams occur mainly during rapid eye movement (REM) sleep. REM sleep also known as paradoxical sleep is characterized by high levels of brain activity, including increased activity in the areas of the brain associated with emotions, memory, and visual processing. The implication is that dreams may be a way for the brain to process and consolidate memories, emotions, and experiences from the day. Its interpretation is common practice in many African cultures and this role is vested in unqualified persons, such as diviners, priests, and healers. Their unprofessional activities have led to dangerous consequences such as anxiety, depression, loss of material possessions, bodily harm, family, or community conflicts, or even death.

Materials and methods: This review manuscript sought to unravel the mystery of dreams from a scientific perspective to educate the scientific community, especially in the developing world.

Results: This review manuscript unravelled the enigma of dreams by delving into the mechanisms underlying their occurrence, exploring the brain processes that shape their content, discussing different types of dreams, and examining the potential scientific basis for interpreting their significance.

Conclusions: The scientific study of dreams and their interpretation has provided fascinating insights into the neural processes, cognitive functions, and emotional dimensions of this intriguing phenomenon.

We recommend that there should be an interdisciplinary collaboration from various fields such as neuroscience, psychology, cognitive science, and even cultural studies. Collaborations between researchers from different disciplines can provide a more holistic understanding of dreams and their interpretation.

Effect of Daydreaming on clinical symptom and cognitive function in patients with obsessive compulsive disorder

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Introduction: Obsessive-compulsive disorder (OCD) is characterized by significant cognitive impairments, including deficits in error monitoring (EM). While Daydreaming (mind wandering, MW) and intraindividual reaction time variability (IIRTV) are implicated in cognitive dysfunction in other disorders, their role in OCD's EM deficits and their relationship with clinical symptoms remains unclear. This study aimed to investigate the associations between MW, IIRTV, EM, and clinical symptoms in OCD patients.

Materials and methods: Eighty-seven OCD patients and 49 healthy controls (HC) completed a revised Sustained Attention to Response Task (SART) to assess EM (error awareness, EA; post-error adjustment, PES), IIRTV, and MW (frequency, content, and variability). Clinical symptoms were assessed using standardized questionnaires. Group differences in SART performance and MW were analyzed using independent t-tests. Correlations between SART measures, MW, and clinical symptoms were examined.

Results: Compared to HC, OCD patients showed impaired EM (lower EA, less PES) and increased MW frequency and variability. OCD patients also exhibited greater IIRTV and lower accuracy on No-go trials. In the OCD group, IIRTV was positively correlated with lower EA. Lower MW variability and IIRTV were associated with reduced post-error slowing. PES was positively correlated with OCD, anxiety, and depression symptoms.

Conclusions: Our findings highlight significant deficits in error monitoring and increased mind wandering in OCD patients, which are associated with clinical symptom severity. IIRTV and MW variability may contribute to the impaired error monitoring observed in OCD, suggesting a complex interplay between spontaneous thought, behavioral variability, and cognitive control in this disorder. These results provide further support for understanding the cognitive and neural mechanisms underlying OCD and may inform the development of targeted interventions.

Effects of a new rocking apparatus on sleep and memory in young adults

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Introduction: Continuous overnight rocking stimulation is a promising intervention for enhancing both sleep quality and memory, through the modulation of NREM brain oscillations. This in-lab study aimed to confirm the beneficial effects of rocking on sleep and memory in healthy adults, using a new rocking prototype which can be fitted to any bedframe, with the long-term objective of applying this approach at-home.

Materials and methods: Following a habituation polysomnographic (PSG) night, nineteen healthy good sleepers (24.9±3.6 years, 53% female) completed 3 PSG nights under the rocking condition (ROCK) and 2 stationary nights (STAT), in a counterbalanced order separated by one week. The rocking prototype induced a continuous back-and-forth movement with a lateral displacement of 10.5 cm at 0.25 Hz (as described by Bayer et al., 2011 and Perrault et al., 2019) but was delivered by a homemade electrically-powered rail system.

From EEG data preprocessed according to the AASM guidelines, we extracted macroarchitecture outcomes, as well as spindle and slow oscillations (SO) characteristics on Fz and Pz during N2 and N3, using automated detection methods (Ray et al. 2015; Staresina et al. 2015). Subjective sleep quality was assessed with questionnaires in the morning. All analyses examined the Condition effect (ROCK vs STAT) during the first night only. Effects after the two subsequent consecutive nights of rocking are detailed in a companion abstract (Phillips et al.).

Declarative (word paired-associate task; 46 pairs) and procedural (finger tapping task; 5 digits over 30-second trials) memory performance were assessed in 3 phases: a learning phase followed by immediate recall in the evening then delayed recall in the morning. We compared the overnight change in accuracy (morning minus evening) between Conditions.

Results: The rocking stimulation did not impact overall sleep architecture (i.e., TST, SE, SOL, WASO; all $p > .05$). However, a significant Condition*Stage interaction highlighted a detrimental change in sleep stage proportion (%TSP; $F(1,18)=28.95$, $p < .001$), such that, compared to STAT1, participants spent more time awake, in both N1 and N2 when rocked, to the expense of N3 and REM (all $p < .05$). Spindle and SO activity were largely unaffected at ROCK1 ($p > .05$), and overnight memory performance improvement was not enhanced by the rocking stimulation ($p > .05$). Although participants were mostly satisfied with their sleep when rocked ($p = .01$), they generally reported more frequent awakenings

($p=.03$) and being disturbed by the noise levels ($p=.001$) and the movement (7/19). Accelerometric data comparing the new prototype and the rocking bed used by Bayer and Perrault revealed a maximal acceleration of around 20 cm/s^2 , contrasting with the expected 26 cm/s^2 . Moreover, the velocity and acceleration signals of the prototype had noticeably more variability than the rocking bed in the form of abrupt bouts of acceleration and deceleration ($p=0.031$).

Conclusions: Our results suggest that after one night, this rocking prototype did not improve sleep architecture or memory consolidation. These findings highlight the importance of optimizing rocking parameters (i.e., jerk, motion control, noise levels) to achieve beneficial effects on both objective and subjective sleep quality, as well as memory performance.

Effects of Binaural Beats on Sleep Initiation and Cognitive Control: A Neurobehavioral Study

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Introduction: Binaural beat (BB) stimulation is known to modulate electroencephalographic activity by brain entrainment, but only a few studies have established whether BB can affect the sleep onset process and daytime executive functioning. Sleep has a particularly detrimental effect on executive functioning involving response inhibition (RI), which plays a central role in regulating and modulating behavioral responses (Schiller et al., 2014). By prioritizing the enhancement of sleep quality, we can effectively enhance RI. In this study, BB stimulation as a sleep intervention was administered for two weeks in which the participant was exposed to 20 minutes of 4-Hz binaural beats before sleep. The primary aim of this study was to investigate the effects of BB stimulation on both sleep parameters and RI, assessed at electrophysiological and behavioral levels.

Materials and methods: The study used a cross-over experimental design, with a sample of 20 participants (age 28.37 ± 2.06 years). Each participant underwent three nights consisting of an adaptation night (T0), a baseline night (pre-intervention without BB) (T1), and a post-intervention night (after two weeks of BB intervention) (T2). Sleep was analyzed using polysomnography on T1 and T2. To evaluate cortical arousal during wakefulness, 5-minute resting-state EEG recordings were conducted on T1 and on T2, before sleep. RI was measured using the Go/NoGo task, programmed in PsychoPy (version 3.0.2). The task was designed in a way that allowed us to study the dynamic RI using mouse tracking to differentiate between the aware and unaware errors.

Results: BB intervention significantly reduced sleep latency and cortical arousal, as reflected by decreased beta and gamma power in resting-state EEG in post-intervention as compared to the baseline condition. The participants demonstrated improved RI following BB intervention in terms of increased response times and correct Go responses and a reduction in unaware commission errors and omission errors.

Conclusions: These findings suggest that BB intervention effectively attenuates high-frequency brain activity associated with alertness and cognitive processing. The observed reduction in beta power implies a shift toward a more relaxed, internally directed neural state. Similarly, the decrease in gamma power may indicate reduced cognitive load or internal information processing demands. At the behavioral level, improvements on the Go/NoGo task suggest enhanced RI following BB intervention. Participants exhibited a reduction in unaware commission errors following the BB intervention compared to the baseline condition, indicating increased attention and improved monitoring of inhibitory control processes. Taken together, the results support the notion that BB may promote better sleep quality, which in turn facilitates improved response inhibition. Thus, BB stimulation appears to offer dual benefits—enhancing both sleep onset time and daytime executive functioning, particularly in the domain of cognitive control.

Effects of sleep inertia, fatigue and boredom on crew performance in reduced crews - a flight simulator study

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Introduction: In view of the latest technological developments in commercial aviation, flights with reduced crews appear possible. In so-called *extended minimum crew operations* (eMCOs), one pilot is in control of the aircraft ('Pilot Flying') while the other pilot is allowed to rest and sleep ('Pilot Resting'). Sleep inertia - a state of cognitive impairment immediately after waking up - is a potential safety risk if the Pilot Resting has to act upon awakening. In addition, fatigue and boredom can increase for the Pilot Flying due to flying alone for an extended period. This study aimed to examine how eMCO segments in a high-fidelity flight simulator scenario affect sleep, sleep inertia, fatigue, boredom and crew performance of commercial pilots.

Materials and methods: Five crews (n = 10 pilots) participated in the study at the AVES flight simulator center of the German Aerospace Center and completed one of two conditions: aborted vs. non-aborted eMCO segment. In both conditions, the crews flew together for 30 minutes, followed by an eMCO segment in the new Pilot Flying (PF) and Pilot Resting (PR) roles. In the aborted condition, the eMCO segment ended unexpectedly after a 60-minute sleep opportunity for the PR, with an engine fire occurring immediately upon awakening. In the non-aborted condition, the eMCO segment ended as planned after 2.5 hours without interruption, with the engine fire occurring 30 minutes after the end of the eMCO segment. Sleep was objectively recorded using a wireless EEG system and a flexible, unobtrusive electrode grid with high wearing comfort. Self-assessments of fatigue, workload and boredom were collected every 30 minutes. Crew performance was operationalized as speed and success in handling the engine fire.

Results: In the non-aborted condition, pilots slept for 99 minutes on average out of a 130-minutes sleep opportunity. Beneficial effects of the nap on subsequent fatigue levels were mixed. Fatigue and boredom of the PF were higher during the eMCO segment than before or after the segment. Workload during the engine fire was perceived as slightly higher in the aborted eMCO than the non-aborted eMCO condition. Out of three crews in the aborted eMCO condition, one PR did not deem himself fit to act upon awakening, leaving the PF to -successfully- deal with the fire on his own. Crew performance speed (i.e., how fast the fire was resolved) did not differ between the two conditions.

Conclusions: In this particular scenario and based on a limited sample size, sleep inertia, fatigue and boredom had no effect on crew performance when an engine fire occurred. The investigation of further safety-relevant eMCO scenarios, e.g. increasing sleep inertia during night flights, is warranted.

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Exacerbated Negative Impact on Sleep, Mood, Cognition and Daytime Functions in Comorbid Frequent Nightmares and Insomnia

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Introduction: Insomnia often co-occurs with frequent nightmares. While previous studies have examined the independent effects of insomnia and nightmares, few studies have investigated the impact of the comorbidity of these conditions. This study aims to determine whether frequent nightmares exacerbate impairments in sleep, mood, cognition, and daytime functioning in individuals experiencing insomnia, compared to those with insomnia alone.

Materials and methods: This is a cross-sectional study recruited adults aged 18 to 70 with insomnia symptoms (Insomnia severity index, ISI $\geq$ 10) in Hong Kong. Participants completed online questionnaires on sleep and mood, clinical interviews (The Structural Clinical Interview for DSM-5 Disorders, SCID-V) for psychiatric diagnoses, and mobile cognitive tests assessing attention (The Psychomotor Vigilance Test, PVT), risk-taking propensity (Balloon Analogue Risk Task, BART), inhibition control (Go/No-go Task) and working memory (N-back Task). Frequent nightmares were defined as occurring more than once a week over the past three months (Nightmare Frequency Questionnaire).

Individuals with post-traumatic disorder (PTSD, identified by SCID-V) were excluded. Group comparisons (insomnia with vs without nightmares) were analysed using Pearson's chi-square test and Wilcoxon rank-sum test. Associations between frequent nightmares and outcomes were further examined using linear and logistic regression.

Results: A total of 230 participants (median age 43 years; 75.7% female) with complete clinical interview, questionnaire, and cognitive task data were included. Individuals with comorbid frequent nightmares (N=53, median age 37 years; 77% female) exhibited greater insomnia severity, pre-sleep arousal, mood disturbances, suicidal ideation, somatic symptoms, and less satisfaction with surrounding environment compared to those with insomnia alone. After adjusting for covariates (age, gender, income, psychiatric diagnoses and insomnia severity), frequent nightmares remained significantly associated with higher depressive severity ($\beta = 1.55, p < .05$), rumination ($\beta = 4.16, p < .05$), suicidal ideation (OR = 2.34, $p < .05$), attention deficits (longer PVT reaction time: $\beta = 55.63, p < .01$; higher Go/No-go omission rate: $\beta = 4.86, p < .05$), and somatic symptoms ($\beta = 1.72, p < .01$). Adjusting further for depressive and anxiety symptoms, frequent nightmares still demonstrated significant associations with greater pre-sleep cognitive arousal ($\beta = 1.84, p < .05$), reflective rumination ($\beta = 0.86, p < .05$), attention deficits (longer reaction time in PVT: $\beta = 55.05, p < .01$; higher omission rate in Go/No-go Task: $\beta = 5.50, p < .01$), and somatic symptoms ($\beta = 1.44, p < .05$).

Conclusions: Frequent nightmares comorbid with insomnia exacerbated pre-sleep arousal, reflective rumination, attention impairment, and somatic symptoms beyond the impact of insomnia alone, independent of insomnia severity and mood disturbances. These findings suggest that intervention targeting both nightmares and insomnia should be incorporated into management of comorbid insomnia and nightmares.

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Examining the Clinical Characteristics Associated with Weekly Nightmares among U.S. Veterans at Risk for Suicide

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Introduction: Sleep disturbances have been implicated as a potentially modifiable risk factor for suicide. Nightmares, in particular, are associated with suicidal ideation, mood disorder symptoms, and premature termination from sleep-focused psychotherapy. Military Veterans are at particular risk, given high frequencies of both nightmares and posttraumatic stress disorder (PTSD) symptoms compared to the general population. Less is known, however, about the associations of nightmares among Veterans in psychiatric inpatient or other high-risk settings. This study aimed to explore (1) the prevalence, demographics, and clinical characteristics of Veterans with weekly nightmares, and (2) differences in clinical characteristics between U.S. Veterans at risk for suicide with and without weekly nightmares.

Materials and methods: Cross-sectional data were drawn from an ongoing VA study on the relationship between sleep and suicide among U.S. Veterans at risk for suicide (n = 66). Participants were sampled from a hospital inpatient psychiatric setting and suicide prevention coordinator office referral. Weekly presence of nightmares was determined through the Pittsburgh Sleep Quality Index, and psychiatric diagnoses were determined through the staff-administered QuickSCID assessment. Those reporting weekly nightmares were compared to those without on demographic characteristics, self-reported psychiatric symptoms (e.g., symptoms of depression, anxiety, alcohol use, and substance use disorders), and staff-rated suicidal thoughts and behaviors (e.g., suicide ideation intensity, lifetime presence of suicidal behaviors). Linear regression models controlled for age; to reduce potential impact of treatment, sensitivity analyses were conducted without participants currently prescribed medications to treat nightmares (n = 63).

Results: A majority of participants reported weekly nightmares (n = 40, 60.6%). Among those with weekly nightmares, the mean age was 45.3 years old, 83% were male, 65% were White/Non-Hispanic, and 60% received service-connected disability for a mental health condition. Among a subsample of those with weekly nightmares who completed the QuickSCID assessment, 74.4% met criteria for PTSD, 59.0% for a substance use disorder (SUD), 51.2% for a major depressive episode (MDE), 48.7% for generalized anxiety disorder, and 43.6% for alcohol use disorder. Groups (i.e., those with and without

weekly nightmares) did not differ on demographic characteristics, psychiatric symptoms, or suicide-related characteristics in unadjusted, adjusted, and sensitivity models.

Conclusions: In a sample of U.S. Veterans at risk for suicide, a majority reported nightmares at a frequency of at least weekly. Among those with weekly nightmares, frequent mental health diagnoses included PTSD, SUD, and MDE. Similarities between those with weekly nightmares and without might reflect the high acuity within the present sample. Future research should examine the longitudinal relationship between nightmares and clinical outcomes within high-risk Veteran samples.

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Exploring nightmares, associated factors and their relationship with externalising behaviours in complex psychiatric populations: A systematic review and clinical case review

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Introduction: Dreaming allows for emotional processing. However, for those with psychiatric disorders, dream disturbances - namely nightmares- are prevalent. Nightmares disrupt this emotional processing, and their distress has demonstrated links to worsening clinical symptoms and increased suicide risk. Despite this, nightmares receive limited clinical attention in complex psychiatric populations. This is surprising when considering how these populations exhibit increased risk factors, such as trauma and distress, which may contribute to unique experiences of nightmares and increased association with externalising behaviours. Few studies focus on the link of nightmares to self-injurious behaviour (SIB). Systematic reviews on psychiatric populations have also failed to capture a broad understanding of nightmares in psychiatric inpatients alone. Forensic psychiatric sampling for nightmare research is particularly scarce, warranting investigation.

Materials and methods: A systematic review using Reflexive Thematic Analysis explored the nature, underlying mechanisms and correlating factors of nightmares in psychiatric inpatient populations. Titles were screened from eleven databases. Data extraction, quality assessment and inter-rater reliability were performed adhering to PRISMA guidelines. This systematic review identified variables for a review of collateral clinical information of detained forensic patients, utilising a structured clinical assessment tool, the Self-injurious behaviour Management and Behavioural Assessment (SIMBA). The SIMBA gathers clinical information based on staff reporting on mental illness, externalising behaviours and importantly, sleep challenges, including whether nightmares have presented. Mixed methods using Reflexive Thematic Analysis and regression explored what was reported about nightmares in these patients and associations with incidents of externalising behaviour.

Results: In relation to the systematic review, of the 9,534 titles screened, a total of 35 papers were included for review. Themes described the chronic and replicative nature of nightmares in psychiatric inpatients, including their violent, trauma-related and disturbing content. Underlying mechanisms of inpatient nightmares centred on trauma and emotional dysregulation, often with early onset. Inpatient nightmares demonstrated bidirectional links with exacerbating clinical symptoms, negative cognitions, distress and other sleep disturbances. The impact of nightmares on risk of suicidality was apparent. Patients in the case study papers were reported as keen to explore their nightmares, while other studies highlighted the unexplored therapeutic potential of nightmares. The methodologies and quality of the included papers varied. In the SIMBA study, nightmares were reported in 23% of the 78 patients reviewed. Themes highlighted how nightmares present as part of wider sleep disturbance, centre around trauma, and have multifaceted impacts. Patients appeared to discuss their sleep problems, yet limitations presented in staff reporting of nightmares. Nightmares qualitatively showed relationships with SIB but did not statistically predict externalising behaviours.

Conclusions: Both reviews overlapped in findings and provide initial understanding of the distressing nature of nightmares in complex psychiatric populations, their underlying mechanisms, interaction with psychiatric symptoms and limitations around assessment. Building on these results, a large study plans to explore nightmares from the perspective of male forensic inpatients and test the feasibility of a brief nightmare intervention. It is hoped that by addressing nightmares, sleep disturbances in high-risk populations can be addressed and patient wellbeing improved.

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Factors and Issues Affecting Sleep Quality in Elderly Hong Kong Residents: A Cross-Sectional Survey, 2024-2025

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Introduction: Sleep is a vital component of health and well-being. Older adults in high living density living environments may experience disproportionately higher levels of sleep disturbances, reducing the quality of sleep. This study investigates the factors associated with poor sleep quality among Hong Kong adults aged 65 and older, with the aim of identifying modifiable targets for evidence-based interventions.

Materials and methods: Between December 2024 to April 2025, a cross-sectional random telephone survey was conducted on community-dwelling older adults (n=723). The Pittsburgh Sleep Quality Index (PSQI) was used to assess overall sleep quality, alongside questions regarding the sleep environment, substance use, and pre-sleep cognitive activity. Multiple linear regression models, adjusted for age, gender, education, and income, were applied to identify predictors of PSQI scores.

Results: Among the older age participants (59.9% female), respondents reported an average of 29 minutes to fall asleep, resulting in a mean total sleep duration of 6.45 hours/night (SD= 1.34). Of the sample, 24.9% reported less than 6 hours of sleep/night. Significant sleep impairments were observed, with 71.1% reporting difficulty initiating sleep and 93.1% struggling with sleep maintenance. Regression analysis identified three key predictors of PSQI scores: nocturia ($\beta=0.988$, $p<0.001$), pre-sleep cognitive arousal ($\beta=3.223$, $p=0.001$), and trends indicating that substance use, specifically smoking ($\beta= 0.258$, $p=0.26$), was associated with reduced sleep efficiency. Breathing difficulties, loud cough/snoring, feeling cold/ hot, bad dreams and pain were not significantly associated with PSQI scores.

Conclusions: This study highlights the complex interplay of physiological, psychological, and behavioral factors contributing to sleep deficits among older adults in Hong Kong. Addressing these determinants could alleviate the healthcare burden associated with geriatric sleep disorders and enhance the quality of life for this vulnerable population.

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Induction of local sleep in a visual processing brain network in humans

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Introduction: Sleep loss often impairs emotional regulation and social functioning, leaving us irritable, impulsive, or less inclined for social contacts. Recent studies suggest that such deficits may stem from local sleep-like episodes - brief intrusions of slow waves similar to those of sleep - in specific cortical networks during wakefulness. These episodes become more frequent with sustained regional activity (use-dependent process) and transiently disrupt the cognitive functions of the affected areas.

While previous work has focused on motor, spatial navigation and executive networks, it remains unclear whether local sleep can affect restricted sensory brain regions, such as those involved in visual processing. Can the brain, for example, grow "tired" of seeing smiling faces?

In this work, we tested whether repeated exposure to faces with emotional expressions could induce local sleep episodes in visual brain regions, and whether such induction alters the perception of facial expressions.

Materials and methods: Participants completed a three-phase paradigm. 1) In the pre-test, we measured baseline performance on a facial expression recognition task using a 2-alternative forced choice (happy vs. angry) on faces morphed across a happy-angry continuum. 2) Then, during an intervention phase, we presented participants with many pictures of happy faces (group 1) or of angry faces (group 2) to induce local sleep for a targeted emotional expression. 3) Finally, participants

performed the same task than the pre-test to measure changes in facial expression recognition. EEG was recorded throughout, and source reconstruction was used to quantify slow-wave density in face-processing brain areas.

Results: Following prolonged exposure to a target emotional expression (e.g., happiness), participants were significantly more likely to interpret ambiguous expressions as the opposite emotion (e.g., anger). This perceptual bias was accompanied by a selective increase in miscategorization of the target emotion, with no comparable effect for the control emotion. Crucially, the degree of miscategorization of the target emotional expression correlated with slow-wave density in visual areas implicated in face processing.

Conclusions: Our findings demonstrate that local sleep-like episodes can be experimentally induced in visual-processing networks through targeted sensory stimulation. These episodes are characterized by wake slow waves that share key features with sleep slow waves, albeit with lower amplitude and spatially restricted expression.

Investigating Task Switching Performance in a 31h Total Sleep Deprivation Protocol

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Introduction: In 24/7 operational environments, managing multiple complex tasks in rapid succession can be cognitively demanding. Managing multiple tasks requires ongoing attention, often requiring the operator to shift their attention between tasks, a phenomenon called task switching. Under conditions of extended wakefulness, the added workload caused by task switching, can slow cognitive processing, impair attention, and increase error rates. This study examined the effects of 31 hours of sustained wakefulness on task-switching performance between a visual and working memory task and the cost of switching on overall performance.

Materials and methods: Twenty-six healthy participants completed a 31-hour sustained wakefulness protocol in a controlled laboratory environment, with testing sessions across the wake period at 11:00h, 17:00h, 23:00h, 05:00h, and 11:00h. Participants were presented with a switching task, where a spatial-rotation (manikin) task was presented on the left and a math task on the right. An arrow indicated which task participants had to respond. Performance measures included mean reaction time (RT), accuracy (proportion correct), and throughput (a measure of speed-accuracy trade-off), analysed across four transition types: math-to-math, manikin-to-manikin, manikin-to-math, and math-to-manikin. Mixed-effects models were used to analyse changes in mean RT, accuracy, and throughput separately as a function of transition type and hours of wakefulness, with random intercepts for participants.

Results: Hours of wake had a significant main effect on mean RT ($p < .001$), throughput ($p < .001$) and accuracy ($p < .001$) with poorest performance at 05:00h respectively. Significant main effects of transition type on RT ($p < .001$) and throughput ($p < .001$) were observed but not for accuracy ($p = .972$). Transitioning from 'different', i.e., manikin-to-math, to 'same', i.e., manikin-to-manikin, there was a reduction in mean RT compared to 'same', i.e., manikin-to-manikin transition types ($p < .001$), no interaction effects were found.

Conclusions: Impairments due to switching were dependent on the preceding and proceeding task. When transitioning between two different tasks, there was a speed/accuracy trade-off observed with participants slowing down to maintain accuracy. To improve/maintain switching performance during around-the-clock operations, it is vital to be aware of the cost of switching multiple different tasks where possible, identify strategies within teams to reduce the number of switches completed by individuals. Future studies should look at human-centred interfaces which are designed to strategically implement cuing in a task that can help mitigate cognitive demands and maintain attentional focus during fatigue.

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Investigating the effects of REM sleep fragmentation on emotional memory and psychophysiological reactivity

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Introduction: Sleep plays a fundamental role in the processing of emotional experiences. Emotional events undergo a priority reactivation during sleep that promotes the consolidation of salient information, while attenuating the associated emotional charge, thus reducing the subsequent physiological reactivity. Replay during slow-wave sleep seems to be primarily involved in improving memory, whereas the processing and attenuation of affective tone has been proposed to be mediated by replay during REM sleep, an optimal continuous period of silencing in noradrenergic activity. Consistently, recent evidence has shown that, in patients with sleep disorders, REM sleep fragmentation (frequent cortical arousals and sleep stage transitions disrupting REM sleep continuity) is associated with the lack of physiological habituation to emotional experiences, possibly due to increases in REM noradrenergic levels associated with arousals. However, multiple sleep macro- and microstructural alterations, beside those affecting REM sleep, often characterize sleep disorders and could contribute to the emotional dysregulation in these patients. To disentangle the specific effect of REM sleep fragmentation from other confounding, we experimentally induced REM sleep fragmentation in good sleepers via vibrotactile stimulation and evaluated its effect on overnight processing of emotional stimuli.

Materials and methods: Seventeen healthy participants (23.18 ± 3.94 y, 3 males) underwent two experimental conditions (*Fragmentation/Control*) in counterbalanced order involving a nocturnal polysomnography (with/without REM sleep fragmentation) and 3 assessments of memory and psychophysiological reactivity to emotional stimuli (T0: pre-sleep baseline; T1: morning after sleep; T2: follow-up 48hrs later). REM sleep continuity was disrupted in the *Fragmentation* condition by eliciting cortical arousals through vibrotactile stimulation, while undisturbed sleep was allowed in the *Control* condition. The effect of the experimental manipulation was assessed on self-report evaluations (Self-Assessing Manikin), physiological responses (Skin Conductance Response, SCR; Heart Rate Deceleration, HRD), and recognition memory (Old/New paradigm) for negative and neutral stimuli. Data were compared via linear mixed model with *Condition*, *Valence* and *Time* as factors and their interactions, including random intercepts per subject and stimulus.

Results: The vibrotactile stimulation was effective in disrupting REM sleep continuity during the *Fragmentation* night and resulted in a reduction of REM sleep duration parallel to increases in NREM1 ($p < 0.001$) compared to the *Control* night, without altering other macrostructural variables ($p > 0.170$). Statistical analyses revealed that REM sleep fragmentation didn't influence subjective ratings of stimuli pleasantness and arousal, or recognition memory performance (all $p \geq 0.116$), while it significantly affected emotional physiological reactivity as measured by HRD ($p = 0.002$). Specifically, HRD values decreased significantly after undisturbed sleep in the *Control* condition ($p = 0.007$) and then remained stable until T2 ($p > 0.999$), whereas no change occurred over sessions in the *Fragmentation* condition ($p \geq 0.529$).

Conclusions: A single night with REM sleep fragmentation after exposure to emotional stimuli impairs the sleep-dependent processes responsible for psychophysiological habituation the following day. Importantly, the dysregulated emotional responses persist for 48hrs, despite two intervening nights of undisturbed sleep. The results support the importance of REM sleep continuity for healthy overnight processing of emotional experiences and its protective role against long-lasting dysfunctional emotional reactivity.

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KNOWLEDGE AND ATTITUDES TOWARDS DREAMS AMONG MEDICAL STUDENTS IN ABAKALIKI NIGERIA: A DESCRIPTIVE STUDY

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Introduction: Dreams represent the activities of the brain during sleep and occur in all stages of sleep, though vivid dreams occur mainly during rapid eye movement (REM) sleep. There are limited scientific studies on dreams in Sub-Saharan Africa despite the growing knowledge in other parts of the world. This research study investigated the level of knowledge about dreams and explored the attitudes of clinical students towards dreams and their relevance in healthcare.

Materials and methods: This cross-sectional observational study was undertaken among the medical students of 2 public institutions in Nigeria from 25th September to 3rd October 2023.

Results: Out of 353 medical students (males- 48.4% and females- 51.6%) with a mean age of 24.3 ± 2.5 years that were studied, 15.6% know that dreams arise from brain activity during sleep (good knowledge), 82.1% believe that dream is spiritual while 2.3% had no idea about the origin of dream. The main source of knowledge of dreams was from the teachings in the church and bible- 68.8%, from home and community- 16.7%, and from personal studies- 14.4%. Nightmares were common and the predominant subject was the death of a loved one (61.3%), a threat to life (26.1%) and failure in examination and life (12.6%).

The actions taken after a nightmare include praying and nullifying the nightmare- 79.9%, requesting their parents and spiritual leaders for a nullification prayer- 14.2%, while 5.9% would do nothing.

Conclusions: The knowledge and attitudes towards dreams are poor among medical students in Nigeria.

Their knowledge and attitude towards dreams can be improved through incorporating Dream Education into the Curriculum, regular seminars and workshops on dreams, the creation of Dream Journals, the formation of peer Discussion Groups and offering research opportunities in the field of sleep and dreams to interested students.

By implementing these recommendations, medical students in Nigeria can develop a better knowledge and attitude towards dreams, sleep, and their relationship with mental health. This can lead to more comprehensive patient care in the future and contribute to a better understanding of mental health in the medical field.

Linking Childhood Trauma to Suicidal Ideation through Nightmares in Youth

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Introduction: Childhood trauma, encompassing experiences such as emotional abuse and neglect, often leaves profound and lasting effects. One of the lesser-recognized consequences of such trauma is its association with frequent nightmares, which may, in turn, contribute to the development of suicidal ideation. This study seeks to examine the relationship between childhood trauma, nightmares, and suicidal ideation, focusing on the impact of both single and multiple types of trauma on frequent nightmares. Additionally, the study aims to explore the mediating role of nightmares in the association between trauma and suicidal ideation and to assess the possible moderating effect of sex on these relationships.

Materials and methods: Youth aged 12–25 years ($n=6145$) participated in an online survey assessing childhood trauma, nightmares, and suicidal ideation. Logistic regression analyses were employed to investigate the relationship between distinct types of childhood trauma and frequent nightmares. Cumulative scores and latent class analyses were applied to identify multiple childhood traumas. Furthermore, moderated mediation analyses were conducted, considering childhood trauma as the independent variable, suicidal ideation as the dependent variable, nightmare frequency as the mediator, and sex as the moderator.

Results: After controlling for a range of covariates, emotional abuse (OR: 1.45, 95%CI: 1.23–1.87) and emotional neglect (OR: 1.19, 95%CI: 1.03–1.37) were found to be significantly associated with an increased likelihood of experiencing frequent nightmares. A dose-response relationship was observed, where a higher number of trauma types was linked to a greater likelihood of experiencing nightmares. Latent class analysis identified three trauma patterns: “low abuse, low neglect (62.4%, $n = 3837$),” “low abuse, high neglect (34.0%, $n = 2089$),” and “high abuse, high neglect (3.6%, $n = 219$).” The latter two patterns were associated with an increased likelihood of nightmares by 26% and 47%, respectively,

compared to the first pattern. Furthermore, nightmare frequency was found to significantly mediate the relationship between childhood trauma and suicidal ideation, accounting for approximately 4.11% of the total effect, even after adjusting for relevant covariates. However, no significant moderating effect of sex was observed, suggesting that both male and female individuals may be equally influenced by trauma-related pathways.

Conclusions: The findings of this study contribute to a deeper understanding of the heterogeneity in childhood trauma and its potential implications for the occurrence of nightmares. They suggest that nightmares may not only reflect the psychological impact of trauma but also serve as a key factor in the development of suicidal ideation. It is possible that interventions targeting nightmares could be effective in mitigating suicide risk in traumatized youth. However, further research is warranted to explore the generalizability of these findings and to evaluate the efficacy of interventions designed to address nightmares in this population.

Long sleep is associated with poor global cognitive function across diverse populations

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Introduction: Associations between suboptimal sleep and reduced cognitive function have been previously reported. However, associations have not been consistently assessed across populations of potentially different characteristics.

Materials and methods: Our analysis included individuals with data from sleep and cognitive exams occurring around the same time and subsequent follow-up cognitive exams in three U.S.-based longitudinal cohort studies: the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) of Hispanic/Latino adults from four metropolitan areas (N= 9217; average age 55 at baseline; 7 years between cognitive exams on average), the Multi-Ethnic Study of Atherosclerosis (MESA) of individuals self-identified as White, Black, Hispanic, or Chinese American, from 6 U.S. six metropolitan areas (N= 1736; average age 67 at baseline; 6.3 years between cognitive exams on average), and the Atherosclerosis Risk In Communities Study (ARIC) of White individuals from three metropolitan areas (N= 1664; average age 63 at baseline; 15 years between cognitive exams on average). In each cohort, global cognitive function (GCF) was defined as the first principal component from analysis of standardized cognitive tests and poor GCF as falling 1 standard deviation (SD) below the age-adjusted study median. Harmonized sleep phenotypes included objectively-measured obstructive sleep apnea (OSA), and self-reported excessive daytime sleepiness (EDS), insomnia symptoms, and short and long sleep durations. We estimated associations between sleep variables and GCF at baseline, and incident poor GCF. Analyses were performed separately in each cohort, adjusted for age, sex, study site, race/ethnic background (when applicable), and education at baseline. Estimates were then meta-analyzed across cohorts.

Results: Long sleep (≥ 9 hours) was consistently associated with reduced baseline GCF (HCHS/SOL beta: -0.32; 95% confidence intervals (CI) -0.42; -0.23; MESA beta: -0.09 95% CI [-0.25; 0.06]; ARIC beta: -0.19 95% CI [-0.40; 0.015]; meta-analysis beta: -0.25, 95% CI [-0.33; -0.17]). Elevated insomnia symptoms was associated with reduced GCF (meta-analysis beta: -0.07, 95% CI -0.13; -0.01); however, results were driven by data from HCHS/SOL (HCHS/SOL beta: -0.17 95% CI [-0.26; -0.09]), with more variable associations in MESA (beta: -0.05; 95% CI -0.19; 0.09) and ARIC (beta: 0.06; 95% CI -0.04; 0.16). Short sleep duration (≤ 6 hours) had statistically significant association with reduced GCF only in

MESA (beta: -0.23; 95% CI -0.45; -0.01); meta-analysis beta: -0.06, 95% CI -0.16; 0.03. Long sleep was also suggestively associated with higher likelihood of incident poor GCF (HCHS/SOL risk ratio (RR): 1.27; 95% CI 0.94; 1.72; MESA RR: 1.00; 95% CI 0.54; 1.87; ARIC RR: 1.50; 95% CI 0.72; 3.16; meta-analysis RR: 1.24, 95% CI [0.96; 1.60]), an analysis with lower sample size (overall N=6648). Patterns of associations of OSA and EDS with cognitive measures were inconsistent across studies and none were statistically significant.

Conclusions: Long sleep duration is associated with reduced GCF across populations of diverse race/ethnicities, with suggestive albeit non-significant associations with incident poor GCF.

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Magnitude and associated factors of poor sleep hygiene practice among Chinese married persons: A cross-sectional study

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Introduction: Due to the responsibility to take care of families, married people may expose to a high risk of poor sleep hygiene, but we do not know the situation. This study aims to evaluate sleep hygiene practices among those population.

Materials and methods: 176 married persons were included in this study. Demographic data, Sleep Hygiene Practice Scale, and Pittsburg Sleep Quality Index were collected. Pearson correlation and multiple linear regression analysis were applied by SPSS 22.0.

Results: Overall, 97 (55.1%) of married persons had poor sleep quality. The score of sleep hygiene was 77.06 ± 21.54 , while in detail, the score of arousal-related behaviors, sleep scheduling and timing scored, eating/drinking behaviors, and sleep environment was 24.26 ± 7.59 , 22.96 ± 6.12 , 12.53 ± 5.29 , and 17.31 ± 7.24 , respectively. Pearson correlation analysis showed that age, body mass index, length of marriage, children with university degree or above, monthly income, drinking, smoking, exercise habit, and perceived health status were negative related to maladaptive sleep hygiene. Interestingly, male's sleep hygiene behaviors were worse than females. Further analysis indicated that, children with university degree or above ($\beta = -11.335$, $P = 0.016$), drinking ($\beta = -14.513$, $P = 0.011$), and exercise habit ($\beta = -7.972$, $P = 0.026$) were the predictors of poor sleep hygiene.

Conclusions: The sleep hygiene practice of Chinese married people was in the lower middle level, and its worse for men's. Nurses should pay attention to married people's children, drinking, and exercise habits to improve their sleep behavior, and thus enhance sleep quality.

Musical harmony is differentially processed during sleep: Evidence from EEG recordings

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Introduction: Musical chords are the smallest musical elements that convey emotional information. While different chord categories (e.g., major or minor) elicit distinct emotions and neuronal correlates during wakefulness, it remains unclear whether the brain continues to differentially process these musical chords during sleep. We hypothesized that musical harmony is differentially processed by the sleeping brain.

Materials and methods: To address this question, we presented musical chords over loudspeakers to 47 healthy young participants (19-25 years) during nocturnal non-rapid eye movement (NREM) sleep. The chords were tone triads with major, minor or dissonant harmonic properties. Chords were subjectively rated before sleep. During the night, sleep was recorded by polysomnography in a sleep laboratory.

Results: Consistent with our hypothesis, event-related responses (ERPs) during sleep significantly differed between the three chord types: major chords elicited the highest negative amplitude in a peak-to-peak (PTP) analysis at approximately 800 ms after chord onset. The PTP responses were intermediate for minor chords, and lowest for dissonant tone triads. These particular response patterns were similar in N2 and slow-wave sleep (SWS), with generally higher PTP amplitudes during N2 sleep.

Importantly, differential responses of the sleeping brain to chord categories were stronger in participants who played a musical instrument compared to participants who never played an instrument.

Conclusions: In conclusion, our findings suggest that the differential processing of single musical chords persists during sleep, influenced by harmonic features and musical expertise in the context of Western musical conventions. Future research should explore whether also longer and more complex harmonic features (e.g., chord sequences or musical pieces) are also differently processed by the sleeping brain.

Napping and cognition in older adults-context matters: reasons for napping, nap timing, and overall sleep health

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Introduction: While midday napping in younger persons benefits cognition, napping in older persons tends to be associated with poorer cognitive outcomes, leading to the view that napping may be 'symptom' of age-related degradation in sleep neurobiology. However, whether naps are maladaptive or productive for older adults may depend on the reason behind the nap and must be understood in the context of overall sleep health as these may underlie negative associations. To rule this out, we examined associations between napping and cognition in a group of older adults with relatively good sleep health (7-10h average TIB, having no trouble falling asleep and/or staying asleep for ³ 5 nights/week, no sleep disorders).

Materials and methods: Older adult healthy sleepers (n = 393) aged between 67-80 years (mean age: 73.8 years, SD: 2.7 years) completed neurocognitive testing and questionnaires probing nap behaviour. Nap frequency (no naps, 1-2 naps/week, 3-6 naps/week, daily naps), nap duration (≤ 30 mins, 31-60 mins, > 60 mins), nap timing (morning, afternoon, evening), nap intention (unintentional, intentional) and reasons for napping (slept poorly the night before, felt tired, boredom, habit) were assessed. Linear regression models were used to determine the effects of nap characteristics on cognitive domains (global cognition, speed of processing, executive function, attention, language, verbal, visual, and visual-spatial memory). Models adjusted for age, gender, years of education, smoking, high blood pressure, diabetes, and history of cardiovascular events and organ disease.

Results: Napping to counter tiredness was associated with better verbal memory (B = 2.47, CI₉₅ = 0.29-4.66) and language (B = 2.08, CI₉₅ = 0.07-4.09) compared to napping because one slept poorly the night before. Napping in the afternoon was associated with better visuospatial memory compared to napping in the morning (B = -5.77, CI₉₅ = -10.55--0.99). Napping daily was also associated with better verbal memory (B = 0.58, CI₉₅ = 0.00-1.17) and language (B = 0.64, CI₉₅ = 0.10-1.17) compared to not napping at all, but with relatively small effects.

Conclusions: In older adults with 'intact' sleep health, napping in the afternoon in response to tiredness cues is associated with better memory performance. Our findings suggest that whether or not napping is a 'symptom' or a 'strategy' for better daytime function may depend on its use patterns and the overall sleep health of an older person.

Night Shift Work Impairs Team Performance and Cohesion

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Introduction: Many safety-critical industries require distributed teams, who collaborate across location and times, to work during the night outside of the conventional '9-to-5' hours, such as healthcare, emergency services, transportation and military settings. Distributed teams that are cohesive and adaptive are essential for maintaining productivity and safety in these continuous, shift-working conditions. Despite their essential nature, there are repercussions for those working at night when their

bodies are most primed for sleep. Nightwork disrupts biobehavioural functions which follow inherent circadian rhythms, requiring the body to be awake during the day and asleep during the night. Circadian disruption associated with night work systematically and negatively impacts health and performance, which are likely to harm distributed team dynamics. In addition to working during the biological night, the complexities associated with working in distributed teams, such as lack of face-to-face interactions and trouble coordinating and collaborating with fellow team members over varying geographical locations and times, further exacerbate these dynamics. Despite the prevalence of night work for distributed teams, little to no research has investigated the impact. Thus, this study aimed to assess the impact of working through the biological night on distributed team performance, dynamics and cohesion.

Materials and methods: Six teams of four, young healthy individuals ($N=24$, $M\pm SD=25.38\pm 6.53$ years, 9f) completed an in-laboratory study consisting of one night of 32h of wakefulness. Simulated night shift work, including COHESION, a computer-based team task, was undertaken by participants during the wake period. Teams were physically isolated every four hours while completing COHESION as to assess distributed team performance, cohesion and dynamics across the biological night (6pm, 10pm, 2am, 6am, 10am). COHESION required distributed team members to move resources into a target zone, while avoiding visible and invisible barriers. Each team member was responsible for a subset of barriers visible only to them and session time could be spent cooperating (revealing barriers to all) or attempting productivity (resource drops). Cooperative and productivity behaviours were analysed at the individual level. Team-level metrics included distributed team performance (team successful resource drops) and team dynamics (dispersion of barrier-reveal attempts within the team). Team cohesion and alertness measures were also administered after each COHESION test. Data were analysed using linear mixed models.

Results: There were significant main effects of clock time on individual alertness ($F(4,96)=27.59, p<.001, \eta_p^2=.74$), cooperative behaviours (barrier reveals, $F(4,96)=3.26, p=.015, \eta_p^2=.12$) and productivity behaviours (resource drop attempts, $F(4,96)=4.01, p=.005, \eta_p^2=.14$). There were also significant main effects of clock time on distributed team performance (team resource drops, $F(4,24)=3.54, p=.021, \eta_p^2=.37$), dynamics ($F(4,24)=4.30, p=.009, \eta_p^2=.42$) and team cohesion ($F(4,92)=16.30, p<.001, \eta_p^2=.41$).

Conclusions: This study found clear deficits in team outcomes during night work, particularly during the circadian low. At this time of the night, distributed teams exhibited increased fatigue, reduced cooperation among team members, and diminished productivity, leading to poorer team performance, dynamics, and cohesion. The circadian system played a crucial role in modulating distributed team performance and cohesion. This is especially problematic in safety-critical, shift-working industries such as healthcare, military, and transport, where effective team work and cohesion across geographical locations and times are essential.

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No association between sleep and dishonest behavior in healthy school-age children

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Introduction: Short sleep duration is associated with poorer executive functions which are crucial for goal-directed behavior and moral decision-making, such as cheating and lying. While previous research on school-age children has uncovered relationships between executive functions and dishonest behavior, little is known about the association between sleep and dishonest behaviour. This study aimed to examine whether short sleep duration, as well as poor sleep quality, were associated with dishonest behaviour and lie sophistication in healthy school-age children.

Materials and methods: The sample consisted of 46 healthy school-age children (19 female, aged 7-12 years) whose sleep was tracked with actigraphy for 8 nights during a school term. Sleep parameters were averaged across days. With parental consent, the Temptation Resistance Task was administered the morning after the final actigraphy night to assess dishonesty. In this task, children completed an

unsupervised trivia quiz containing one unanswerable question. They were told they would be rewarded for answering all the questions correctly and were instructed not to peek at the answers on the back of the page before being left alone to complete the quiz. A hidden camera recorded their behaviour during this task. They were later asked if they had peeked, and if they could guess the content of the answer sheet (each answer was accompanied by a symbol that depicted a unique object in a different colour). Among the lie-tellers, lie sophistication was based on whether they lied about the object of the symbol accompanying the answer to the unanswerable question, its colour, or both aspects (unsophisticated = 0 aspect; slightly sophisticated = 1 aspect; sophisticated = 2 aspects). Children were debriefed after the task. Group differences in sleep parameters were examined using ANCOVAs with age and sex as covariates.

Results: “Non-peekers” (n = 28) and “peekers” (n = 18) did not significantly differ in any of the sleep parameters: time in bed (mean $\pm$ SEM: 534.0 ± 9.7 vs 533.7 ± 10.4 minutes), total sleep time (467.3 ± 7.4 vs 473.6 ± 11.0 minutes), sleep efficiency (87.4 ± 0.8 vs $88.7 \pm 0.9\%$), wake after sleep onset (40.4 ± 3.2 vs 37.4 ± 3.0 minutes), and sleep latency (15.8 ± 2.1 vs 14.0 ± 2.4 minutes) (all $p > 0.05$). Among the “peekers”, only one child did not lie; thus, differences in sleep between lie-tellers and non-lie-tellers could not be examined. Among the lie-tellers, the unsophisticated (n = 3), the slightly sophisticated (n = 8), and the sophisticated (n = 6) groups did not differ in any of the sleep parameters (all $ps > 0.41$).

Conclusions: In healthy school-age children, sleep duration and quality did not appear to be associated with dishonest behavior or lie sophistication, suggesting that the relationship between sleep and higher-order cognitive functions, such as deception, may be more trivial than those with basic cognitive functions found in previous studies.

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Objective markers of in-dream speech and audition in narcoleptic lucid dreamers

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Introduction: The functional significance of dreams and dream-related content remains unknown. Therefore, investigating objective markers of dream content may clarify the underlying neurobiological basis of dream generation and paint a clearer picture of the function of dreaming. Recent studies conducted on REM sleep behaviour disorder (RBD) patients suggest that dream content relies on wake-like cerebral pathways, as conversation properties are highly conserved between wake and dreams. This suggests that in-dream conversations are generated and processed similarly those during waking. The possibility remains that speech-related muscle activation during REM sleep mirrors waking neural pathways. As no objective markers of speech and audition during have been identified, this project aims to identify these markers and relies on a lucid-dreamer model for real-time validation.

Materials and methods: To investigate the dynamics of muscle twitches during the night, we recruited 11 volunteers (6 females, 5 males), including lucid (n=4) and non-lucid dreamers (n=7). Lucid participants were all narcoleptic (type 1 or 2) patients who suspended their treatment during the experiment to increase the occurrence of an early REM episode during naps. 64-channel EEG, EMG electrodes, and respiratory belts were used to assess brain and muscle activity. Middle ear muscle activity (MEMA) was measured using earplugs. Participants underwent overnight and nap recordings, with dream content collected after awakening. Sleep stages and muscle activity were manually scored. All experimental procedures involving human participants were reviewed and approved by the Comité de Protection des Personnes Ouest III. Written informed consent was obtained from all participants prior to inclusion in the study.

Results: Overnight recordings show that spontaneous activity of the laryngeal and orbicularis muscles decreases with NREM stages, but is significantly higher in REM sleep, primarily as short twitches. Similarly, MEMA increases during REM sleep. Overnight, no correlation was found between the incidence of muscle twitches and the breathing phase. In lucid dreamers, reports of speech were often associated with increased laryngeal and orbicularis muscle activity, and preliminary results suggest that stronger muscle activity is associated with reports of louder in-dream conversation. However, MEMAs could not be associated with acute reports of sounds.

Conclusions: Our study shows that speech-related muscles are more active during REM sleep. Reports from lucid dreamers suggest that in-dream speech leads to activation of the dreamers' lips and larynx. These results support the idea that the neural mechanisms of speech production is conserved in dreams. However, results with MEMA do not correspond to acute listening, although they may reflect anticipatory processes. Our results highlight the value of lucid dreamers in identifying objective physiological measures of dream processes. These findings shed light on the interplay between dream content and peripheral muscle activation and provide new avenues for investigating this mental state.

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Offline by Design: Cortical Mechanisms of Partial Sensorimotor Disconnection Across Sleep Stages and More

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Introduction: Partial sensorimotor disconnection is a defining feature of sleep, during which we spend approximately one-third of our lives functionally detached from the external environment—often unaware of potential threats. However, the mechanisms underlying this intriguing sensory and motor gating across sleep stages are poorly understood. When arousal thresholds are assessed using peripheral stimuli, they are typically higher during deep non-rapid eye movement (NREM) sleep than during rapid eye movement (REM) sleep. Interestingly, for example, locus coeruleus neurons show no response to mild auditory stimuli during REM sleep, whereas responses are present in NREM sleep. The cerebral cortex is widely regarded as the neural substrate of awareness. It also contributes to disconnection, but its specific role across different sleep stages remains unclear.

Materials and methods: Here we tested in mice whether optogenetic activation of cortical neurons in posterior parietal cortex (PtA) or medial prefrontal cortex (mPFC) is sufficient for arousal from NREM or REM sleep. Adult CaMKIIα::ChR2 mice of both sexes (> P56, 12 mice) were chronically implanted with optic fibres at PtA or mPFC, intracortical laminar probes and surface electrodes for electroencephalographic (EEG) recordings, as well as nuchal and vibrissal electromyographic (EMG) electrodes. To compare with sleep, experiments were also performed in two progressively deeper unresponsive states: a coma-like state by midbrain muscimol injection through pre-implanted bilateral cannulas, and anaesthesia by sevoflurane-dexmedetomidine co-administration. Finally, our ongoing work investigates arousal threshold during fast-induced torpor in adult C57BL6/J male mice implanted with EEGs and EMGs (8 mice) using brief auditory tones (1–11 kHz, 1 sec duration).

Results: We found that cortical laser stimulation (square pulses or 4–8 Hz train pulses lasting 1–5 sec) in either PtA or mPFC could always awaken the mice from NREM or REM sleep (8 mice). Interestingly, the awakening from REM sleep required significantly more laser power and/or longer stimulation compared to awakening from NREM sleep ($p = 2.6 \times 10^{-5}$). PtA stimulation was significantly more effective than mPFC stimulation, i.e. with PtA stimulation weaker and/or shorter pulses were required to induce arousal ($p = 7.7 \times 10^{-5}$). In addition, optogenetic cortical stimulation was also able to arouse mice from coma (12 mice) and produce cortical activation from anaesthesia (9 mice). Preliminary finding on torpor showed that the auditory arousal threshold in this largely unexplored physiological state was surprisingly lower than NREM sleep.

Conclusions: These findings demonstrate that direct activation of cortical neurons in mice is sufficient to disrupt the disconnection from sleep—as well as to induce behavioural and/or cortical arousal from deeper unresponsive states i.e. brainstem coma and general anaesthesia. Activation of cortical neurons awakens mice more easily from NREM sleep than from REM sleep, suggesting that disconnection during NREM sleep may notably result from corticothalamic slow-wave activity—disruption of which readily triggers awakening—whereas in REM sleep, it is largely driven by other mechanisms such as the lack of noradrenaline.

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Personality, cognitive performance and perceived workload in young adults with unmanaged sleep disorders after 20 hours of extended wake

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Introduction: There are inter-individual differences in the effects of extended wake on cognitive performance, including a potentially modifying influence of personality trait dimensions. Greater extraversion has previously been associated with poorer psychomotor vigilance performance during extended wake in young adults with healthy sleep.

Performance may also be worsened in individuals with sleep disorders. Up to 20% of young adults have sleep disorders that require clinical investigation and up to 80% of these disorders are undiagnosed. Yet, young adults with sleep disorders are poorly represented in existing studies of extended wake. The aim of this study was to determine associations between sleep disorders, cognitive performance and perceived mental workload after extended wake in young adults, and explore whether personality dimensions modify any observed associations.

Materials and methods: Data from 24 young adults aged 18 – 32 years (Mean(SD) = 25.0(3.9), 42% female) were included. Participants first completed a Structured Clinical Interview (SCISD) and NEO Personality Inventory (NEO-PI-R) with a trained psychologist. All participants included in analyses met diagnostic criteria for insomnia (n=14) or delayed sleep wake phase disorder (DSWPD; n=10) according to DSM-5-TR criteria but had no prior diagnosis or treatment for a sleep disorder at baseline.

Participants underwent a diagnostic polysomnography with sleep onset and offset times aligned with their habitual bedtime before commencing extended wake. The psychomotor vigilance task (PVT) was performed at 2 hours and 20 hours after wake. Reciprocal reaction time (RTT; 1/ mean reaction time) and number of lapses in attention were used to determine changes in performance and were the primary performance outcomes. The NASA Task Load Index (NASA-TLX) assessed subjective workload immediately after each PVT (performance, effort, frustration, and mental, physical, and temporal demand) on a 0-100 scale. Data were analysed in R Studio, using a combination of linear regression and mixed effects regression in the *lmer* package.

Results: We observed the anticipated effect of extended wake on PVT metrics, with reduced RRT (reflecting poorer performance, 3.02(0.56) v 2.22(0.77), $p < 0.001$), and increased PVT lapses (3(7) v 15(13), $p < 0.001$). All indicators of subjective mental workload on the NASA-TLX were elevated at 20hours wake compared to 2hours (all $p < 0.05$), with the exception of temporal demand ($p = 0.42$). Time by personality dimension interactions on PVT performance were not significant (all $p > .05$), suggesting cognitive performance was not modified by personality dimensions. However, extraversion modified the association between extended wake and mental workload, where higher extraversion was associated with higher perceived temporal demand ($B = 1.04$, 95%CI = 0.41, 1.68, $p = .002$), poorer perceived performance ($B = 0.79$, 95%CI = 0.08, 1.49, $p = .031$), and greater frustration ($B = 0.96$, 95%CI = 0.09, 1.83, $p = .033$).

Conclusions: Extraversion may modify the perceptions of performance and mental workload more broadly in young adults with sleep disorders. Unlike healthy sleepers, extraversion in young adults with sleep disorders modified the association between 20h of extended wake and subjective performance, but not objective performance. Personality-task mismatch on monotonous tasks may be an issue for extroverts who are entering healthcare professions, who may feel greater frustration and perceive poorer performance when sleep deprived.

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Preferences and Expectations of Mothers When Choosing Digital Medicine to Improve Their Babies' Sleep: An Analysis of 653 Global Surveys

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Introduction: Sleep disorders in infants aged 0 to 3 years are an increasing concern for parents, and many seek digital solutions to address them. With the rise of digital medicine, it is important to understand what parameters mothers value when choosing these approaches to improve infant sleep. This study aims to identify mothers' preferences and expectations regarding digital medicine, exploring factors such as professional training, personal experience, and expected outcomes.

Materials and methods: A total of 653 surveys were conducted with mothers seeking digital solutions through the professional Instagram account @AnaMariaSilvaPediatria. The sample was divided into three groups: 354 pregnant women (54.21%), 280 mothers with infants aged 0 to 4 months (42.88%), and 19 mothers with infants aged 4 to 36 months (2.91%). The surveys were completed by women from 26 countries, with the highest participation from Colombia (63.5%), the United States (7.21%), Venezuela (4.60%), Mexico (2.91%), and Argentina (2.61%). Data was collected on occupation, socioeconomic status, and expectations related to infant sleep. Data collection took place over a 6-month period, from July to December 2024.

Results: The main expectations of mothers were for their babies to sleep through the night (53.91%), to avoid dependency on breastfeeding or other sleep associations (24.50%), to improve naps (12.25%), and to get their babies to sleep in their own crib or room (9.34%). Regarding the factors influencing the choice of digital medicine, experience, testimonials, and results were the most relevant factor (36.84%), followed by the professional's medical training (31.58%) and social media content (15.79%). 10.53% of mothers valued methods that did not involve "letting the baby cry," and only 5.26% considered social media recognition of the doctor important.

Conclusions: The results suggest that mothers particularly value evidence of effectiveness through previous experiences and testimonials, as well as the medical training of the professional offering the digital solutions. The preference for methods that do not involve letting the baby cry reflects an interest in respectful approaches that are sensitive to the emotional needs of the baby. Despite the cultural and socioeconomic diversity in the sample, common expectations point to a significant improvement in infant sleep quality, underscoring the relevance of digital medicine in this context. This study contributes to understanding the factors motivating mothers to choose digital options for managing infant sleep and can guide the development of more effective and accessible intervention programs.

Sleep disorders after mild traumatic brain injuries in young female patients

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Introduction: . Aim of this study was to present cases of sleep disorders after mild traumatic brain injuries in young male patients(<40 years old).

Materials and methods: 10 cases are presented.10 young male patients. Range of age 18-40 years old. Some common symptoms were: 4 of patients have insomnia, 2 patients have sleep apnea, 2 have hypersomnia, and 2 have narcolepsy.

Results: All of them received :Cognitive behavioral therapy (CBT),Natural sleep-inducing remedies, Pharmacotherapy and continue Neurological, Psychological and Psychiatric Support. Good results in 9 patients (90%) and moderate in 1 (10%).

Conclusions: Multidisciplinary approach is essential to achieve optimal results for our patients.

Sleep Macro- and Microarchitecture in Major Depressive Disorder with Sleep State Misperception

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Introduction: Sleep state misperception, also known as paradoxical insomnia, is a phenomenon characterized by a mismatch between subjective and objective sleep assessment. It is highly prevalent among individuals with depression, yet its physiological underpinnings remain poorly understood. This study aimed to determine the associations between multidimensional sleep features and the presence of sleep perception impairment (SPI) in patients with depression, using both features of sleep macro-architecture and micro-architecture derived from polysomnography (PSG).

Materials and methods: We enrolled 63 patients (aged 18–65 years) meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria for major depressive disorder. Based on either a ≥ 60 -minute discrepancy in total sleep time or a $\geq 15\%$ gap in sleep efficiency between subjective sleep diary and objective PSG, participants were classified into sleep perception impairment (SPI; $n = 26$) or non-SPI ($n = 37$) groups. All underwent overnight PSG and completed standardized assessments, including the Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HAM-D), and cognitive testing using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). We extracted sleep macro-architecture (e.g., sleep efficiency, latency, apnea-hypopnea index [AHI]) and micro-architecture features (e.g., band power, spectral ratios). Additionally, we calculated sleep temporal entropy (STE)—a novel marker reflecting the fragmentation and irregularity of transitions across sleep stages—to capture dynamic aspects of sleep stability. Between-group comparisons used appropriate statistical tests. Logistic regression models examined associations with SPI: Model 1 adjusted for demographic variables; Model 2 added PSQI score, cognitive function, and HAM-D score; Model 3 further included AHI, periodic limb movement index (PLMI), health status, and comorbidities.

Results: Compared to patients without SPI, those with SPI exhibited significantly lower PSG-derived sleep efficiency (mean $\pm$ SD: $71.2\% \pm 10.3\%$ vs. $83.4\% \pm 8.1\%$, $p < 0.01$), longer sleep latency (28.7 ± 15.9 vs. 17.1 ± 10.2 minutes, $p < 0.01$), and greater subjective-objective mismatches in total sleep time and sleep efficiency (both $p < 0.01$). In univariate logistic regression, increased gamma power (OR = 2.15, 95% CI: 1.24–3.75, $p < 0.01$), higher overall sleep temporal entropy (OR = 2.47, 95% CI: 1.29–5.08, $p < 0.01$), and elevated REM theta/beta ratio (OR = 2.04, 95% CI: 1.17–3.52, $p = 0.01$) were significantly associated with SPI. These associations persisted after adjustment for demographic and clinical covariates. In the fully adjusted model, higher whole-night STE (OR = 2.62, $p = 0.01$) and an increased theta/beta ratio during REM sleep (OR = 2.19, $p < 0.01$) remained independently associated with SPI. Metrics from the STE and Ratios domains showed consistent and robust associations across all models, highlighting their potential utility as objective markers of sleep misperception in depression.

Conclusions: Our findings suggest that alterations in both sleep macro- and micro-architecture are closely associated with subjective-objective sleep discrepancy in individuals with depression. Digital biomarkers such as spectral ratios and entropy-based fragmentation metrics may provide insight into the neurophysiological mechanisms underlying subjective-objective sleep discrepancy in depression. They support the differentiation between perception-based and physiology-based sleep phenotypes, facilitating phenotype-driven intervention strategies.

Sleep Restriction Affects Sequential Updating Through Increasing Reward Sensitivity

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Introduction: Bayesian cognitive theories propose decision-making involves the integration of prior knowledge with new evidence to form updated judgements. This framework has been used to understand how sleep restriction (SR) impairs integration of information, with findings suggesting SR biases individuals toward relying more on prior knowledge and less on new evidence. However, previous work has employed static decision-making tasks where information needed to make the decision on each trial is provided afresh, and feedback does not influence decisions on subsequent trials. This limits insight into how SR affects more dynamic, experiential learning processes. In everyday settings, decision making often involves *sequential updating*, an iterative process where outcomes of decisions are continuously learned and integrated into future behaviour. This process is critical for adapting to changing environments, yet its relationship with sleep loss remains poorly understood. To address this gap, we used a probabilistic reversal learning paradigm, requiring participants to learn reward schemas iteratively and adjust to changing reward contingencies.

Materials and methods: 36 healthy participants (25F, 11M; $M_{age} = 24.46$, $SD_{age} = 5.07$) underwent two experimental conditions in counterbalanced order: Well-Rested (7 nights of 9h sleep opportunity) and Sleep-Restricted (7 nights of 5h sleep opportunity). Each was preceded by a 5-night wash-in period (8–9h sleep opportunity). Sleep schedules were implemented at home and monitored via actigraphy, diaries, and voicemail check-ins. On the last day of each condition, participants completed a 150-trial probabilistic reversal learning task, where participants selected between two options with 70% and 30% reward probabilities. Reward contingencies switched between options with 10% probability per trial.

To decompose task performance into its underlying cognitive components, we fitted an asymmetric Rescorla-Wagner model implemented within a Bayesian hierarchical framework, providing estimates of reward and nonreward sensitivity parameters. Additionally, a choice consistency parameter captured levels of decision noise in participants' choice patterns. To the model, we also included offset parameters capturing the amount of deviation in each base parameter attributable to SR. Lastly, task accuracy was analysed using a mixed-effects logistic regression.

Results: Computational modelling results revealed a significant increase in reward sensitivity under SR, indicating enhanced learning from positive outcomes. There were no significant effects of SR on nonreward sensitivity or choice consistency parameters. Task accuracy did not differ between conditions.

Conclusions: Although reward sensitivity was heightened following SR, this is not necessarily benign. Enhanced sensitivity to positive feedback may reflect a bias toward reward-driven behaviour at the expense of balanced information integration during sequential updating. In real world decision contexts, such as gambling or financial decisions, heightened reward sensitivity following SR may reinforce maladaptive risk-taking behaviour when rewards are delivered intermittently. Additionally, participants' altered reward sensitivity was not reflected in task accuracy, indicating conventional summary metrics of performance may overlook meaningful cognitive changes.

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Sleep Restriction Increases Propensity to Seek Instrumental Information during Decision Making

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Introduction: Previous research shows chronic sleep restriction (SR) reduces reliance on new information during decision-making, leading individuals to rely more on familiar, easy-to-understand prior knowledge. It remains unclear whether SR also reduces the motivation to seek out information that could support better decisions. In everyday settings, people often choose to acquire additional information to improve judgements and guide future behaviour, a process known as instrumental information seeking. If SR reduces reliance on new information, it may also reduce the drive to obtain it. To test this hypothesis, we used a task designed to measure willingness to seek instrumental information.

Materials and methods: 36 healthy participants (25F, 11M; $M_{age} = 24.46$, $SD_{age} = 5.07$) completed an at-home sleep protocol involving two experimental conditions in counterbalanced order: Well-Rested (7 nights with a 9-hour sleep opportunity) and Sleep-Restricted (7 nights with a 5-hour sleep opportunity). Each condition was preceded by a 5-night wash-in period (8–9 hours sleep opportunity). Adherence was ensured via actigraphy, sleep diaries, and daily voicemail check-ins. On the final day of each condition, participants completed an Instrumental Information-Seeking Task (IIST) based on an optional-stopping paradigm. Each trial displayed a grid of cells, with some contents (gold or rock) visible and others concealed. Concealed cells were equally likely to contain either resource. Participants could choose to pay in-game money to reveal more cells, then guessed whether gold or rock constituted the majority of the grid. Correct guesses yielded in-game money; incorrect guesses earned none. To maximise earnings, participants needed to weigh the cost of seeking additional information against its potential informational.

We fitted mixed-effects logistic regression models to assess whether SR altered the likelihood of

seeking additional information on the IIST. Interactions between sleep condition and key task features, including initial number of cells concealed, expected value of information (EVI) offered by revealed cells, and offer cost, were tested in a hierarchical regression framework. Lastly, increasingly complex random-effects structures were compared to determine optimal model fit.

Results: The best-fitting model included no interaction terms and a random slope for EVI, indicating SR did not interact with task features to predict information seeking. Model results showed, after controlling for task features, SR increased the likelihood of seeking additional information on the IIST.

Conclusions: Contrary to predictions based on prior findings, participants in the SR condition were more likely to seek additional information. This occurred independently of changes in sensitivity to EVI or cost, suggesting a general shift in information-seeking behaviour. Sleep-restricted individuals may engage in compensatory behaviour to offset SR-induced cognitive impairments. Alternatively, they may experience greater discomfort with uncertainty and increased motivation to reduce it. In real world settings where decisions involve uncertainty, such as financial or medical decision making, SR-induced increases in information-seeking behaviour could result in inefficient or excessive use of information, particularly when acquiring additional information is costly or does not improve quality of judgements.

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Sleep's Protective Effect on Fear Overgeneralization: The Role of REM Sleep and Theta Oscillations

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Introduction: Fear overgeneralization, defined as the excessive fear response to non-threatening stimuli, is a hallmark of anxiety-related disorders. Sleep has long been recognized as a critical factor in the consolidation and processing of fear memories, with research suggesting that different sleep phases, particularly with rapid eye movement (REM) and non-rapid eye movement (NREM) sleep, thought to have distinct roles. However, how sleep influences fear generalization remains largely unknown. This study systematically investigates the dynamic effects of sleep phases and their associated neural oscillations on fear generalization recently after sleep manipulation and remotely one week later.

Materials and methods: In a randomized controlled, between-subjects design, 126 participants were assigned to four groups: total sleep deprivation (SD, N=16), early-night (dominated by NREM sleep) SD (N=36), late-night (dominated by REM sleep) SD (N=38), and total sleep (N=36). Participants completed the fear conditioning test before the sleep intervention, followed by a recent fear generalization test after sleep, and the remote fear generalization test one week later. Both task-related neuroimaging data and behavioral data (subjective risking and objective skin conductance responses) were synchronously collected to analyze brain functional changes during generalized stimuli processing.

Results: Sleep, particularly REM sleep phase, inhibits fear generalization, whereas late-night SD, by reducing REM sleep, induces fear overgeneralization comparable to total SD. To further validate the specific role of REM sleep in fear generalization, we employed a support vector machine model (AUC = 0.81), and identified REM percentage as the dominant discriminant feature (weight = -1.23) between higher and lower generalization subtypes. The percentage of REM sleep was negatively associated with the degree of fear generalization ($\beta = -0.47$, $p < 0.001$, $R^2 = 0.21$), and positively correlated with dorsolateral prefrontal cortex (MNI: x = 39, y = 44, z = 6) activity during the recent generalization test ($r = 0.43$, $p_{\text{fwe}} < 0.001$). Notably, prefrontal theta oscillations mediated 44% of REM sleep's effects on fear generalization (indirect effect = -0.40, $p < 0.001$).

Conclusions: In summary, the present study suggests that the reduction of REM sleep following fear conditioning increases the risk of fear overgeneralization and alters related prefrontal activity. It enhances our understanding of the pivotal role of theta oscillations in the prefrontal cortex in mitigating fear overgeneralization during REM sleep. Our findings identify specific sleep phase, electrophysiological activities, and brain targets, opening potential avenues for non-invasive neuromodulation in the treatment of fear overgeneralization-related disorders.

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Sleep Surprises Questionnaire: Using Expectancy Violations from Naturalistic Behavioural Experiments to Enhance Sleep-Wake State Curiosity

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Introduction: Surprises, triggered by expectancy violations, drive new learning, reshape expectations, prompt adaptive behaviours, and generate evolving perceptions, creating further curiosity in a cycle of resilience. Surprises abound in sleep and waking, arising from naturally-occurring behavioural experiments and challenging our assumptions about sleep-wake states, next-day alertness and energy. The Sleep Surprises Questionnaire (SSQ) captures these expectancy violations in non-insomnia and (potentially) insomnia populations, promoting trust in sleep self-regulation, and gathering evidence that promotes curiosity about sleep-wake states. This oral presentation will explore how the SSQ's design and scoring illuminate surprise-driven learning, encouraging behaviours that enhance perception of sleep robustness with implications for preventive sleep health strategies.

Materials and methods: The SSQ, comprising 22 items across naturalistic behavioural experiments (eg, sleeping after an evening coffee or cinema screening), sleep-wake discrepancies (eg nearby sounds incorporated into dreams, time distortions), and next-day functioning (eg surprising alertness after broken sleep), uses a unified response scale:

N/A (never experienced), not surprised (0), mildly surprised (1), quite surprised (2), or very surprised (3). Scores sum across items (max 66, N/A excluded) with categories: little surprise (0–22), some surprise noted (23–44), very attentive to sleep surprises (45–66).

Objective is to establish SSQ norms (eg score distributions for 22 items (max 66), categories: 0–22, 23–44, 45–66), validate against ISI (insomnia severity) and DBAS-16 (dysfunctional beliefs), and assess content validity. Sourcing a population of non-insomnia adults (eg general population or students, N≈300 for normative study, N ≥ 100 for EFA, and N ≥ 50 for test-retest, stratified by age, gender). Will include a subset with mild insomnia (eg ISI 8–14) for comparison. Rationale is to gauge if SSQ scores reflect openness to surprise and correlate inversely with ISI and DBAS-16 scores. Will recruit participants using convenience sampling (eg universities, online platforms) or random sampling for representativeness, and obtain informed consent & ethics approval. Initially exclude clinical population (ISI ≥ 15) until second stage of research.

Results: Preliminary findings for 3 participants with mild insomnia (eg Sunday night sleep concerns) score low on both ISI (<15, or Subthreshold insomnia) and SSQ (eg SSQ: 6-10/66, "little surprise"), but individual high-surprise items (eg surprise at alertness after poor sleep) suggest intervention pathways. The preliminary data indicate higher openness & attentiveness to surprises inversely correlates with insomnia severity, offering a streamlined tool to foster adaptive sleep perceptions.

Conclusions: Even in a non-insomnia demographic, negative sleep predictions fuel sleep "safety-seeking" behaviours which reinforce beliefs about sleep fragility, while increased tolerance of the inherent uncertainty of sleep-wake state discrepancies drives optimistic predictions and nonfearful behaviours. Preliminary findings suggest naturalistic behavioural experiments have the potential to raise expectancy violations, reflected in SSQ scores which inversely correlate with insomnia severity & rigidly dysfunctional beliefs about sleep. Surprises disconfirm perceptions of fragile sleep and build confidence in sleep self-regulation. By quantifying surprise, the SSQ supports CBT-I behavioural experiments, creating learning opportunities to explore sleep-wake perceptions with growing curiosity.

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The association of unconsciousness, dreaming, and slow wave activity under general anesthesia

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Introduction: Natural sleep and general anesthesia both produce states of unconsciousness in which the brain becomes disconnected from the external environment, with the distinction being whether the process is spontaneous or artificially induced. Dreaming experiences, considered a form of “disconnected consciousness,” are known to occur not only during natural sleep but also under general anesthesia. Investigating the dreaming experience under anesthesia may offer a window into the neural basis of consciousness. Despite the increasing interest, the physiological mechanisms underlying dreaming experiences under anesthesia remain poorly characterized, and their similarities to dreaming during natural sleep have been scarcely investigated. This study aimed to investigate the neural mechanisms responsible for unconsciousness and dream generation by analyzing intraoperative EEG in patients who underwent surgery under general anesthesia.

Materials and methods: All participants underwent surgery under propofol-based general anesthesia at Stanford University Hospital between 2021 and 2023. Standard ASA (American Society of Anesthesiologists) monitoring and intraoperative EEG monitoring using 4-channel frontal SedLine electrodes were employed. Immediately upon emergence from anesthesia, participants were interviewed regarding the presence and content of any dreaming experiences. Data from 62 patients (mean age: 47.6 ± 14.6 years) who reported dreaming and 48 patients (mean age: 55.1 ± 13.9 years) who did not report dreaming were included in the analysis. EEG recordings were assessed using visual inspection, power spectral analysis, and time-frequency analysis, and comparisons were made between the dreamer and non-dreamer groups.

Results: 1. The time from slow wave activity (SWA) disappearance to emergence was significantly longer in patients who reported dreaming after surgery compared to those who did not ($p = <0.001$, $d = 1.36$). 2. The EEG during the pre-emergence period in the dreamer group was characterized by a gradual decline in alpha activity and a rapid increase in fast-wave activity in the gamma band.

Conclusions: These findings suggest that dreaming experiences under general anesthesia occur during the period between the cessation of SWA and emergence, indicating that “disconnected consciousness” is induced as a transitional state from the unconscious state to awakening. Furthermore, the present results also suggest that frontal alpha and/or beta activity serves as a potential marker of the dreaming experience during this period. The observed relationship between SWA and unconscious state, as well as between frontal alpha/gamma power and dreaming, provides novel insights into the neural substrates of consciousness and dreaming.

The effects of intense theatrical training on sleep structure of the following night

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Introduction: Research on sleep regulation has traditionally focused on the role of wake duration. However, there is now substantial evidence that sleep characteristics also depend on wake intensity (the degree of cognitive and physical activity). Data on humans mainly come from research on sleep-memory relationships, with numerous studies showing sleep changes after bedtime administration of different cognitive tasks. However, more ecological studies have almost exclusively been conducted on animals, through the enriched environment paradigm. Here we investigate sleep features after a day including a theatrical workshop session, compared to sleep following an ordinary day, in a group of young adults.

Materials and methods: Eighteen young women (mean age 21.4 ± 2.2) participating to a theatre workshop (26 sessions over 6 months) were recruited for the study. Their night sleep is monitored (by means of the Somno-Art® portable sleep device) at 4 different times: a Baseline night (BL), following a day with ordinary (routine) schedule, as monitored through a day log, and 3 post-training nights (TR), i.e., following the 2nd, 14th and 26th workshop session. Here we present preliminary data on 11 participants: specifically, we compared sleep features of BL with those of the first TR night through paired t-test.

Results: No between-conditions differences emerged for any sleep parameter: Time in Bed, Total Sleep Time, Sleep Latency, Wake After Sleep Onset, Sleep Efficiency, N1+N2 duration, N3 duration, REM duration, number of awakenings, of state transitions and of sleep cycles (all p 's $>.05$).

Conclusions: In contrast with literature conducted on animals with the enriched environment paradigm, our preliminary results suggest that, in humans, a similar paradigm does not produce acute sleep modifications. A plausible hypothesis is that intentional (rather than incidental) learning is necessary in humans to show acute effects on post-learning sleep, as suggested by data from the sleep-memory literature. Also, we know from previous literature that the effects of training on sleep quality could be detected only provided that baseline sleep is somehow impaired (especially in terms of reduced sleep depth and efficiency). Finally, we cannot rule out that cumulative effects of the long-term learning experience (i.e., the theatrical workshop) will emerge on subsequent post-session nights.

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The effects of poor sleep on empathy: A systematic review and meta-analysis

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Introduction: Recent research has explored whether poor sleep can reduce empathy, a cornerstone of human cooperation and social interaction. Empathy includes both cognitive aspects (understanding another person's emotional state) and affective aspects (sharing the feelings of someone else). The findings have been decidedly mixed, with some studies highlighting the causal link between poor sleep and reduced empathy, and others finding either no significant effect, or the exact opposite: an increase in empathy after experiencing poor sleep. The extant literature on the topic has also been mixed regarding methodology, whether by examining healthcare workers or the general population, for example, or focusing on different aspects of empathy. Thus, to better understand the effect of poor sleep on empathy, and whether we can pinpoint potential sources of heterogeneity in the field, the current study presents a systematic review and meta-analysis of the existing literature.

Materials and methods: We searched EBSCOHost, PubMed, and SCOPUS, for articles related to "sleep", "sleepiness", "insomnia", and "empathy" and "cognitive empathy". The search yielded 362 unique peer-reviewed articles on the impact of sleep disruptions on empathy in humans. Studies which examined the effect of empathy on sleep were not included. Studies were excluded if they did not include a direct examination of how poor sleep impacts empathy, if they were conducted on children, or if the empathic measure was not on the same individual (e.g., a patient rating physician empathy before and after the patient experiences disruptions in their sleep). Seventeen studies and 30 effect sizes were included in the final analysis. The meta-analysis followed the PRISMA guidelines in methodology and reporting standards.

Results: Results of the meta-analysis suggested a moderate and negative relationship between poor sleep and empathy (Hedges' $g = -0.38$, with a 95% confidence interval ranging from -0.55 to -0.22), such that poor sleep was associated with lower levels of empathy. Significant heterogeneity was observed ($I^2 = 74.5\%$, $Q(26) = 90.53$, $p < .0001$), suggesting meaningful variability in effect sizes across studies. Studies were conducted mostly in western countries (UK, US, Canada, Italy, Israel, Switzerland, and Sweden), except for two studies, one of which was conducted in China, and the other in Saudi Arabia.

Conclusions: Results indicated that overall, poor sleep negatively impacts empathy. This effect has been found both in experiments and in ecological, observational, settings. For example, impaired empathy due to lack of sleep has been shown in paramedics, doctors, nurses, and other healthcare professionals, suggesting that lack of sleep due to long or late shifts may impact patient care. Results also indicated significant heterogeneity across studies, which may derive from differences in populations (general population compared to healthcare workers, for example), or variability in measurements of both sleep and empathy. A summary of the literature regarding these sources of heterogeneity, and the implications of the meta-analytic results will be discussed.

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The Impact of Sleep Deprivation on Superiority Illusion

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Introduction: Superiority Illusion (SI) is common cognitive bias which healthy individuals usually have the tendency to overestimate their abilities than others. Lower SI ability has been proved linked to various mental health problems, including generalised anxiety disorder, depression and bipolar disorder. Previous studies found that cognitive function would be impaired by sleep deprivation. However, the change on SI remains unexplored. This study aims to elucidate the effects of sleep deprivation on SI and the related psychological mechanisms.

Materials and methods: Healthy adults from universities aged 18–28 years completed a repeated-measures cross-over design, including 2 sessions conducted in a counterbalanced order—one after a normal night of sleep (SR) and one after 24 h sleep deprivation (SD). Sleep status control prior to the experiment includes actigraphy devices and sleep diaries for more than seven consecutive days. On the night preceding SR session, polysomnography (PSG) was conducted. On the morning of the behavioral task, affective states were assessed through the Positive and Negative Affect Schedule (PANAS) and the Brief Fear of Negative Evaluation Scale (BFNES). The core SI task consists of 60 trials, incorporating two dimensions (positive and negative words).

Results: Data from 47 participants (mean age 23.0 ± 1.0 years, 27 women) were included in the final analysis. A significant reduction on SI scores in SD (mean difference = -0.184 , 95%CI = $[0.050, 0.317]$, $t = 2.775$, $p = 0.008$), a significant main effect of sleep condition ($F_{(1, 46)} = 7.701$, $p = 0.008$, partial $\eta^2 = 0.143$) and a significant main effect of valence ($F_{(1, 46)} = 19.151$, $p < 0.001$, partial $\eta^2 = 0.294$) were found, whereas the interaction between these factors was nonsignificant ($F_{(1, 46)} = 0.004$, $p = 0.948$). In positive-word trials, SD led to a marginal reduction in SI scores (mean difference = -0.181 , 95%CI = $[-0.371, 0.009]$, $t = 1.918$, $p = 0.061$), whereas in negative-word trials, the reduction was statistically significant (mean difference = -0.187 , 95%CI = $[-0.308, -0.065]$, $t = 3.095$, $p = 0.003$). Correlational analyses under SD revealed total task scores had positive correlations with PANAS positive affect scores ($r = 0.353$, $p = 0.015$) and negative correlations with PANAS negative affect scores ($r = -0.343$, $p = 0.018$) and BFNES scores ($r = -0.421$, $p = 0.003$).

Conclusions: The present findings indicate that SD results in a significant decline in SI scores. Meanwhile, the SD scores correlate to post-deprivation emotional states. These results provide novel insights into the role of sleep in self-referential cognitive processes and offer a theoretical foundation for understanding sleep deprivation.

The Impact of Sleep Loss on Decision Making - Opening the Cognitive Black Box

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Introduction: The detrimental effect of sleep loss on decision making is well-known, but identifying cognitive mechanisms by which sleep deprivation impairs decision-making remains difficult. This stems largely from a widespread reliance on global behavioural metrics of cognitive tasks, providing performance summaries but offering limited insight into the latent processes driving behaviour. To address this gap, we highlight the cognitive "black box" problem in sleep research and demonstrate how computational cognitive modelling can be used to clarify the mechanistic effects of sleep loss on decision making.

Materials and methods: Progress in sleep and decision-making research requires moving beyond surface-level behavioural summaries and into the domain of computational cognitive modelling. These models quantify latent cognitive processes, such as reward value sensitivity and decision noise, providing a more nuanced view of how cognitive processes are disrupted by sleep loss and affect behaviour downstream. To demonstrate this approach, we reanalysed Iowa Gambling Task data

previously published in a paper investigating the effects of 51h and 75h of total sleep deprivation (TSD). Two cognitive process models, the Prospect Valence Learning-Delta (PVL-D) and the Value plus Sequential Exploration (VSE) model, were fit using Bayesian estimation, allowing us to isolate changes in underlying decision mechanisms across time spent awake.

Results: Model comparisons indicated the VSE model was a superior fit of the data. Accordingly, our reanalysis showed TSD increased decision noise and further reduced sensitivity to gains and losses, effects not otherwise detected through relying on the conventional IGT score. Specifically, by 51h TSD, participants exhibited significantly lower choice consistency, indicating noisier and less goal-directed behaviour. By 75h TSD, value sensitivity was also significantly impaired, indicating diminished ability to differentiate between advantageous and disadvantageous outcomes. These findings provide complementary insight into results reported by the original paper.

Conclusions: This reanalysis provides new insights into the cognitive processes underlying how sleep loss degrades decision-making: by decreasing behavioural consistency of responses and decreasing sensitivity to differential rewards. These mechanisms cannot be detected by traditional global behavioural metrics. Computational cognitive modelling offers a powerful tool to complement traditional quantitative methods, providing higher-resolution insights into sleep-related cognitive impairments and aligning sleep research with the latest models in cognitive neuroscience. Incorporating such models can inform targeted interventions aimed at mitigating decision errors in sleep-deprived individuals, particularly professionals working in high-stakes environments who face chronic sleep loss as a result of scheduling demands.

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The Interplay of Sleep and Cognition: Amnesic MCI and Severe OSA in the Elderly

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Introduction: 79-year-old gentleman who sought medical attention due to concerns about failing memory. Although retired, he remains active in business. His family has observed that his immediate memory is poor, leading to frequent repetitions of events and conversations. Additionally, he sometimes shows confusion with dates and the context of events. Despite being aware of these issues, he attributes them to aging, saying, "what can you expect after 75?" He weighs 90 kgs, has a history of a sedentary lifestyle in recent years but was active during middle age. He describes himself as a "light sleeper" with frequent nocturnal awakenings and has a long-standing history of snoring. Despite not feeling refreshed upon waking, he believes his sleep is acceptable, although he is more concerned about his forgetfulness.

Materials and methods: Plan of Assessment:

1. Biochemistry, MRI Brain & Neuropsychological assessment
2. Indication for Sleep study: His history of long-standing snoring, frequent nocturnal awakenings, and non-restorative sleep, along with his ability to nod off easily when not engaged in goal-directed tasks, strongly suggest a possible sleep disorder.

Results: Sleep Study results indicate several important findings:

1. Sleep efficiency was 95%
2. Sleep Stage Percentages -
 - N1 - 23.7%
 - N2 - 57.1%
 - N3 - 11.4% (Normal N3 sleep 15-20%)
 - R - 7.8% (Normal R sleep 20-25%)
3. Obstructive apnea - 331, Hypopnea - 141
4. Apnea Hypopnea index (AHI) - 59 events/hr. An AHI of 59/hour is classified as severe obstructive sleep apnea.

5. The average oxygen saturation was 96% & lowest 78%
6. He spent 5 minutes of his sleep time below 90% of SpO₂
7. Total Arousals - 257
 - Respiratory arousals - 129
 - PLMS - 76
 - Spontaneous arousals - 52

Interpretation: Severe obstructive sleep apnea with secondary poor fractionation of deep sleep

Conclusions: Cognition and Sleep:

1. Deep Sleep (N3) - Slow-wave sleep (SWS), is essential for consolidating declarative memories (e.g., facts and events). During this phase, the brain replays and strengthens memories from the day, integrating them into long-term storage.
2. REM Sleep is crucial for procedural memory consolidation (e.g., motor skills) and emotional regulation.
3. Glymphatic System - It is a waste clearance system in the brain that removes metabolic waste products, including amyloid-beta and tau proteins, which are associated with neurodegenerative diseases. This system is most active during sleep, especially during deep sleep (N3)
4. Autophagy activation - REM sleep has been shown to be important for neuronal autophagy, aiding in the removal of cellular debris and damaged proteins, thereby supporting overall brain health
5. OSA leads to repeated interruptions in sleep which can impair the glymphatic system's ability to clear waste products effectively, potentially exacerbating cognitive decline and increasing the risk of neurodegenerative diseases.
6. Ensuring good sleep health and addressing sleep disorders like OSA are vital steps in supporting cognitive function and reducing dementia risk

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The Myth of Male Vulnerability: Exploring Sex Differences in Physiological Risk for Drowsy Driving

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Introduction: Drowsiness accounts for ~20% of all motor vehicle crashes, and young male drivers are overrepresented in drowsiness-related crash statistics. This is in contrast to laboratory and shift worker literature showing that women are vulnerable to sleep loss, relative to men. Despite 75% of drowsiness-related crashes being caused by men, there is a paucity on research examining the causes of this overrepresentation. Understanding whether young men have a physiological vulnerability to drowsy driving, or whether they are overrepresented due to behavioural and environmental factors is important for developing campaigns and interventions to curb drowsy driving behaviour. This study aimed to examine whether men and women showed differential vulnerability to drowsy driving in a controlled track environment, following total sleep deprivation, where behavioural and environmental factors had been removed.

Materials and methods: Thirty-two healthy, young, experienced drivers (N=16 women; N=16 men) aged 21-35 were recruited from the community. Participants completed two counterbalanced 2h daytime track drives in a fully instrumented vehicle: one after an 8h sleep opportunity (well-rested) and one after a night of no sleep (sleep deprived). Drives were completed in an automatic transmission vehicle equipped with a forward-facing camera around a closed-circuit track designed to mimic suburban driving conditions. Participants were accompanied by an experienced driving instructor and a

study technician. Lane deviations and near-crashes were used to measure driving impairment. Subjective sleepiness was measured every 15 min with the Karolinska Sleepiness Scale and Likelihood of Falling Asleep scale, and participants completed the Symptoms of Sleepiness Questionnaire at the end of each drive.

Results: As expected, total sleep deprivation resulted in an increase in lane deviations ($p < .001$), near crash risk ($p < .001$), subjective sleepiness ($p < .001$), subjective likelihood of falling asleep ($p < .001$) and symptoms of sleepiness ($p < .001$). Following a night of no sleep, 75% of women and 44% of men experienced a near crash ($OR = 3.9$, $\chi^2 = 3.2$, $p = .072$). With 50% of women experiencing a near crash after 66 min of driving. On average, women exhibited 4.0 lane deviations per 5 min of driving, whereas men experienced 2.9 lane deviations/5 min. There was no effect of sex, or interaction between sex and sleep deprivation for lane deviations or subjective outcomes ($p > .208$).

Conclusions: Young men do not show a physiological vulnerability to drowsy driving when compared to young women. Over-representation of men in drowsiness-related crash statistics is likely due to behavioural, lifestyle and environmental factors such as increased risk-taking behaviours, and differences in attitudes towards sleep, drowsy driving, and driving safety. Education campaigns targeting drowsy driving need to focus on a shift of attitudes towards drowsiness, risk taking behaviour, and driving in young men. Women were 3.9x more likely to crash following total sleep deprivation. Given women show differential vulnerability to sleep loss across the menstrual cycle, further investigation into women's vulnerability to crash risk is warranted.

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The neural pathway from glutamatergic neurons in the lateral hypothalamus to the rostromedial tegmental nucleus mediates defensive behaviors in mice

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Introduction: Defensive behaviors responding to actual or perceived threats are essential for survival, encompassing flight, avoidance, and hiding. Although these behaviors are adaptive, excessive or maladaptive defensive responses are implicated in the pathogenesis and progression of various psychiatric disorders in humans. The underlying neural circuit mechanisms governing defensive behaviors remain poorly understood. In this study, we investigated the role of the neural circuit from lateral hypothalamic (LH) glutamatergic neurons to the rostromedial tegmental nucleus (RMTg) in defensive behaviors in mice.

Materials and methods: Adult male vesicular glutamate transporters (Vglut2)-Cre mice (8–10 weeks old) were randomly assigned to either a control group (mCherry) or an experimental group (ChR2). The control group received bilateral injections of AAV2/9-EF1 α -DIO-mCherry-WPRE-pA into the LH, while the experimental group received AAV2/9-EF1 α -DIO-ChR2-WPRE-pA. Optical fibers were implanted in the RMTg of all mice. After three weeks for recovery from surgery and sufficient viral expression, behavioral tests—including the open field test, real-time place preference (RTPP) test, and hiding box test—were conducted. Following the experiments, viral infection was confirmed by mCherry expression in the LH, and c-Fos expression in the RMTg was assessed to validate the activation of the pathway from LH glutamatergic neurons to the RMTg upon 473 nm laser stimulation.

Results: During a 473 nm laser stimulation of RMTg GABAergic terminals in the LH, mice in the ChR2 group exhibited significantly increased velocity in the open field test, indicative of escape behavior. In the RTPP test, these mice spent less time on the preferred side, suggesting avoidance behavior. Additionally, the latency to enter the hiding box was significantly reduced, reflecting enhanced hiding behavior. The expression of c-Fos in the RMTg was elevated in ChR2-expressing mice following laser stimulation, confirming successful pathway activation.

Conclusions: Activation of the LH glutamatergic neuron projections to the RMTg promotes defensive behaviors in mice. These findings provide insights into the neural basis of defensive behaviors and may inform future research on mental diseases.

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The role of sleep-related dysfunctional beliefs in the effect of cognitive behavioral therapy on the severity of insomnia

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Introduction: Dysfunctional beliefs are an important characteristic of patients with chronic insomnia. Unreasonable sleep beliefs will aggravate the severity of insomnia and affect the normal life of patients. Cognitive behavioral therapy for Insomnia (CBT-I) is currently the first-line treatment for insomnia in the world. However, there is a lack of specific research on the role of changes in sleep-related dysfunctional beliefs in the treatment process. Therefore, the purpose of this study was to explore the changes of dysfunctional beliefs in different dimensions and their effects on the severity of insomnia during CBT-I.

Materials and methods: 120 patients with insomnia were included. They were randomly assigned to CBT-I group (n=30), cognitive therapy for insomnia group (CT-I, n=30), behavioral therapy for insomnia group (BT-I, n=30), and conventional treatment group (TAU, n=30). Patients in all three treatment groups received treatment once a week for eight weeks. The Insomnia Severity Index (ISI) and the Brief Version of Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16) were used to assess changes in insomnia severity and sleep-related dysfunctional beliefs at baseline, 4th week, and 8th week, respectively. The parallel process latent growth curve model (PP-LGCM) was used to analyze the mediating role of dysfunctional beliefs in the process of cognitive and behavioral techniques to improve sleep quality. The Cross-Lagged Panel Model (CLPM) was used to explore the interaction between dysfunctional beliefs and insomnia severity over time.

Results: CBT-I, CT-I, BT-I can effectively improve the severity of insomnia and reduce sleep-related dysfunction beliefs ($p<0.001$). Sleep-related dysfunctional beliefs fully mediated the effect of CT-I on insomnia severity and partially mediated the effect of CBT-I. However, the mediating effect of sleep-related dysfunctional beliefs was not found in the BT-I group. In CBT-I group, insomnia severity at week 4 significantly predicted the scores of perceived consequences of insomnia ($p=0.011$) and scores in the medication dimension ($p=0.020$) at week 8. In CT-I group, the baseline medication dimension scores significantly predicted the severity of insomnia in 4th week ($p=0.015$), which can significantly predict the total score of dysfunctional beliefs ($p=0.002$) and the scores of perceived consequences of insomnia ($p<0.001$) at 8th week. While in BT-I group, the severity of insomnia in 4th week can predict the total score of dysfunctional beliefs ($p=0.003$) and the scores of medication dimension ($p<0.001$) in 8th week.

Conclusions: This study investigated the relationship between sleep-related dysfunctional beliefs and the severity of insomnia in different treatment methods. The results showed that sleep-related dysfunctional beliefs mediated the effects of CBT-I and CT-I on the severity of insomnia. It was also found that the severity of insomnia can predict changes in sleep-related dysfunctional beliefs.

Time-Varying Effects of Deep Learning-Based Physical Activity Patterns on All-Cause Mortality: the NHANES 2003–2006 study

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Introduction: Average total activity count (TAC), a single dimension of objective physical activity (PA), showed time-varying effect in all-cause mortality, while not considering the complex interaction among PA features. Convolutional Long Short-Term Memory (Conv-LSTM) architecture can fully extract all PA features and comprehensively evaluate the objective PA pattern (PAP). The main goal of this study was to analyze whether PAP can present stronger prediction performance on all-cause mortality than TAC.

Materials and methods: We focus on PAP and TAC extracted from a hip-mounted accelerometer from the 2003 to 2004 NHANES cycle. For PAP, the reshaped three-dimensional physical-activity matrices were fed into a two-stage deep-clustering framework. During the first stage, a Conv-LSTM auto-encoder was pre-trained, and the resulting latent vectors were subjected to k-means initialization with the number of clusters (k) empirically set to 2–5. In the second stage, an Improved Deep Embedded Clustering algorithm jointly fine-tuned the auto-encoder and its trainable clustering layer, ultimately assigning a cluster label to every participant. Internal validity was quantified with the silhouette coefficient, Calinski–Harabasz index and Davies–Bouldin index. For TAC, participants were stratified into distinct groups based on the optimal number of clusters of PAP. We then tested two models. The first model fit was a Cox proportional hazard model with fixed time effects of PAP and TAC on risk of mortality. The second model fit was a Cox model with time-varying coefficient for PAP and TAC.

Results: This study ultimately enrolled 6,546 participants aged 18 years and older, all of whom had high-integrity accelerometer measurement data and complete mortality follow-up records. The mean follow-up of this study is 10.21 years, and we observed 961 deaths with a mean time to event of 8.41 years. The optimal clustering performance for PAP was achieved at $k = 2$ (silhouette = 0.925; Calinski–Harabasz = 306 348.60; Davies–Bouldin = 0.092). Accordingly, the cluster labels obtained with $k = 2$ (high- and low-PAP groups) were retained for all downstream analyses. For TAC, participants were stratified into high- and low- TAC groups based on median TAC values. The results of the Wald test indicated that the first model in both PAP ($p=0.025$) and TAC ($p=0.034$) may not be appropriate, for the strong time-varying effect of PA on mortality. In the second model, the estimated HR of PAP and TAC is 0.386 (95%CI 0.25–0.597; $p < 0.001$) and 0.392 (95%CI: 0.234–0.657, $p < 0.001$), respectively. As for the time-varying effect, the HR increases at a rate of 5.4% per year ($HR=1.054$, 95%CI 1.054–1.008; $p = 0.02$) in PAP model, whereas in the TAC model it increases by 4.8% per year ($HR = 1.048$, 95% CI 0.997–1.102; $p = 0.065$).

Conclusions: Both PAP and TAC were significantly associated with reduced all-cause mortality risk, with comparable overall protective effects. However, only the PAP demonstrated a statistically significant time-varying effect, suggesting that its association with mortality attenuated more clearly over time. These findings highlight the potential of deep learning-based PAP analysis to capture multidimensional PA features in mortality risk prediction, informing more precise health interventions and preventive strategies.

Toward a Rocking Apparatus at Home: Effects of Continuous Rocking Stimulation Over Consecutive Nights on Sleep

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Introduction: This study investigates whole-night continuous rocking stimulation, an emerging approach with potential benefits for improving sleep quality through the modulation and entrainment of sleep spindles and slow oscillations (SO's). Prior research has been conducted mainly over one night, limiting real-world applicability. This in-lab pilot study aimed to assess the efficacy of a new rocking bed prototype on sleep quality over multiple consecutive nights, in young, healthy participants.

Materials and methods: We developed a rocking bed prototype that replicated the rocking parameters used by Bayer et al. (2011) and Perrault et al. (2019), who demonstrated benefits for sleep and memory in healthy and good sleeper young adults. The new apparatus consisted of rails with acceleration and braking capabilities powered by an electric motor that moved the mattress laterally (21 cm every 4

seconds; 0.25 Hz).

Following an adaptation night, 19 participants (age=25±3.62; 10F) completed three consecutive nights with rocking stimulation (ROCK1-2-3) and two stationary nights (STAT1-2) one week apart, in a randomized counterbalanced order. Whole night polysomnography including EEG (24 scalp electrodes), EOG, EMG, and ECG were recorded at each night. Sleep scoring (AASM) and EEG preprocessing (artefact/arousal) were performed manually using Wonambi Python toolbox. Macro-architecture was extracted using the Seapipe Python toolbox. Sleep spindle and SO's were automatically detected and extracted based in Fz and Pz with methods described by Ray et al. (2015) and Staresina et al. (2015), using an individually adapted frequency bandwidth. We assessed the probability of their appearance being influenced by the bed's motion (i.e., entrainment). Analyses examined the Visit*Condition interaction and post-hoc analyses.

Results: On Night 1, rocking (ROCK1) slightly disrupted sleep, with increased wake time, N1, and N2, at the expense of N3 and REM (all $p<.05$), alongside a modest decrease in fast spindle density ($p=.033$; corrected threshold: $p<.013$) compared to STAT1. Across subsequent nights, both conditions showed improved sleep architecture (reduced wake and N2, increased REM; all post-hoc $p<.05$), with rising sleep efficiency ($p=.012$). This improvement was more pronounced in the rocking condition from ROCK1 to ROCK2, reaching levels comparable to STAT2 ($p=.259$). Fast spindle density also increased in ROCK2 (Condition*Visit interaction: [N2] $p=.010$; [N3] $p=0.008$) and were maintained at ROCK3, likely due to emerging entrainment (Chi-square: $p=0.10$). SO's were entrained from the first night but we observed no effect of condition or visit on their characteristics.

Conclusions: Despite initial disruption, a rebound effect was observed in both conditions, with greater improvement in the rocking condition, suggesting that rocking benefits may take longer to emerge with our prototype. The early entrainment of SO's (Night 1) and later spindle entrainment (Night 2) suggest an immediate neural response to stimulation, though improvements at the sleep architecture level may require more time. These findings highlight the need to refine motion parameters, as further discussed in a complementary abstract (see Barbaux et al.). While our results differ from the literature, a longer protocol may have revealed eventual benefits. Future studies should explore long-term effects and feasibility in home settings, particularly for individuals with sleep disturbances.

Trait-level mindfulness, objective and subjective sleep, and risk for hypertensive disorders of pregnancy

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Introduction: Poor sleep is pervasive in pregnancy and increases risk for hypertensive disorders of pregnancy. Mindfulness, defined as paying attention to the present moment non-judgmentally, is associated with fewer insomnia symptoms and better sleep quality in non-pregnant adults. However, the associations among mindfulness and sleep in pregnancy, and their associations with hypertension risk, are unknown.

Materials and methods: We evaluated associations among self-reported mindfulness (using the Five Facets of Mindfulness Questionnaire), objective (7 days of actigraphy) and subjective (Pittsburgh Sleep Quality Index, PSQI) sleep, and 24-hour ambulatory blood pressure in a sample of pregnant women at risk for hypertensive disorders of pregnancy. Analyses were conducted using IBM SPSS v.25.

Results: Participants were 137 pregnant women at risk for hypertensive disorders of pregnancy according to American College of Obstetricians and Gynecologists criteria and were enrolled in an ongoing trial of prenatal mindfulness training (NCT04626245). Participants were 32 years old (SD=5), 18 weeks' gestation (SD=1) at the time of data collection, and 45% were pregnant with their first baby. 27% of participants were Hispanic, 23% were Black, and 53% were non-Hispanic White. Average total sleep time from actigraphy was 377 minutes (SD=87, range: 187-671). Average global sleep quality as measured by the PSQI was 8 (SD=4, range: 1-17). 69% of the sample had poor sleep quality (> 5 on PSQI). We performed linear regression analyses, adjusting for parity, income, education, ethnicity, and race, to examine associations among trait-level mindfulness, objective and subjective sleep, and daytime and nighttime blood pressure. Results revealed that trait-level mindfulness was significantly associated with subjective sleep quality, such that higher scores on subscales 'acting with awareness' (focusing attention on one's current activity; (B=.32, $p<.001$)) and 'non-judging of inner experiences'

(experiencing thoughts/feelings without judging them or criticizing oneself; $B=.32$, $p<.001$) were associated with better global sleep quality on the PSQI. Actigraphy-measured total sleep time was associated with lower nighttime systolic ($B=-.24$, $p=.027$) and diastolic blood pressure ($B=-.22$, $p=.046$). Better PSQI-measured global sleep quality was also associated with lower nighttime systolic ($B=-.22$, $p=.023$) and diastolic ($B=-.20$, $p=.032$) blood pressure. There were no associations between trait-level mindfulness and blood pressure measures.

Conclusions: Overall, participants at risk for hypertensive disorders had short sleep duration (less than 7 hours of sleep per night) and poor subjective sleep quality. Higher trait-level mindfulness was associated with better subjective, but not objective, sleep quality. Shorter sleep duration and poorer subjective sleep quality were associated with higher blood pressure during the night. Lastly, trait-level mindfulness was not significantly associated with blood pressure. Future studies are needed to evaluate interventions aimed at improving prenatal sleep health and decreasing risk for adverse obstetric outcomes.

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Who Benefits — and Who Doesn't — from a Nap? Diverging Cognitive Outcomes Predicted by Insomnia Severity, Fatigue, and Sleep Quality

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Introduction: Daytime naps improve cognitive performance, but individual differences in sleep history and fatigue may moderate the benefits. Insomnia severity (ISI), functional fatigue (FSS), and global sleep quality (PSQI) are overlapping yet distinct constructs. We investigated how each uniquely predicted improvements following a 30-minute nap across cognitive domains of working memory, sustained attention, and emotion processing.

Materials and methods: Young adults ($n=47$; males=5) completed performance testing before-and-after counterbalanced nap and wake conditions. Difference scores (post-pre, nap-wake) were calculated for outcomes. To investigate the unique predictive value of ISI, PSQI, and FSS on performance following a nap, hierarchical regressions were employed. In each model, total sleep time (TST) and the two non-target sleep-related variables were entered simultaneously in Step1 to control for shared variance. The primary predictor (ISI, PSQI, or FSS) was entered in Step2. Good and poor sleepers were recruited: 32 participants scored >5 on PSQI (mean=7.2, range:3-15), 18 scored >8 on ISI (mean=6.96, range:0-21), and 25 had clinically significant fatigue on FSS (mean=35.11, range:14-51). TST in the nap ranged 10-29min (mean=23min). We assessed working memory with a 2-back task, sustained attention with a Reaction Time (RT) task, and emotion processing with a facial categorization task displaying Happy, Sad, Angry, Fearful faces.

Results: **Insomnia severity (ISI)** significantly predicted change in RT to errors in **working memory** following the nap. Controlling for TST, FSS, and PSQI, ISI explained additional variance ($\beta=-.601$, $p=.025$); participants with greater insomnia symptoms experienced larger gains (i.e., faster responses indicating improved cognitive efficiency). ISI also predicted WM accuracy, controlling for TST and either FSS or PSQI, but did not survive as a unique predictor when adding both FSS and PSQI.

Fatigue (FSS) significantly predicted improvements in **sustained attention** following a nap. Controlling for TST, ISI, and PSQI, FSS explained additional variance for mean RT ($\beta=-.350$, $p<.029$) and RT instability (composite of RT standard deviation, 10% slowest RTs, number of lapses) ($\beta=-.336$, $p<.035$), indicating higher fatigue was associated with greater reductions in mean RT and instability, reflecting improved attention due to the nap.

Sleep quality (PSQI) significantly predicted changes in **emotion categorization accuracy** after a nap. Controlling for TST, ISI, and FSS, PSQI explained additional variance ($\beta=-.699$, $p<.001$), showing that poorer sleep quality was linked to diminished recognition of emotional faces, particularly for angry expressions which are salient social cues ($\beta=-.647$, $p=.001$).

Conclusions: **These findings underscore a dissociation among self-report sleep scales and their prediction of cognitive benefits of napping.** FSS, which captures general daytime fatigue, predicted improvements in attentional speed/stability—suggesting individuals experiencing fatigue may benefit from naps as an intervention for vigilance. ISI, reflecting subjective difficulties initiating or maintaining sleep, was associated with working memory improvement, possibly because naps provide compensation for those with reduced nocturnal sleep. PSQI, indexing sleep quality over past month,

was associated with *diminished accuracy* in emotion processing; cumulative sleep debt may have increased sleep inertia or limited restorative potential of the nap. These results highlight the importance of differentiating functional fatigue, acute insomnia symptoms, and chronic sleep quality when assessing who might benefit from napping.

Whose Dream Experiences Are More Intense? An Exploratory Study on the Relationship between Nightmares/Sexual Dreams and Personality Traits

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Introduction: Dream experiences, such as nightmares and sexual dreams, serve as windows into individuals' psychological and emotional health. Guided by the continuity hypothesis of dreaming, this study investigates how personality traits and anxiety predict the intensity of nightmares and sexual dreams in athletes and non-athletes. Athletes, often under high-performance stress, may exhibit distinct dream patterns compared to non-athletes, while sexual dreams reflect aspects of sexual mental health. By comparing these phenomena, this research addresses critical questions: *Which individuals experience more intense nightmares or sexual dreams, and how do personality traits and anxiety contribute to these differences?*

Materials and methods: Two cross-sectional studies were conducted in athletes and non-athletes.

1. **Nightmare Study:** Participants included 187 athletes (mean age = 20.44, SD = 0.85; 91 females) and 90 non-athletes (mean age = 20.34, SD = 1.65; 52 females) reporting nightmares. Tools: Nightmare Experience Questionnaire (NEQ), Zuckerman-Kuhlman-Aluja Personality Questionnaire-Short Form (ZKA-PQ/SF), and Self-Rating Anxiety Scale (SAS).
2. **Sexual Dream Study:** 411 participants (50.12% reporting sexual dreams; 88 athletes [mean age = 21.12, SD = 0.83; 24 females] and 118 non-athletes [mean age = 20.29, SD = 1.58; 71 females]) completed the Sexual Dream Experience Questionnaire (SDEQ), ZKA-PQ/SF, and SAS.

Regression analyses identified predictors of nightmare and sexual dream intensity.

Results: 1. Nightmares

46.5% of athletes reported nightmares. Athletes with nightmares exhibited higher neuroticism ($p < 0.01$) and anxiety ($p < 0.05$) than non-nightmare athletes.

Non-athletes with nightmares scored higher in aggressiveness, neuroticism, and sensation seeking ($p < 0.05$).

Anxiety ($\beta = 0.32$), neuroticism ($\beta = 0.28$), and sensation seeking ($\beta = 0.18$) predicted athletes' nightmare intensity.

2. Sexual Dreams

Athletes with sexual dreams scored lower in aggressiveness and neuroticism than non-sexual dreamers ($p < 0.05$), with no significant anxiety differences.

Anxiety ($\beta = 0.16$) and sensation seeking ($\beta = 0.37$) positively predicted athletes' sexual dream intensity.

Non-athletes with sexual dreams showed higher aggressiveness and neuroticism traits ($p < 0.05$).

Conclusions: Personality traits and anxiety differentially predict intense dream experiences. Athletes' nightmares are linked to neuroticism and anxiety, aligning with performance-related stress, whereas their sexual dreams correlate with lower aggression and higher sensation seeking. Non-athletes' intense dreams reflect broader traits like aggressiveness and sensation seeking. These findings highlight the dual role of personality in shaping nightmares (stress indicators) and sexual dreams (impulse-driven experiences). For mental and sexual health interventions, tailored strategies—stress management for athletes and psychoeducation on emotional regulation—are recommended. This study advances understanding of how individual differences shape dream intensity, offering practical insights for health professionals.

Chronobiology/Circadian Disorders

Abnormal Global Brain Function in Shift Work Disorder Patients: A Resting-State Functional MRI Study

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Introduction: Since the negative influence caused by shift work disorder (SWD), its underlying mechanisms still remain unclear. Thereby, we conducted this study to explore the neuromechanism of SWD due to the disrupted circadian rhythm using Resting-state functional magnetic resonance imaging (rs-fMRI).

Materials and methods: 65 SWD patients and 65 healthy controls (HC) had received assessments of relevant

questionnaires, including PSQI, ISI, ESS, FS-14, PHQ-9, GAD-7, and rs-fMRI scans.

Amplitude of Low Frequency Fluctuations (ALFF), Regional Homogeneity (ReHo)

analyses were performed on rs-fMRI data to compare the differences between the two groups. The peak points, which significantly altered in ALFF and ReHo were chosen as the seed regions to further calculate and Functional Connectivity (FC) of the whole brain. Finally, we performed correlation analyses to assess the association between alterations in brain function and clinical characteristics.

Results: The study included 121 participants (61 SWD, 60 HC). The SWD group showed higher PSQI, ISI, ESS, FS-14, PHQ-9, and GAD-7 scores (all $P < 0.05$) but no demographic differences versus HCs.

ALFF analysis revealed increased activity in frontal regions (left medial superior frontal gyrus, orbital middle frontal gyrus, right dorsolateral superior frontal gyrus) and decreased activity in occipital areas (left middle occipital gyrus, right superior occipital gyrus/lingual gyrus) in SWD. ReHo was reduced in the right middle occipital gyrus. FC analysis showed decreased connectivity between the right superior occipital gyrus and left superior occipital gyrus/cuneus.

Conclusions: The changes of functional brain activities in SWD patients are mainly in the prefrontal and occipital lobes, and related brain network is the default mode network (DMN), which might be potential neuroimaging indicators and therapeutic target brain region for SWD patients.

A direct comparison of sleep loss and circadian effects in sustained attention

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Introduction: Extended wakefulness of up to 30 hours has been associated with severe impairments in performance arising from loss of sustained attention. This impairment of attention is usually attributed to sleep loss. The impairment may not be due solely to sleep loss since considerable recovery of function occurs the next day even with further sleep loss. A circadian effect is likely to be a significant contributor to performance measures and has been apparent in many studies. However, few studies have directly compared the contributions of accumulated sleep loss and circadian rhythm on sustained attention. The aim of the study was to compare the contribution of sleep loss with a linear model and circadian rhythm contribution with a cosine model. We compared both the amplitudes and variances accounted for in the two models.

Materials and methods: We analyzed the data from 38 healthy sleepers (Mean (SD) age = 32.6 (12.9) years) who performed the 10-minute Psychomotor-Vigilance Task (PVT) 10 times equally spaced across a 29-hour period of total sleep deprivation in a controlled laboratory protocol. The number of lapses (Reaction Time > 500 msec) of attention was measured at each testing time. Two curve-fitting approaches were applied: (1) a linear function using least squares method to model time awake effects, and (2) a 24-hour cosine curve to model the circadian component. For both group mean data and individual participant data, we compared the amplitudes and variances accounted for (R^2) between the circadian and linear models. Within-subject statistical comparisons were conducted using paired t-tests.

Results: The 24-hour amplitude of the mean lapses curve was 14.1 lapses in the circadian component and 12.5 in the linear component and the variances were 72.3% and 57% respectively. Individual participant analyses means were 15.0 lapses and 12.75 lapses and variances of 59.5% and 40.4% for the circadian and linear curve fits respectively. Within subjects t-tests showed the circadian component has significantly larger amplitude ($t(37) = 2.56, p < 0.02$) and higher variance accounted for by the circadian curve fit ($t(37) = 5.14, p < 0.001$) than from the linear model.

Conclusions: Across the 29-hour sleep deprivation protocol the circadian model contributes a greater amplitude and variance accounted for in lapses of attention than the linear time awake model. Campaigns to improve public safety should draw as much attention to the danger of the circadian time of operation as to the amount of prior wakefulness.

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AI-enabled discovery of novel circadian-clock markers from overnight PSG

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Introduction: Circadian rhythms orchestrate physiological homeostasis and overall health. However, established circadian biomarkers, such as salivary melatonin, are invasive and poorly suited to large-scale studies, whereas wrist actigraphy lacks direct physiological specificity. Consequently, non-invasive, cost-effective circadian markers that can be deployed at home are needed to enhance health risk stratification. Here, we propose an artificial intelligence-based framework that infers internal circadian timing directly from overnight polysomnography (PSG).

Materials and methods: We fine-tuned a pretrained deep neural network model to predict clock time continuously across the night, using abdominal respiratory and electrocardiogram signals—modalities that can also be captured in ambulatory, non-laboratory environments. The model was trained on 1-hour segments with a 10-minute sliding window. For each individual, it generated a predicted time series across the night, reflecting their internal circadian timing.

Circadian characteristics were quantified by regressing the predicted times against actual clock time, yielding two metrics: (1) Circadian Phase Misalignment (CPM), defined as the absolute angular deviation (in degrees) between the fitted slope's arctangent and the 45-degree reference angle; and (2) Circadian Rhythm Strength (CRS), the regression R^2 , indicating internal rhythm consistency.

Model development used 35,945 overnight PSGs drawn from 13 National Sleep Research Resource cohorts, the Human Sleep Project, and Shanghai Sixth People's Hospital (8:1:1 train/validation/test split). External validation was performed in Multi-Ethnic Study of Atherosclerosis ($n = 2,056$), Sleep Heart Health Study ($n = 5,795$). Logistic regression examined associations between CPM, CRS, and seven self-reported neuropsychiatric and metabolic conditions (anxiety, depression, bipolar disorder, post-traumatic stress disorder [PTSD], Alzheimer's disease [AD], Parkinson's disease [PD], overweight, diabetes), adjusting for age and sex.

Results: The combined development dataset included 35,945 participants (age: 49.0 ± 20.0 years; 44.6% female; 44.4% Non-White). The clock time model achieved a mean absolute error of 1.55 hours in internal validation and 1.39–1.96 hours across external cohorts. Median CPM was 9.83° (range: 0.003 – 75.4°), and median CRS was 0.745 (range: 0–1). A 10° increase in CPM was associated with higher odds of multiple conditions, most notably bipolar disorder (OR = 1.75, 95% CI: 1.54–1.98), AD (OR = 1.71, 95% CI: 1.27–2.30), and PTSD (OR = 1.43, 95% CI: 1.28–1.60). Depression, PD, diabetes, and overweight also showed significant associations (all $p < 0.001$, OR range: 1.04–1.40). A 0.1-unit decrease in CRS was similarly associated with increased odds of AD (OR = 1.27, 95% CI: 1.09–1.48), with consistent but weaker associations across other conditions (all $p < 0.001$; OR range: 1.02–1.19).

Conclusions: This AI-based approach provides a scalable, non-invasive method to quantify internal circadian rhythms from overnight sleep physiological signals. The derived metrics capture biologically meaningful variation in circadian timing and show strong associations with comorbidities, making them a novel tool for circadian phenotyping with clinical and translational relevance.

An iPhone App to Guide the Collection of the Dim Light Melatonin Onset at Home

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Introduction: The dim light melatonin onset (DLMO) remains the gold standard circadian phase marker in humans. We previously developed a proof-of-concept home DLMO kit and demonstrated that valid DLMOs could be collected at home, with objective markers of light exposure and sample timing. Nonetheless, the proof-of-concept kit uses costly external technologies such as photosensors (to monitor light exposure) and MEMS TrackCaps (to monitor sample timing). Here we present a novel iPhone app designed to improve upon the original proof-of-concept kit.

Materials and methods: We have designed an iPhone app that: (1) streamlines the home DLMO collection procedure, (2) maintains the objective assessment of light exposure and sample timing with internal app features, (3) provides real-time feedback on errors in light exposure and sample timing to both participants and externally located researchers, and (4) provides some cost savings over the original proof-of-concept kit. Programming capability includes options to (1) sample saliva at half-hourly or hourly intervals, (2) end sampling at participants' habitual bedtime or up to 3 hours past habitual bedtime, and (3) set a light intensity threshold of choice to alert the research participant and externally located researcher in real-time that melatonin levels may be suppressed. At the conclusion of the home DLMO collection, the app generates a report of light levels and sample timing for the researcher. Saliva samples can then be sent to a qualified laboratory for assay processing.

Results: Flow diagrams of the back-end programming capability available to researchers and the front-end step-by-step display screens guiding research participants will be shown. A demonstration model of the iPhone app will be available for hands on interaction.

Conclusions: A novel iPhone app has been developed to better support the collection of DLMOs at home, and facilitate research examining circadian timing in human populations.

A randomized controlled trial on the effect of a self-help book for shift work disorder

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Introduction: Shift work disorder (SWD) is a circadian rhythm sleep-wake disorder characterized by excessive sleepiness and insomnia due to work hours that overlap with the habitual time for sleep. It is associated with substantial adverse consequences for the individual, employers and society. Previous studies have found self-help therapies to be effective for insomnia. The aim of the present study was to compare the effect of a self-help book for coping with shift work to that of sleep hygiene advice in a randomized controlled trial with follow-up after 6 months.

Materials and methods: Data were collected among 199 health care workers with shift work disorder (SWD) at baseline (86.9% females, mean age 39 years). At follow-up, 136 participants responded, rendering a response rate of 68.3%. The questionnaire included information about SWD, work-related fatigue (the Swedish Occupational Fatigue Inventory), turnover intention, knowledge about shift work, and self-reported sickness absence related to sleep problems. Statistics were conducted among the 136 completers.

Results: Shift work disorder was reduced in both groups, from 100% to 83.1% and 79.0% in the sleep hygiene group and self-help book group, respectively. None of the five dimensions of fatigue changed in the sleep hygiene group. Four dimensions were reduced in the self-help book group; lack of energy (14.9 to 12.3, $p < .001$), lack of motivation (11.7 to 9.9 $p = .004$), sleepiness (14.7 to 12.5, $p < .001$), and

physical discomfort (12.4 to 10.9, $p=.003$). There were significant interaction effects on lack of energy ($p=.017$), lack of motivation ($p<.001$), and sleepiness ($p=.002$), indicating that the self-help book was better than the sleep hygiene advice. Turnover intention significantly increased in the sleep hygiene group (8.04 to 8.62, $p=.044$), but did not change in the self-help book group (7.56 to 7.47, $p=.79$). Mean correct answers out of 13 questions on the knowledge test did not change in the sleep hygiene group (7.2 to 7.1, $p=.57$), but significantly increased in the self-help book group (7.5 to 8.4, $p<.001$), with a significant interaction effect ($p=.005$). Sickness absence related to sleep problems increased in the sleep hygiene group (27.5% to 30.4%) and decreased in the self-help book group (18.6% to 13.6%).
Conclusions: This study suggests that a self-help book may be an effective low-threshold intervention for coping with shift work.

Aripiprazole (Abilify) as a new treatment for circadian rhythm sleep-wake disorders (CRSWDs) and its mechanism of action

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Introduction: Circadian rhythm sleep-wake disorders (CRSWDs), especially delayed sleep-wake phase disorder (DSWPD), are common among young people and are a major problem in sleep medicine. They are usually treated with melatonin, bright light therapy, and lifestyle guidance, but nighttime sleep time is often extended, making them difficult to treat. We have reported that administration of 0.5-3 mg of aripiprazole to 12 patients with CRSWDs resulted in sleep onset time 1 hour earlier, sleep time 1.3 hours shorter, and wake time 2 hours earlier (Omori, 2018). However, the mechanism of action is unknown, which is a drawback in clinical application.

Materials and methods: A total of 10 clinical reports of CRSWDs, DSWPD and non-24-hour sleep-wake disorder have been published in Japan, and a meta-analysis was performed. In vivo and ex vivo experiments were performed in mice to clarify the mechanism of action.

Results: In a total of 45 cases, an average dose of 2.7 mg of aripiprazole resulted in 0.5 hours earlier sleep onset, 1.1 hours shorter sleep time, and 2.5 hours earlier wake-up time. In vivo study involved administering mice with aripiprazole through drinking water and subjecting them to a 6-hour advance jet lag. This administration led to the rapid re-entrainment of the shifted light-dark cycle (Li, 2023). Ex vivo experiments with suprachiasmatic nucleus (SCN) slice cultures have revealed that aripiprazole causes desynchronization of SCN neurons via the serotonin 1A receptor. The mathematical modeling suggests that mild disruption of SCN coupling by aripiprazole enhances photic entrainment without being so disruptive as to cause arrhythmicity.

Conclusions: A meta-analysis confirmed that aripiprazole is highly effective as a treatment option for CRSWDs. It was also confirmed that the mechanism of action is a direct effect on SCN. Melatonin as a therapeutic drug promotes sleep onset, but aripiprazole promotes early awakening, so it is expected that its effectiveness will be enhanced by using it in combination.

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Association between wearable device-measured weekend catch-up sleep and brain health in UK Biobank participants

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Introduction: Sleep deprivation was correlated with risks of brain diseases. However, as a compensation for weekday sleep deficits, the effects of weekend catch-up sleep (WCS) on brain health remain inconclusive. This study investigated the association between WCS and major brain disorders, including depression, anxiety, dementia, stroke, and Parkinson's disease (PD) during a 13.65-year follow-up period, using wearable device data of 93,506 UK Biobank participants.

Materials and methods: A total of 93,506 participants from the UK Biobank were followed for an average of 13.65 years. Accelerometer-measured sleep data were used to classify WCS into four categories: no WCS (≤ 0 hours), short (>0 to <1 hour), medium (≥ 1 to <2 hours), and long (≥ 2 hours). Cox proportional hazards models, adjusting for multiple confounding factors, were used to estimate the association between WCS duration and disease incidence. Restricted cubic spline analyses assessed potential nonlinear relationships.

Results: The fully-adjusted Cox proportional hazards model revealed that medium WCS significantly reduced the risk of depression (HR 0.89, 95% CI 0.81–0.99) and anxiety (HR 0.88, 95% CI 0.79–0.98). Nonlinear dose-response relationships were observed between WCS and depression/anxiety (P for nonlinearity <0.001). No significant associations were found between WCS and dementia, stroke, or PD. Subgroup analyses indicated a significant interaction between WCS and age for anxiety (P for interaction = 0.003).

Conclusions: Medium WCS may be a promising, cost-effective strategy for promoting mental health, specifically reducing the risk of depression and anxiety. However, no significant associations were found with dementia, stroke, or PD. Future research should explore the underlying mechanisms and replicate these findings in diverse populations.

Association of circadian rest-activity rhythm and genetic risk with incident irritable bowel syndrome

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Introduction: Irritable bowel syndrome (IBS) is a common functional bowel disorder characterized by recurrent abdominal pain, altered defecation, or changes in bowel habits. Although the exact mechanisms remain unclear, disrupted communication between the gut and brain has been implicated. The circadian system regulates various gastrointestinal functions, and circadian rhythm disruptions are associated with gastrointestinal diseases. However, prospective studies linking circadian rhythms and IBS risk are limited.

Materials and methods: This study included 86,106 UK Biobank participants who were free of IBS at baseline. Circadian rest-activity rhythm (CRAR) was assessed using non-parametric parameters, including interdaily stability (IS), intradaily variability (IV), activity level during the most active 10 hours (M10), activity level during the least active 5 hours (L5), relative amplitude (RA), M10 onset, and L5R onset. The incidence of IBS was identified using hospital records and a self-assessment questionnaire, and genetic risk was determined using a polygenic risk score (PRS). Cox proportional hazards models were used to examine the association between CRAR and incident IBS.

Results: During 620,851 person-years of follow-up (median follow-up period of 7.8 years), a total of 8,790 new cases of IBS were identified. We found that the risk of incident IBS decreased with increasing RA and M10, with multivariate adjusted hazard ratios (HRs) (95% CI) were 0.86 (0.81, 0.91) for decreasing RA and 0.88 (0.83, 0.92) for high M10. Conversely, high L5, a delayed onset of M10 and an advanced onset of L5 were associated with a higher risk of IBS, with the HRs (95% CI) of 1.06 (1.04, 1.12) for high L5, 1.10 (1.04, 1.16) for delayed M10 onset time, and 1.06 (1.01, 1.12) for advanced L5 onset time. However, the relationships of IS and IV with IBS risk did not reach statistical significance. No significant interactions between CRAR parameters and genetic risk are observed. Additionally, individuals with high genetic risk and poor CRAR parameters showed a significantly higher risk of IBS.

Conclusions: CRAR disturbances, characterized by lower amplitude and abnormal phase, are linked to an elevated risk of developing IBS. These findings underscore the potential of circadian rhythm management as a modifiable risk factor for IBS prevention. Further research is needed to explore the underlying mechanisms linking CRAR disruptions to IBS.

A study of sleep EEG spectral analysis of delayed sleep-wake phase disorder

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Introduction: Delayed sleep-wake phase disorder (DSWPD) is a sleep disorder where sleep architecture is considered normal if individuals sleep at their preferred times aligned with their internal body clock. However, there have been reports of reduced recovery sleep after sleep deprivation in patients with DSWPD under experimental conditions, suggesting a potential alteration of its sleep homeostatic process. To clarify this further, we conducted electroencephalographic (EEG) spectral analysis of DSWPD under normal living conditions in this study.

Materials and methods: The case group consisted of patients who were not on medication, visited the Department of Psychiatry at Fujita Health University Hospital, and were diagnosed with DSWPD based on the diagnostic criteria of the International Classification of Sleep Disorders, 3rd edition (ICSD-3). Healthy individuals were also recruited to serve as the control group. The study was approved by the Ethics Committee of Fujita Health University, and all participants provided written informed consent. The patients spent at least one week on their usual schedule at their home, keeping sleep diaries and wearing an actigraphy. On a day during this period, an overnight EEG with a 2-channel measuring device was conducted, and saliva samples were collected hourly under dim light conditions to determine dim-light melatonin onset (DLMO) in the evening just before the EEG measurement. Melatonin non-delayed and delayed types of DSWPD were defined as having DLMO more than 30 minutes earlier than the patient's desired bedtime or not, according to ICSD-3-Text-Revision. For EEG spectral analysis, the power spectra (μV^2) of the theta and delta bands for each 30-second epoch were obtained by fast Fourier transform. All participants completed the Morningness-Eveningness Questionnaire (MEQ) to determine their chronotype.

Results: Ten DSWPD patients and twenty-one healthy subjects were included in the study. Slow wave power in the delta band during the first two hours after sleep onset was significantly higher in DSWPD patients than in healthy subjects. As for the ratio of theta and delta band slow wave spectral power in the second half to that in the first half, it tended to positively correlate with MEQ across both case and control groups, though there were some exceptions. The melatonin delayed type of DSWPD showed a tendency for slow waves to appear more immediately after sleep onset. In contrast, the non-delayed type showed a tendency for slow waves to remain in the second half of sleep.

Conclusions: Differences in the distribution of slow waves across the sleep period were observed between DSWPD and healthy subjects, as well as between melatonin delayed and non-delayed DSWPD, suggesting that some alteration may occur in DSWPD with regard to sleep homeostatic processes. Further research with a larger sample size is necessary to confirm this finding.

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Automatic sleep-wake classification and Parkinson's disease recognition using multi-feature fusion with support vector machine

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Introduction: Sleep disturbance is a prevalent non-motor symptom of Parkinson's disease (PD), however, assessing sleep conditions is always time-consuming and labor-intensive. In this study, we performed an automatic sleep-wake state classification and early diagnosis of PD by analyzing the electrocorticography (ECoG) and electromyogram (EMG) signals of both normal and PD rats.

Materials and methods: The study utilized ECoG power, EMG amplitude, and corticomuscular coherence values extracted from normal and PD rats to construct sleep-wake scoring models based on the support vector machine algorithm. To evaluate the applicability of the sleep-wake classification

models across different rat groups, we randomly selected the features from 8 rats in the sham group (Sham train) and 8 rats in the lesion group (Lesion train) to train the SVM models, respectively. Subsequently, the remaining sham record (Sham test) and lesion record (Lesion test) were considered as two test data points for cross-validation of the models. The Sham dataset contained 6480 10-second segments labeled by the sleep experts with data encompassing WAKE: 1548, NREM: 4164, REM: 768. Similarly, the Lesion dataset contained 6521 10-second segments labeled by the sleep experts with data encompassing WAKE: 2047, NREM: 3866, REM: 608. The Sham test and Lesion test contained approximately 720 10-second segments, respectively. For comparison, we used ECoG from occipital or frontal cortex regions in the Sham train and Lesion train for feature extraction and model training to construct four different sleep-wake classification models. Finally, by incorporating PD-specific features from frontal ECoG, we developed two models capable of simultaneous sleep-wake state classification and PD detection. By incorporating the previously selected features and expanding the functionality of the model, we achieved simultaneous detection of sleep-wake states and the likelihood of PD in rats.

Results: The highest accuracy was achieved when the model was trained by the Sham train of the occipital ECoG and tested by the Sham test data, at which time the Cohen's kappa value was 0.77 ± 0.05 . Features extracted from occipital ECoG signals were more suitable for constructing sleep-wake scoring models than those from frontal ECoG (average Cohen's kappa: 0.73 vs. 0.71). Additionally, after retraining, the new models demonstrated increased sensitivity to PD and accurately determined the sleep-wake states of rats (average Cohen's kappa: 0.79). A slightly greater level of overall accuracy was noted when conducting classification through a combination of occipital and frontal ECoG, as opposed to relying solely on frontal ECoG ($84.87\% \pm 2.22\%$ vs. $83.90\% \pm 2.50\%$).

Conclusions: This study accomplished the precise detection of substantia nigra lesions and the monitoring of sleep-wake states. The integration of circadian rhythm monitoring and disease state assessment has the potential to improve the efficacy of therapeutic strategies considerably. Furthermore, the algorithms developed in this research exhibit promising potential for future integration into adaptable, wireless, and portable DBS monitoring systems.

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Blue light influences loss aversion

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Introduction: Gambling is a popular and easily accessible activity, with ~1.6 billion people worldwide engaging in gambling activities. The manipulation of gambling product designs, like the ringing bell on the slot machines, have been found to reinforce gambling behaviour. It's possible that the use of light and colour may also enhance gambling behaviour. As decision-making is influenced by underlying cognitive processes directly impacted by circadian photoreception, activation of circadian photoreceptions may alter an individual's sensitivity to loss. We investigated whether circadian photoreception influences loss aversion.

Materials and methods: Fifteen participants (mean age = 20.40, $SD = 2.03$) completed an economic-decision making task under blue-enriched ($\lambda_p = 490$ nm) and blue-depleted light ($\lambda_p = 631$ nm) of the same photopic lux (200 lux). Light conditions were counterbalanced for order of exposures across two sessions, two weeks apart. During the task, participants were required to choose between taking a risky gamble of a positive or negative outcome, or take a guaranteed, less risky outcome.

Results: Using Hierarchical Bayesian Modelling to derive individual parameter estimates for loss aversion, we found that individuals were less loss averse under blue-enriched light compared to blue-depleted light. Linear mixed models were used to analyse trial-by-trial performance, and the best-fit model indicated light condition significantly affected the loss aversion parameter, with blue-enriched light associated with a .43 decrease in loss aversion. Significant sex differences were also found, with men showing decreased loss aversion across both light conditions.

Conclusions: This is the first study to demonstrate that light that preferentially targets circadian photoreception influences loss aversion. Our key finding was that blue-enriched light significantly decreased loss aversion, suggesting that when under this light, individuals are relatively more

comfortable to take a risk and demonstrate a reduced sensitivity to loss. With virtually all machines used for gambling employing LED/LCD displays which are known for their blue-enriched light content, targeting the reduction of “blue” light content in gambling scenarios may be a promising target for reducing gambling behaviour by promoting greater loss sensitivity.

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Chronotherapy in Acute Psychiatry: Light conditions in hospitals can reduce aggression

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Introduction: Severe mental illness is often marked by unpredictable and sometimes dangerous behaviors. In acute psychiatric settings, aggression poses a dual threat: it endangers staff and undermines therapeutic relationships, reducing opportunities for effective treatment. Managing aggression is therefore a critical challenge. We have previously shown that sleep is related to aggressive behaviors for patients in acute psychiatric hospitals, and that modifying the evening light environment according to chronobiological principles can have effects on the circadian system, sleep, and arousal in healthy individuals. In this study, we investigated whether patients admitted to an acute psychiatric inpatient unit with a evening blue-depleted light environment (BDLE) exhibited lower levels of aggressive behavior compared with patients in admitted to standard lighting conditions (SLE). All patients additionally received treatment as usual – including pharmacological treatment, consistent routines, and milieu therapy.

Materials and methods: This study is a secondary analysis of BDLE's effects on aggression across diagnostic subgroups. Participants (N = 475) admitted to a newly built acute psychiatric unit were randomized to BDLE or SLE. Aggressive behavior was assessed using the Brøset Violence Checklist (BVC), recorded three times daily by the responsible nurse based on a one-hour observation of the patient at the beginning of each shift. BVC scores >2 indicated serious aggressive incidents. Mixed-effects models were used to examine BDLE's effects on aggression, with subgroup analyses for four ICD-10 diagnostic categories: severe depressive episode, manic episode, psychotic disorders, and “other diagnoses”. Models were adjusted for baseline variables including age, sex, psychiatric diagnosis, comorbid personality or substance use disorder, admission status (voluntary/involuntary), and prior admissions in the past two years.

Results: In SLE, a total of 73 serious aggressive events were recorded, compared to 8 events in BDLE. Patients in BDLE experienced an estimated 0.25 fewer serious aggressive events during their admission (95% CI: -0.38 to -0.12, $p < 0.001$) compared to SLE, despite receiving identical psychiatric care. Among patients with a manic episode (N = 31), the reduction was most pronounced, with a mean of 1.27 fewer events (95% CI: -2.39 to -0.15). For the “other diagnosis” group (N = 329), BDLE also led to a significant reduction of 0.14 fewer events (95% CI: -0.24 to -0.04). No significant effects were observed for psychosis (N = 87) or depression (N = 28), though a non-significant trend suggested fewer aggressive events in psychosis (-0.42, 95% CI: -0.89 to 0.05, $p = 0.08$).

Conclusions: We have showed that modifying the evening light environment in an acute psychiatric ward appeared to «dial down» aggression, with the strongest effects seen in patients with mania. All patients received standard treatment, meaning these reductions occurred in addition to any improvements achieved through usual care. Our findings highlight this targeted chronotherapeutic intervention as a promising, non-invasive tool for managing aggression in the acute phase of severe mental illness.

Chronotype and infradian rhythms: the influence of solar and lunar cycles on sleep duration and phase

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Introduction: The geophysical properties of the Earth, Moon, and Sun dictate the timing of a variety of biological cycles on our planet. While it is known that lunar phases and photoperiod length can influence the human sleep/wake cycle, the existence of different chronotypes suggests the presence of various, individual degrees of entrainment to astronomical cues.

This study aimed to characterize circannual and circalunar variations in sleep phase and duration across chronotypes. We hypothesized that individuals with extreme chronotypes (i.e., evening and morning types) maintain their circadian rhythms out of phase from the day/night cycle because they are less responsive to sunlight entrainment signal or more able to neutralize it. This could hinder their ability to adjust their sleep behavior to seasonal variations in daylength. Additionally, we proposed that evening types' sleep behavior may align with changes in the lunar phases, as they are more likely to extend wakefulness beyond sunset, possibly increasing their exposure to moonlight.

Materials and methods: A total of 402 healthy volunteers (29.91 ± 13.36 ys; 45.5% females; 66.9% intermediate types, 17.9% evening types, 15.2% morning types) wore an actigraph for an average of 7 days, resulting in 2844 valid night sleep episodes, from which the sleep midpoint and the total sleep time were derived. Participants completed the reduced Morningness/Eveningness Questionnaire to determine their chronotype. Periodic splines with two knots at the tertiles modelled the day of the year and of the lunar cycle. Random-effect linear models were fitted to assess the predictive power of lunar and solar cycle variables on sleep duration and phase among the different chronotypes. All models were adjusted for age and sex.

Results: Intermediate types exhibited circannual variations in sleep duration that closely mirrored seasonal photoperiod changes, with maximum sleep duration near the winter solstice and minimum near the summer solstice. Conversely, evening types showed sleep duration and timing variations aligned with the lunar cycle, displaying the shortest sleep duration and the most delayed sleep phase around the full moon. Moreover, in intermediate types only, the photoperiod length significantly predicted total sleep time ($\beta = -0.070$, $p = 0.007$), indicating that longer daylight periods were associated with shorter sleep durations. For evening types, increased lunar illumination significantly predicted a delay in sleep midpoint ($\beta = 40.02$, $p = 0.035$), when adjusting for moonrise time.

Conclusions: Intermediate chronotypes adapt their sleep duration in response to seasonal photoperiod fluctuations, whereas evening types are more influenced by lunar phases. The differential adaptation to the circannual rhythm may arise from genetic differences in photoreceptivity or from varying abilities to neutralize solar cues through behaviors such as artificial light exposure. In this perspective, moonlight exposure may be the cause of the disruption of evening types' seasonal synchronization. Both usual late bedtime and increased sensitivity to moonlight spectrum (richer in red light than the sunlight spectrum) can explain evening types' alignment with the lunar cycle. Further investigations are warranted to elucidate the underlying mechanisms behind chronotype-dependent variations in infradian rhythm entrainment.

Chronotype, Sleep and Stress: A Comparative Study of International Students in Georgia and Spain

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Introduction: Numerous studies have shown that university students experience constant stress and sleep deprivation, while international students, especially medical students, are at greater risk of mental and general health problems, as they face other stressors in addition to academic and financial problems, such as language and cultural differences, stereotypes, etc., making them particularly vulnerable to health-related problems.

The aim of this study is to understand whether chronotype (individual preferences for sleep and daytime activity), influence the risk of sleep disturbances and stress in international students from two universities: Georgian American University (GAU, Georgia) and University of Jaen (UJA, Spain), with a focus on evening chronotypes, which are associated with poorer health outcomes.

Materials and methods: 160 international **medical** students at GAU and 185 international students from **non-medical** programs at UJA participated in the study. Data was collected by the Morningness/Eveningness Questionnaire (MEQ), the Epworth Sleepiness Scale (ESS), the Pre-Sleep Arousal Scale (PSAS), and the Student-Life Stress Inventory (SLSI).

Results: Evening chronotype subjects reported significantly higher levels of daytime sleepiness, pre-sleep arousals, and stress compared to intermediate and morning chronotypes. Specifically, evening chronotype sample were found to have higher rates of excessive daytime sleepiness (ESS score ≥ 11) compared to morning chronotypes, with 10.6% of evening chronotypes and 12.0% of intermediate chronotypes reporting sleepiness, versus 3.7% of morning types.

Somatic and cognitive PSAS were more prevalent among evening chronotypes, with 71.3% of evening types reporting somatic arousal compared to 48.1% of morning types, and cognitive arousal was higher in evening types (25.8 ± 7.6) compared to intermediate (20.8 ± 7.2) and morning types (17.3 ± 7.2). Total PSAS score was also higher for evening chronotypes.

Evening chronotypes also reported the highest total stress levels, with a Total SLSI score of 141.9 ± 28.3 , significantly higher than intermediate types (141.9 ± 28.3) and morning types (123.9 ± 28.2). In the total sample ($n = 345$), significant correlations were found between daytime sleepiness (ESS) and somatic PSAS ($r = 0.442$, $p < 0.001$), and between cognitive PSAS and overall stress ($r = 0.519$, $p < 0.001$).

In evening chronotypes ($n = 92$), significant correlations between somatic and cognitive PSAS ($r = 0.529$, $p < 0.001$) and total pre-sleep arousal ($r = 0.755$, $p < 0.001$) indicated that both somatic and cognitive PSAS contribute to sleep difficulties. No significant correlations were found between chronotype and overall stress in individual groups, suggesting that while evening types report higher stress, other factors also contribute to stress perception.

Conclusions: The results show that evening chronotypes are more vulnerable to both sleep problems and stress-related problems. The results highlight the important role of chronotype, especially evening chronotype, in exacerbating sleep problems and stress in international students. The study provides further evidence for the need for interventions for international students and specific coping strategies tailored to chronotype preferences to reduce stress and improve sleep quality, especially for evening chronotypes who are at higher risk of adverse health outcomes.

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Chronotype Stability in Childhood and its Link to Sleep Problems

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Introduction: Chronotype reflects one's innate preference for specific periods of the daily 24-hour cycle for rest and activity, and varies between individuals. Cross-sectional studies show that chronotype is ontogenetic and varies between age groups. However, longitudinal studies examining the temporal stability of chronotype are scarce, especially during childhood when significant developmental changes occur. Moreover, the relationship between chronotype stability and sleep remains unclear. Our study addresses these research gaps by investigating chronotype stability between preschool- and school-age, and its association with sleep problems.

Materials and methods: Data were drawn from 256 children in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth-cohort study. Chronotype was assessed at 4.5 and 8 years old using

the Children's Chronotype Questionnaire (CCTQ). The CCTQ provides an overall morningness/eveningness (M/E) score, with higher scores representing greater eveningness and lower scores representing greater morningness. To examine the change in chronotype between timepoints, we calculated chronotype delta by subtracting M/E scores at 4.5 years old from the repeat measurement at 8 years old. Sleep problems were evaluated at 8 years old using the Children's Sleep Habits Questionnaire (CSHQ). The CSHQ measures total sleep problems by summing subscale scores for Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Wakings, Parasomnias, Sleep Disordered Breathing and Daytime Sleepiness. Both measures were parent-reported. We performed Pearson's correlation analysis and calculated an intraclass correlation coefficient to examine the stability of M/E scores between preschool- and school-age. Linear regressions were conducted to examine the association between chronotype delta and sleep problems measured on the CSHQ.

Results: M/E scores showed moderate test-retest reliability ($r=.60, p<.001$) and stability ($ICC=.59$) between 4.5 and 8 years old. Mean M/E scores at 4.5 and 8 years old were 30.45 ± 5.60 and 28.94 ± 5.19 respectively. The t -test revealed a slight but significant shift towards morningness at school-age ($t(255)=5.05, p<.001$). Chronotype delta among individual subjects ranged between -19 to 14 points. Linear regressions revealed that chronotype delta was associated with daytime sleepiness ($B=.181, 95\% \text{ CI}:.094 \text{ to } .268, p<.001$) and total sleep problems ($B=.257, 95\% \text{ CI}:.084 \text{ to } .430, p=.004$). These results suggest children who experience shifts towards eveningness between preschool- and school-age are susceptible to adverse sleep problems at school-age.

Conclusions: Our results indicate overall moderate stability of chronotype in children as they transition from preschool to primary school. The shift towards morningness at 8 years old may potentially be accounted for by early primary school schedules in Singapore, and suggests amenability of chronotype. Moreover, we observed individual variability in chronotype stability, with shifts towards eveningness linked to daytime sleepiness and total sleep problems. Better understanding of individual differences in chronotype stability may facilitate identifying children at greater risk for sleep problems and inform preventive strategies.

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Circadian Amplification in Diabetic Retinopathy: A Pilot Study

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Introduction: Diabetic Retinopathy (DR) affects more than 450 million individuals worldwide. Emerging data suggests that type 2 diabetes (T2D) with DR is associated with a dysregulated 24-h melatonin rhythm, likely due to a loss of intrinsically photosensitive retinal ganglion cells, a crucial component for circadian entrainment. The lack of strong photic synchronizers in T2D with DR is associated with significant sleep disturbances, particularly irregular sleep, which was linked to increased systemic inflammation. This pilot study explored the effects of "Amplify-RHYTHM", a novel intervention to regularize sleep timing and strengthen photic circadian cues, on sleep, circadian and cardiometabolic outcomes in T2D with DR.

Materials and methods: Eight T2D persons (5M/3F) with DR participated in a 6-week "Amplify-RHYTHM" intervention (NCT06183476) consisting of two components: 1. sleep regularization (remote weekly coaching aiming at keeping bedtimes and wake times within a 60-min window with 7-9 hours of time in bed, verified by an activity monitor (Fitbit®), and educational content), and 2. timed light exposure (30-minute morning light exposure via Luminette® glasses, evening blue light blocking glasses for 2 hours before bedtime, and sleep mask at night). Study measures were collected at baseline and during last 2 weeks of the intervention. Primary outcomes were insomnia symptoms and 14-day actigraphy-derived sleep parameters. Circadian related parameters included rest-activity rhythm

parameters, dim light melatonin onset (n=5) from home saliva samples, and overnight urinary 6-sulfatoxymelatonin (aMT6s) secretion. Cardiometabolic parameters included mean glucose level from 14-day continuous glucose monitor (CGM), high sensitivity c-reactive protein (hs-CRP), blood pressure and heart rate. Satisfaction (scale 1-7) was collected. Statistical analysis was performed using paired t-test or Wilcoxon signed rank test.

Results: Mean (SD) age was 57.2 (5.6) years, and mean HbA1C was 7.5 (0.8)%. Compared to baseline, after Amplify-RHYTHM intervention, insomnia symptoms significantly decreased 2.50 (1.92) vs. 4.25 (2.49), $p=0.041$. Sleep regularity improved as there was a reduction in variation of sleep midpoint; 0.90 (0.27) vs. 1.33 (0.39) h, $p=0.018$. Sleep efficiency trended toward significant improvement ($p=0.075$) while sleep duration did not change. For rest-activity parameter, intra-daily variability significantly reduced, 0.82 (0.13) vs. 0.95 (0.21), $p=0.049$, suggesting less fragmentation of rest-activity rhythm, while relative amplitude and inter-daily stability did not change. Urinary aMT6s remained low, 6.3 (7.6) vs. 5.7 (5.6) ng/mg, $p=0.600$, and DLMO pattern did not change. For cardiometabolic parameters, hs-CRP was significantly reduced, 1.58 (2.29) vs. 2.36 (3.3) mg/L, $p=0.011$, and heart rate tended to decrease ($p=0.065$), while there was no significant change in mean glucose level from CGM or blood pressure. Participants found that Amplify-RHYTHM was easy to implement (a mean score of 6.63) and overall satisfaction was high (a mean score of 5.88). One person experienced progression of DR deemed to be related to baseline DR severity.

Conclusions: Amplify-RHYTHM, a novel intervention to enhance sleep and circadian regulation in persons with T2D with DR, resulted in positive health outcomes including less severe insomnia symptoms, more regular sleep, reduced behavioral circadian fragmentation, and reduced systemic inflammation. These emerging data should be confirmed in a larger, randomized study.

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Circadian Rhythm Dysregulation in patients with bipolar disorder: correlations with Inflammatory markers and suicidal risk

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Introduction: Bipolar disorder is a chronic and disabling psychopathological condition that is associated with a significant risk of suicide, possibly resulting from the interaction of genetic and environmental factors. It is considered a priority to improve our understanding of the mechanisms involved in the development and maintenance of Bipolar Disorder in order to identify early markers that may help in screening, diagnosing, and treating strategies. Evidence suggests that Bipolar disorder is also associated with alterations in the circadian system. According to the "circadian hypothesis of mood disorders," mood symptoms would be caused by the misalignment of the circadian system due to the desynchronization of the master biological clock of the hypothalamus, i.e., the suprachiasmatic nucleus. Recent years have seen a growing body of evidence suggesting a potential link between the immune system, and more broadly, inflammation, and mood disorders. Given that sleep plays a pivotal role in regulating inflammatory indices it is plausible that sleep disorders may contribute to inflammation and dysregulation of neuroendocrine systems that promote bipolar disorder as well. This study aimed to assess the correlations between circadian rhythm alterations and inflammatory markers in patients with bipolar disorder

Materials and methods: A consecutive series of patients who were hospitalized at the Psychiatric Unit, University of Pisa Italy, with a diagnosis of Bipolar Disorder type I and II according to DSM-5-TR were evaluated. All participants were clinically assessed with a set of questionnaires that included the assessments of circadian rhythm disorders during the previous two weeks with the Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) depressive, manic symptoms and suicidal risk with the Beck Depression Inventory (BDI-II), the Young Mania Rating Scale (YMRS) the Scale for Suicide Ideation (SSI). Inflammatory parameters, including the Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), and Systemic Inflammation Index (SII), were also measured at the time of the evaluation.

Results: The final sample consisted of 103 individuals. Patients who experienced circadian rhythms alterations during the previous two weeks demonstrated higher suicidal risk, more severe depression, and showed elevated levels of inflammatory markers. Logistic regression analysis indicated that suicidal

risk was predicted by circadian rhythm disturbances (OR=7.64, 95% CI 1.92-27.86, $p=0.005$), and inflammation indices such as NLR (OR=4.00, 95% CI 1.14-13.99, $p=0.030$). Mediation analyses showed that inflammation indices played a mediation role between circadian dysregulation and suicidal risk.

Conclusions: Chronobiological alterations directly contributed mood symptoms and suicidal risk. Chronobiological alterations may be impacted on inflammatory system hence indirectly contributing to bipolar disorder severity and suicidal risk. These findings call for the systematic screening of these dysrhythmicity dimensions when considering suicidal risk in individuals with Bipolar disorder.

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Clinical Trial of Solriamfetol in Early Morning Shift Workers

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Introduction: Shift work is common and in a quarter of individuals leads to a diagnosis of shift work disorder (SWD), characterized by excessive sleepiness accompanied by short sleep duration and/or insomnia. While more individuals work early morning shifts than overnight shifts, few studies have investigated this population. We aimed to evaluate the efficacy of solriamfetol for the treatment of excessive sleepiness during workdays in participants with SWD who work early-morning shifts.

Materials and methods: We conducted a randomized, double-blind, placebo-controlled 4-week clinical trial in early morning shift workers (shift start 3-7AM). Participants who reported excessive sleepiness and were at high risk for SWD as determined by a SWD questionnaire were selected. Following screening and 2 weeks of baseline, participants were randomized into 4 weeks of placebo or solriamfetol (150mg taken after waking on workdays). Outcome measures included severity of illness as measured with Clinical Global Impression of Severity (CGI-S) scale, global functioning, daily activity and work productivity impairments as measured with Sheehan Disability Scale (SDS) and Work Productivity and Activity Impairment-Specific Health Problem (WPAI:SHP) scale with excessive sleepiness as the specific health problem, and objective sleep duration or sleep quality as assessed with actigraphy-derived total sleep time and sleep fragmentation index from the main sleep episodes. Mixed-effects and logistic regression models were used to analyze the data.

Results: 74 participants completed the study (median age 37 [28-46]; 27 females); 38 in the solriamfetol group and 36 in the placebo group. A significantly greater percentage of participants treated with solriamfetol showed improvement on CGI-S compared to those who received placebo (76% vs. 53%, OR=2.8, 95% CI 1.0-7.5, $p=0.04$). Patients treated with solriamfetol reported greater improvement in global functioning (SDS: -3.7, $p=0.04$) as well as in daily activity and work productivity impairments due to excessive sleepiness (WPAI-overall work impairment: -16.7, $p=0.03$; productivity impairment: -15.5, $p=0.03$; activity impairment: -16.9, $p=0.01$). There was no significant difference between the groups on sleep duration or sleep fragmentation assessed with actigraphy (all p -values >0.05).

Conclusions: Solriamfetol significantly reduced the severity of illness and improved subjective functioning compared to placebo in participants with SWD who work early-morning shifts.

www.clinicaltrials.gov (NCT04788953).

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Comparative Analysis of Mid-Sleep Point Calculation Methods Using Actigraphy: Relationship with Sleep Quality and Chronotype

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Introduction: The mid-sleep point (MSP) is a widely used marker of circadian phase and sleep timing in chronobiological research, particularly useful in non-invasive field studies. However, different calculation approaches can yield divergent MSP values, potentially influencing their associations with sleep quality and chronotype. This study aimed to: (1) compare two MSP calculation methods: $MSP_1 = \text{Sleep Onset} + (\text{Total Sleep Time} / 2)$ and $MSP_2 = \text{Sleep Onset} + ((\text{Sleep Offset} - \text{Sleep Onset}) / 2)$, where $(\text{Sleep Offset} - \text{Sleep Onset})$ represents the total Time in Bed; (2) examine how the selected method influences the relationship between MSP and subjective sleep quality; (3) assess the role of chronotype in moderating discrepancies between the two methods.

Materials and methods: 400 healthy adults (54% female; mean age = 29.91 years, SD = 13.36), contributing a total of 2420 single nights of sleep data, were included. Sleep was recorded using actigraphy, providing parameters including Total Sleep Time (TST), Sleep Efficiency (SE), Wake After Sleep Onset (WASO), and sleep onset/offset times. Subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), and chronotype was determined through the reduced Morningness-Eveningness Questionnaire (rMEQ). Two mid-sleep point values (MSP_1 and MSP_2) were calculated from actigraphic data. Agreement between the methods was evaluated through Bland-Altman plots and mixed-effects linear regression models, with age, gender, WASO, SE, PSQI, and chronotype as predictors.

Results: Data showed a mean TST of 7.23 hours (SD = 1.09), SE of 90.81% (SD = 6.97), and a PSQI score of 5.19 (SD = 2.39), with 39% of the sample classified as poor sleepers (PSQI > 5). Chronotype distribution included 269 neither-types, 71 evening-types, and 60 morning-types. The two MSP methods generally showed close agreement, with differences clustering around zero. For participants with WASO < 30 minutes, Bland-Altman analysis indicated minimal bias and narrow limits of agreement, suggesting high consistency between MSP_1 and MSP_2 . However, mixed-effects modeling revealed that WASO ≥ 30 minutes was significantly associated with greater discrepancy between methods ($\beta = 30.11$, $p < .001$), highlighting the influence of fragmented sleep on MSP computation. Gender also emerged as a significant predictor, with males exhibiting slightly higher MSP discrepancies ($\beta = 2.35$, $p = .001$). Conversely, M-types and N-types showed significantly smaller discrepancies compared to E-types ($\beta = -5.01$, $p = .022$; $\beta = -5.76$, $p < .001$, respectively). No significant difference in MSP discrepancy was observed between good and poor sleepers as classified by PSQI ($p = 0.287$).

Conclusions: The choice of computational method for determining the mid-sleep point yields largely comparable results under conditions of consolidated sleep but diverges meaningfully in the presence of increased WASO. These findings underscore the critical importance of considering sleep continuity characteristics and individual circadian profiles when selecting MSP calculation methods in both research and clinical practice, particularly given the divergence observed in fragmented sleep. While a 30-minute cutoff for WASO was adopted, future research should identify the precise WASO threshold for significant divergence and, critically, determine which method provides the most reliable MSP estimates for individuals with fragmented or poor sleep.

Darkness Metaphors for Depression: A Case of Impaired Non-Visual Photoreception?

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Introduction: The use of darkness language to describe depression is both ancient and cross-cultural, appearing in linguistic expressions from Japanese (*kurai*, meaning depressed mood and physical darkness), Greek (*melaina chole*, "black bile"), and Mesopotamian texts (*tādirtu*, meaning both melancholy and physical darkness). Foundational metaphors originate from the systematic pairing of sensory experiences with specific emotion states. We propose that darkness metaphors for depression likely stem from a neurobiological basis: individuals currently experiencing depression show impaired non-visual photoreception, unlike those with only a history of depression who maintain normal light sensitivity. This impairment in the brightness detection system during depressive states potentially forms a neurobiological basis for the metaphorical experience of 'darkness' in depression. We

investigated: (i) whether depression symptom severity predicts metaphorical language, including darkness metaphors, and (ii) the relative predictive capacity of darkness metaphors for depression symptom severity compared to anxiety, insomnia and eveningness.

Materials and methods: A global online survey captured participants' free-text descriptions of depression between 2020-2021. Participants with diagnosed or suspected depression completed the DASS-21, Morning-Eveningness Questionnaire, and Insomnia Severity Index (N=488). Using Braun & Clarke's thematic analysis approach, we identified metaphor types and constructed dictionaries of terms for darkness, descent (e.g. "feeling down"), and weight (e.g. "burdened") metaphors. Logistic and linear regression models examined relationships between metaphor use and depression severity.

Results: Higher depression scores predicted the higher likelihood of using darkness language (OR = 1.40, 95% CI [1.02, 1.93], $p = .039$), with each standard deviation increase in depression scores (~12 points) predicting higher likelihood of using darkness metaphors by 40%. Darkness language significantly improved prediction of extremely severe depression symptoms beyond an initial model including only anxiety, insomnia, and chronotype ($\chi^2(1) = 10.22$, $p = .001$). Darkness language predicted the risk experiencing extremely severe depression group by 250% (OR = 2.50, 95% CI [1.42, 4.47], $p = .002$), a larger effect than standard deviation increases in anxiety (OR = 2.15), insomnia (OR = 1.47), or morningness (OR = 0.66). Depression scores were not related to the use of descent or weight language.

Conclusions: Darkness metaphors uniquely contribute to identifying extremely severe depression symptoms beyond established correlates such as anxiety, insomnia, and eveningness. Our findings demonstrate that extremely severe depression specifically relates to darkness metaphors rather than to metaphorical language broadly. This suggests that as depression becomes more severe, the subconscious pairing of darkness with emotional state becomes more salient in how individuals conceptualise their experience. Given that individuals currently experiencing depression have impaired non-visual photoreception sensitivity, their heightened use of darkness metaphors may represent an implicit recognition of how this sensory impairment shapes their emotional experience. The stronger association between darkness language and extremely severe depression compared to other predictors points to potential clinical utility in using linguistic markers to differentiate depression severity levels. These results support investigating whether variations in non-visual photoreception sensitivity influence the propensity to use darkness metaphors in describing depression.

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Developing a Pragmatic Online Behavioural Intervention for Shift Work Disorder in NHS Staff

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Introduction: Shift work disorder (SWD), characterised by complaints of insomnia and excessive daytime sleepiness attributed to shift work, affects around 27% of workers. SWD is often associated with poorer physical and mental health. Cognitive behavioural therapy for insomnia (CBT-I) has shown suboptimal results in achieving clinically significant changes in insomnia symptoms among shift workers. This suggested that a more tailored behavioural approach, addressing the insomnia symptoms and daytime sleepiness associated with SWD, may be beneficial. This study outlines the development process of a novel, online, and pragmatic behavioural intervention for shift workers employed by the National Health Service (NHS) in England.

Materials and methods: The Oxford Behavioural Intervention for Shift workers (OxBIS) has been co-developed by researchers and individuals with lived experience of shift work. A four-member core intervention development team, consisting of sleep and circadian scientists and a clinical psychologist, reviewed existing literature and drew upon clinical experiences from working with shift workers to inform the development process. Patient and public involvement have been integral throughout the development, with 10 diverse individuals with lived experience forming the NHS Nightshift Workers

Research Advisory Group (RAG). The RAG held regular meetings to provide advice on intervention development, specifically regarding content and delivery. Additionally, the RAG was responsible for testing content materials and providing feedback and suggestions.

Results: Seven meetings were held with the RAG members, shaping the three iterations of the intervention. Their firsthand experience as NHS shift workers provided valuable insights into the realities of shift work culture. The resulting OxBIS programme consists of six one-to-one sessions lasting 1-1.5 hours, to be delivered online by trained facilitators. Key intervention targets include enhancing sleep and circadian knowledge, optimising the sleep-wake schedule, scheduled light exposure and blockade, adjusting lifestyle factors, implementing stimulus control, and managing maladaptive sleep-related thoughts using cognitive strategies. Their feedback was crucial in the intervention development. The RAG members supported content refinement, ensured appropriate terminology throughout the materials, contributed to the creation of a shift worker-specific sleep diary, prioritised suitable outcome measures, and advised on practical and logistical considerations, such as recruitment strategies.

Conclusions: The OxBIS intervention reflects a comprehensive and tailored approach for addressing behavioural, circadian, and lifestyle factors that perpetuate SWD. Co-development with individuals who have lived experience ensures that the intervention is patient-centred and focused on the specific needs of shift workers in the NHS. A feasibility and acceptability trial for the OxBIS intervention is currently underway (Ref: PID 18679). The trial aimed to provide empirical evidence on its suitability and inform future implementation.

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Differences in sleep and circadian health in short-sleeping adolescents with and without *MTNR1B* risk variant rs10830863

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Introduction: The melatonin receptor 1b gene (*MTNR1B*) risk variant rs10830963 (C/G; ~20-30% minor allele frequency) is an independent risk factor for type 2 diabetes and has been associated with extended duration of endogenous melatonin production with later morning melatonin offset (dim light melatonin offset, DLMO_{off}) in adults. However, the functional impact of the variant is not well understood, and adolescents have been underrepresented in this research. The goal of the current study was to examine differences in sleep and circadian health in adolescents with and without the *MTNR1B* risk variant.

Materials and methods: Thirty-seven adolescents with <7h sleep/night participating in a larger randomized clinical trial on cardiometabolic health consented to optional genotyping procedures. Of these, 27 samples were able to be analyzed using a Taqman assay (age=16.1±1.2, 85.2% female, 77.8% non-Hispanic White, BMI_{ile}=57.6±28.1). Participants completed in-home actigraphy monitoring during one week of typical sleep during the academic year followed by an overnight in-lab study visit with AM and PM serial salivary dim-light melatonin sampling and an intravenous glucose tolerance test to measure insulin sensitivity (Si). Summary measures are reported for those with and without the risk variant (GG/GC vs. CC) as median [interquartile range]. Wilcoxon, chi-squared or Fisher's exact statistics tested for differences between groups.

Results: 52% had the G allele (GG n=4, or GC n=10) while 48% (n=13) did not (CC). Participants with the risk variant compared to those without had shorter sleep onset latency (5.3min [3.8,8.8] vs. 10.0min [7.6,13.8]; p=0.01) and greater variability in bedtime (1.1h [0.8,2.9] vs. 0.6h [0.5,0.7]; p=0.007) and sleep midpoint (1.1h [0.7,2.4] vs. 0.5h [0.4,0.8]; p=0.02) across the home monitoring week. Those with the risk variant trended towards earlier dim light melatonin onset (DLMO_{on}; 20:06 [19:36,20:30]

vs. 21:06 [20:54,21:06]; $p=0.05$). There were no differences between groups for sleep duration, waketime, DLMOff, melatonin duration, or Si.

Conclusions: In this sample of habitually short-sleeping adolescents, those with at least one copy of the *MTNR1B* risk (G) variant had some differences in sleep and circadian rhythms compared to those without, but findings are limited due to the small sample size. Further research in larger and more diverse samples is recommended.

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Differential Light-Induced Phase Shifts in the Circadian Rhythms of Cardiovascular Autonomic Function in Hypertensive and Normotensive Rats

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Introduction: Previous clinical studies have found that shift workers with abnormal blood pressure are at risk of cardiovascular disease. However, there is still a lack of integrated studies to discuss the pathophysiological mechanisms associated with abnormal circadian rhythms in shift work and jet lag, and the pathophysiological effects of combined hypertension. Therefore, this study aims to investigate the differential changes of various physiological signals in normotensive Wistar-Kyoto rat (WKY) and spontaneously hypertensive rat (SHR) during and after light-induced phase shift process by using the established wireless multi-channel physiological recorder.

Materials and methods: We recorded physiological signals from WKY and SHR rats over 17 consecutive days before, during, and after a light-dark cycle phase-shift intervention, and analyzed the circadian rhythms of the brain waves, sleep architecture, and cardiovascular parameters using various linear methods.

Results: It was found that the blood pressure, heart rate, and cardiovascular autonomic function of both WKY and SHR rats were affected by the phase shift of the light-dark cycle, with changes in the phase and amplitude of their circadian rhythms. Compared with WKY rats, the acrophase of blood pressure and vascular sympathetic function in SHR was more profoundly affected by the light-induced phase shift. Moreover, the amplitude of the circadian rhythm was smaller in SHR than in WKY. In addition, the circadian rhythms of R-R intervals, as well as cardiac parasympathetic and sympathetic functions, were more significantly altered by the light phase shift in SHR, exhibiting greater phase shifts, increased frequency, and reduced amplitude.

Conclusions: Compared to normotensive individuals, those with hypertension may be more susceptible to the adverse effects of jet lag or shift work on cardiovascular function.

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Dim light melatonin onset is later in post-menopausal women following Breast Cancer compared with controls

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Introduction: One year after treatment for breast cancer, >80% post-menopausal women in remission from breast cancer complain of poor sleep-quality, which may be a consequence of circadian misalignment. The aim of this study was to compare central circadian timing via nocturnal melatonin-secretion, in post-menopausal women in remission from breast cancer (≥ 12 -months) (BCG), with age-matched post-menopausal women with no cancer history (CG).

Materials and methods: Participants were recruited from outpatient breast cancer clinics (BCG: $n=6$) or the community (CG: $n=10$). Sleep and psychological symptoms were assessed using the Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS) and the Depression, Anxiety, Stress Scale (short form; DASS-21). Habitual bedtime (HBT) was quantified using actigraphy (7 days). Overnight in-laboratory polysomnography was performed, and saliva samples collected under strict lighting conditions (<1 Lux; 13 samples in total) 5 hours prior to HBT until 2 hours after habitual wake time. Salivary melatonin was quantified by radioimmunoassay. Individual melatonin profiles were analysed for the; (1) Clock-time when melatonin concentrations reached 4pg/mL (DLMO), (2) Area under the melatonin curve (AUC), and the Time-interval between HBT and DLMO (PA). Group data were summarised as median (interquartile range) and compared through 2-sided Mann-Whitney U-tests. $p < 0.05$ indicated statistical significance.

Results: There were no significant differences ($p > 0.20$) in age (BCG: 62.5 (59.5-67.3) vs. CG: 58.5 (54.0-66.3) years), body-mass indices (BCG: 28.0 (24.0-30.5) vs. CG: 25.1 (22.1-29.9) kg/m²) or HBT (BCG: 22:49 (21:46-23:38) vs. CG: 22:16 (21:59-22:21)). Neither group had evidence of negative emotional state (DASS-21; BCG: 8.5 (2.8-9.5) vs CG: 5.0 (2.8-9.0) au), sleepiness (ESS; BCG: 8.0 (5.0-9.0) vs. CG: 3.5 (1.8-6.3) au) or severe obstructive sleep apnoea (OSA) (Apnoea-hypopnoea index; BCG: 9.0 (6.6-10.3) vs. CG: 6.9 (2.4-21.3) events/hr), all having $p > 0.10$. Compared to CG, BCG tended to have higher PSQI (BCG: 8.5 (5.3-10.8) vs. CG: 4.0 (3.8-5.5) au; $p=0.07$) and ISI scores (BCG: 10.5 (5.5-17.3) vs. CG: 5.5 (3.8-8.0) au; $p=0.07$), lower AUC (BCG: 97.3 (83.7-125.0) vs. CG: 170.8 (96.6-250.3) pg/mL; $p=0.09$), and shorter PA (BCG: 1.4 (1.0-2.4) vs CG: 3.6 (2.2-3.9) hrs; $p=0.09$). BCG had significantly delayed DLMO compared to CG (20:46 (20:01-22:03) vs 18:40 (17:55-20:07); $p=0.03$).

Conclusions: In this small cohort, in the absence of severe OSA, negative emotional state or sleepiness, post-menopausal women in remission from breast cancer tended to report poorer sleep-quality, increased insomnia symptoms, with lower overnight melatonin secretion, altered circadian-sleep alignment, and a significantly delayed melatonin onset. We speculate poor sleep-quality and insomnia symptoms following breast cancer treatment attribute to circadian-sleep misalignment from delayed central circadian timing.

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Disease-Based Chronoseasonal Patterns in Emergency Department Visits Reflecting Traditional and Emerging Trends

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Introduction: Seasonal variation in emergency department (ED) visits reflects underlying chronobiological rhythms shaped by environmental exposures, temporal patterns in disease incidence, and healthcare utilization behaviors.

In recent years, global shifts in climate and human behavior have raised questions about the consistency of these seasonal trends. This study investigated whether traditional seasonal patterns in ED utilization have continued across different disease categories and age groups.

Materials and methods:

We retrospectively analyzed 420,000 ED visits from two regional hospitals in Korea (2020–2024). Patients were stratified into three age groups (pediatric, adult, older adults), and symptoms/diagnoses were mapped to clinically relevant categories based on ICD codes, with expert-reviewed reclassification by organ system. To model seasonal trends, we used generalized additive models with quasi-Poisson distribution and cyclic cubic splines for month, adjusting for year, hospital, age, and sex.

We fitted a quasi-Poisson model with cyclic splines for months that varied by age group, and used a Wald test to assess differences in seasonality across age groups. Relative risks were calculated relative to the trough month, and the peak-to-trough ratio (PTR) was defined as the ratio of the peak to the trough predicted count.

Results: From 2020 to 2024, the mean age and proportion of elderly ED visitors steadily increased (46.66 to 50.55 years; 26.1% to 35.8%). Seasonal variation was most pronounced in pulmonary and infectious diseases, with peaks in January and July, respectively (PTR = 1.58 and 1.46). Notably, this seasonal pattern was attenuated during the early COVID-19 period and gradually recovered in subsequent years, likely reflecting the impact of public health measures such as mask-wearing and social distancing. Orthopedic and trauma surgery showed summer peaks in June and August, respectively (PTR = 1.27 and 1.40). Acute cardiovascular events, including myocardial infarction and stroke, did not show apparent seasonal variation in our data. In general, seasonal variation was attenuated in older adults compared to younger ones, possibly due to a smaller sample size. However, nephrology-related visits were significantly more common among older adults. No nocturnal or diurnal differences were observed in the ED presentation of any symptoms or diseases.

Conclusions:

This study demonstrates that seasonal variation in emergency care differs by disease and age group. Pulmonary and infectious diseases maintain consistent seasonal patterns, while trauma and cardiovascular conditions display altered or absent seasonality compared to traditional reports. The attenuation and partial recovery of seasonality during the COVID-19 period highlight the influence of behavioral and environmental factors on temporal disease dynamics. Reduced seasonal variation in older adults, with a disease-specific exception, warrants further investigation with a larger sample. These findings underscore the complexity of seasonal rhythms in emergency care and the importance of considering demographic and environmental contexts in temporal analyses.

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Diurnal light exposure and circadian rest-activity rhythms with the risk of metabolic dysfunction-associated fatty liver disease

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Introduction: Metabolic Dysfunction-Associated Fatty Liver Disease (MASLD) is the most prevalent liver disease worldwide, affecting approximately 32% of the population. Despite the lack of approved therapies or specific pharmacological treatments for MASLD, prevention has become the primary focus of its management, particularly identifying and addressing modifiable risk factors. The circadian clock regulates various hepatic functions, including glucose, triglyceride, and cholesterol metabolism, and disruptions in circadian rhythms are associated with metabolic disorders and exacerbated liver pathologies. However, research examining the relationship between objectively measured circadian rhythm disruptions and MASLD remains limited.

Materials and methods: This prospective cohort study utilized seven days of accelerometer data from the US National Health and Nutrition Examination Survey (NHANES) and UK Biobank. The primary objective was to explore the associations between 24-hour light exposure, circadian rest-activity rhythm (CRAR), and the risk of incident MASLD. We also assessed the impact of light exposure and CRAR on genetic risk and their effects on life expectancy in individuals with MASLD. The analysis focused on five CRAR parameters, including the average activity levels during the least active (L5) and most active (M10) periods, relative amplitude (RA), and the onset times of L5 and M10. Daylight and nighttime light exposures were categorized based on intensity thresholds. We employed Cox regression models to estimate hazard ratios (HRs) for incident MASLD, and subgroup analyses were conducted to assess interactions by polygenic risk, age, and sex.

Results: The study included 7,253 participants from NHANES and 91,349 participants from the UK Biobank, with a median follow-up of 7.93 years. In the UK Biobank prospective analysis, higher RA and M10 levels were associated with a 46% and 37% reduced risk of MASLD, respectively, compared to

the lower group. Higher L5 levels and delayed L5 onset were linked to a 59% and 21% increased risk of MASLD. Moreover, each additional hour of daylight exposure above 6000 lux was associated with a 9% lower risk of MASLD, while each additional 30 minutes of nightlight exposure above 30 lux corresponded to a 22% higher risk of MASLD. Similar associations were observed for fibrosis and cirrhosis risk. Additionally, individuals with optimal CRAR and light exposure had a greater life expectancy compared to those with poor rhythms and light exposure.

Conclusions: This study provides robust evidence that disruptions in circadian rest-activity rhythms and light exposure are associated with an increased risk of MASLD. Our findings highlight the potential of managing circadian behaviors and environmental cycles as an approach to prevent MASLD and other chronic liver diseases.

Diurnal preferences and mental health in dermatological diseases: Population-based evidence from the EPISONO cohort

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Introduction: Dermatological diseases (DD), such as dermatitis, psoriasis, and vitiligo, are commonly associated with pruritus, sleep disturbances, and psychological distress. Growing evidence suggests that pruritus severity may be influenced by individual chronotype. However, population-based studies on the impact of DD on chronobiological aspects and psychological outcomes remain limited. Thus, this study aimed to examine the independent and combined effects of dermatitis, psoriasis, and vitiligo on sleep habits, circadian typology, and psychological outcomes in a representative sample from São Paulo, Brazil.

Materials and methods: This cross-sectional case-control analysis used data from the 4th edition (2018–2019) of the São Paulo Epidemiologic Sleep Study (EPISONO). A total of 743 participants who completed the dermatological section of the general health questionnaire were included. Individuals who self-reported a diagnosis of dermatitis (n=51), psoriasis (n=19), vitiligo (n=8), or overlapping conditions (n=8) were classified as having DD, while the remaining (n=657) comprised the non-DD group. Propensity score matching (PSM) was performed in a 1:1 ratio based on age, sex, ethnicity, and socioeconomic status to generate comparable groups.

Results: Before PSM, participants with DD (mean age: 49.1±14.5 years; 66.3% women) had significantly lower Morningness–Eveningness Questionnaire (MEQ) scores (54.2±11.2 vs. 57.5±11.5) and a smaller proportion of morning types (29.1% vs. 46.6%) compared to the non-DD group (mean age: 48.7±14.9 years; 57.8% women), particularly among those with dermatitis (MEQ: 52.5±10.8; morning types: 25.5%). PSM resulted in 86 well-balanced pairs (mean age: 49.8±14.5 years; 69.8% women). After matching, these differences in morningness preference were no longer significant. No significant differences were observed in social jetlag or mid-sleep on free days corrected for sleep debt on work days (MSFsc). In terms of mental health, the DD group reported 3.8% higher perceived stress and 3.4% lower scores in the psychological domain of the World Health Organization Quality of Life Instrument – Brief Version compared to controls before matching. Post-matching, psychological quality of life became further reduced, the physical domain presented a 5.7% lower score, and the Beck Depression Inventory (BDI) score was approximately 27% higher in the DD group (10.4±7.7 vs. 8.1±6.9).

Conclusions: Individuals with DD presented greater eveningness preference and worse psychological outcomes. Although some differences were influenced by sociodemographic factors, the persistence of reduced quality of life and increased depressive symptoms after adjustment suggests an independent association. These findings support the inclusion of circadian and mental health assessments in dermatological care and reinforce the need for longitudinal studies to clarify causal mechanisms.

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Effect of Acupuncture on Shift Work Disorder : A Randomized Clinical Trial

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Introduction: To observe the efficacy and safety of acupuncture on sleep quality for patients with shift work disorder (SWD)

Materials and methods: This sham-controlled, randomized clinical trial was conducted in China from December 1, 2021 to January 31, 2023. A total 86 SWD patients who met the inclusion criteria were randomized in a 1:1 ratio into manual acupuncture (MA) or sham acupuncture (SA) groups. All the participants received acupuncture or sham acupuncture 10 sessions, once every 2 days. The primary outcomes was Pittsburgh Sleep Quality Index (PSQI). The secondary outcomes included Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Fatigue Scale-14 (FS-14), Patient Health Questionnaire (PHQ-9) and General Anxiety Disorder-7 (GAD-7). Besides, 2-week Actigraphy (ACT) were completed at baseline and post-treatment.

Results: Compared with the SA group, the MA group showed statistical decreases in PSQI ($F = 5.985$, $P = 0.017$), ISI ($F = 4.792$, $P = 0.031$), PHQ-9 ($t = -2.640$, $P = 0.010$), GAD ($Z = -2.483$, $P = 0.013$) at the post-treatment, as well as demonstrated decrease ISI score at the follow-up period ($F = 8.407$, $P = 0.005$). As to ACT data, acupuncture significantly improved in Innerdaily Stability (IS), Intradaily Variability (IV), Fragmentation index (FI) at the post-treatment period ($Z = -2.004$, $P = 0.045$; $t = 3.406$, $P = 0.001$; $t = -3.004$, $P = 0.004$).

Conclusions: Acupuncture can improve subjective sleep indicators in SWD patients, including improving sleep quality, reducing the severity of insomnia, as well as objective sleep indicators such as increasing IS and decreasing IV and FI. Besides acupuncture can alleviate the adverse emotions of SWD patients.

Effect of flight itinerary on jetlag duration: a systematic modelling study

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Introduction: Rapid travel crossing multiple time zones results in jetlag, which affects millions of travellers daily. Flight itinerary is likely to affect the duration of jetlag; however, its effects have not been systematically studied. This study investigates the effects of flight departure time, flight duration, and forced wakefulness at the destination on jetlag duration.

Materials and methods: We used an arousal dynamics model to simulate sleep-wake cycles and circadian dynamics depending on flight departure time (from 00:30 to 24:00), flight duration (from 0.5 to 24 hours), and time zone difference between destination and origin (ΔT from -12 to 12 hours). Simulations were performed with either free sleep or forced wakefulness from 10:00 to 17:00 daily at the destination. To simulate the time and activity at the airport, wakefulness was forced for 3 hours before and 1 hour after flight with airport light of 300 lux. To simulate the take-off and landing, forced wakefulness was applied for 30 minutes at the beginning and end of the flight with in-flight light of 80 lux. During the flight, the light level was 50 lux, and 0 lux during sleep. Sleep was allowed in-flight based on physiological need for sleep during the flight. Jetlag was considered over when the circadian phase at the destination reached values within 30 minutes of the fully entrained to the destination's light-dark cycle. Cognitive performance was predicted in the model using the lapses of attention on the Psychomotor Vigilance Task.

Results: Jetlag occurred for all ΔT s, and larger $|\Delta T|$ resulted in longer jetlag. Adaptation via phase-advancing caused longer jetlag with a larger variance due to the flight itinerary. Light exposure and forced wakefulness caused by different flight itineraries moved circadian clock closer or further away from destination time zone. For the case of free sleep at the destination, flight itinerary affects jetlag duration by up to 8 times. Forced wakefulness at the destination reduced the average jetlag duration

by up to 10 days compared to free sleep; however, it came at the cost of impaired cognitive performance for up to 1 week. For ΔT from 1 to 9 hours, jetlag was shortest for flights departing from 8 AM to 11 AM or arriving from 5 AM to 8 AM in the origin time, and jetlag was longest for flights departing from 11 PM to 3 AM or arriving from 11 PM to 2 AM. The relationship was reversed from the other ΔT s.

Conclusions: Flight itinerary significantly affects the duration of jetlag. Forced wakefulness at the destination can reduce jetlag duration, but it also reduces cognitive performance. Selecting flights based on these findings could reduce jetlag. This study considered the most common scenario; the results may not be directly applicable to other populations.

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Effects of nighttime melanopsin stimulation on sleep architecture

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Introduction: Light plays a fundamental role in visual perception but also in regulating non-visual processes, including the entrainment of circadian rhythms. The pacemaker of the circadian clock, located in the suprachiasmatic nucleus (SCN), receives its primary input from the retina, making it particularly sensitive to light. Among the retinal photoreceptors, intrinsically photosensitive retinal ganglion cells (ipRGCs), which express melanopsin (most sensitive to short-wavelength light), are considered primarily responsible for mediating these non-visual responses. Recent research has used metameric light conditions to disentangle the contributions of specific photoreceptors. These light conditions allow for selective modulation of melanopic activation while keeping cone stimulation constant, isolating the role of ipRGCs. A few studies have used such metamers to compare the effects of high- versus low- melanopic light exposure before and up to shortly after habitual bedtime. Results have consistently shown that higher melanopic light leads to stronger melatonin suppression. However, its effects on sleep remain inconclusive. We aim to extend this line of research by designing metameric light conditions that differ only in their melanopic equivalent daylight illuminance (EDI), while maintaining matched alpha-opic EDI values for S-, M-, and L-cones. By exposing participants to these light conditions during the melatonin plateau, we aim to further investigate the role of melanopsin stimulation on sleep following nighttime light exposure.

Materials and methods: Participants (N=7) were exposed to three light conditions: two metameric lights providing (1) high and (2) low melanopic input, and (3) dim light as a baseline. Each exposure lasted 2 hours, beginning 3.5 hours after individual dim light melatonin onset (DLMO). One hour after the light exposure ended, participants were allowed to sleep until spontaneous awakening. Sleep was monitored using polysomnography, and morning alertness was measured with the Karolinska Sleepiness Scale (KSS).

Results: Light exposure had no effect on the proportion of N1, N2, REM sleep, or awakenings after sleep onset. Total sleep time, time spent in N1, N2, REM, and awake did not differ between light conditions. However, exposure to high melanopic light resulted in a longer duration of N3 sleep. Morning KSS scores did not significantly differ between light conditions.

Conclusions: Exposure to high melanopic light during the night selectively increased N3 sleep duration, suggesting that melanopsin stimulation may enhance restorative aspects of sleep. This is consistent with previous research showing that light exposure during extended wakefulness increases slow-wave sleep. The late scheduled sleep onset in our participants likely caused partial sleep deprivation, which may have influenced the effects of light. These findings highlight the role of melanopsin in regulating restorative sleep and have potential implications for lighting design. Further research should investigate the contributions of classical photoreceptors to the non-visual effects of light.

ADCY3 Ser107Pro links difficulty awakening in the morning to adiposity through circadian regulation of adipose thermogenesis

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Introduction: Modern lifestyles often disturb circadian rhythms, yet the genetic circuits that convert this stress into metabolic dysfunction remain poorly defined.

Materials and methods: We conducted a genome-wide pleiotropy analysis to explore the associations between morning circadian preference and BMI, focusing on the tissue-specific expression and rhythmicity of key genes.

Results: Here, we identify a missense variant in ADCY3 (rs11676272; Ser107Pro) as a pleiotropic regulator of circadian preference and adiposity. Using genome-wide pleiotropy analysis in ~480,000 UK Biobank participants, we show that the G risk allele (Pro107) increases eveningness, BMI, and fat mass in European (N=451,324) and African (N=8,738) ancestry groups, with behavioral amplification by morning difficulty awakening observed in Europeans, and power-limited interaction modeling in other populations. Structural modeling and transcriptomic analysis suggest this allele destabilizes ADCY3 and alters adipose-specific splicing and expression. In mice, *Adcy3* is rhythmically expressed in adipose tissue, with the conserved Pro107 site showing BMAL1 binding and cold-inducible activation. Human adipose ADCY3 expression also increases after weight loss

Conclusions: Together, these findings reveal a genotype-dependent, behaviorally modifiable axis linking difficulty awakening to adipose thermogenesis and obesity risk.

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Evaluation of the Molecular Crosstalk Between Endoplasmic Reticulum Stress and Sleep-Wake Homeostasis

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Introduction: Sleep and circadian disturbances (SCRD) are increasingly recognised as both a **consequence and contributor** to **endoplasmic reticulum (ER) stress**, a cellular condition caused by the accumulation of unfolded or misfolded proteins within the ER. This bidirectional relationship plays a key role in the pathophysiology of numerous sleep disorders, neurodegenerative diseases, and metabolic conditions. In response to ER stress, cells activate the **unfolded protein response (UPR)**, a protective network comprising three signalling branches mediated by **ATF6, PERK, and IRE1**. Together, these pathways function to restore ER homeostasis by enhancing protein folding, reducing global translation, and promoting degradation of misfolded proteins. Targeting components of the UPR has emerged as a promising therapeutic strategy to mitigate SCRD and its systemic effects. Our research investigates **casein kinase 1 (CK1)**—specifically its **δ (delta)** and **ε (epsilon)** isoforms—as modulators of both **circadian rhythms** and **ER stress responses**.

Materials and methods: Using U2OS osteosarcoma and SH-SY5Y neuroblastoma cell lines, we evaluated the effects of pharmacological CK1 inhibition on multiple arms of the UPR. *In vivo*, we conducted a comprehensive characterisation of sleep and circadian behaviour in mice treated with CK1 inhibitors, examining phase shifts and recovery from SCRD. We quantified ER stress markers in both central (brain) and peripheral tissues, comparing outcomes with and without CK1 inhibition. To assess the cognitive impact of SCRD and therapeutic intervention, we employed behavioural assays evaluating spatial memory and executive function.

Results: Our findings reveal that **CK1 inhibition effectively tunes the UPR**, both in vitro and in vivo, and modulates behavioural and molecular outcomes linked to sleep disruption. In cell culture models, CK1 inhibition altered the expression and activation of key UPR components across the ATF6, PERK, and IRE1 pathways. In the mouse model, CK1 inhibitor treatment demonstrated significant effects on circadian parameters and sleep architecture during normal conditions and following induced sleep disruption. Analysis of tissue samples revealed corresponding changes in ER stress markers, with differential responses observed between the central nervous system and peripheral tissues.

Behavioural testing indicated that CK1 inhibition attenuated cognitive deficits associated with sleep disruption, correlating with reduced markers of ER stress in brain regions associated with learning and memory.

Conclusions:

These results position **CK1 as a promising therapeutic target** at the intersection of **circadian regulation, sleep homeostasis, and cellular stress resilience**. By targeting the ER stress response, our work offers translational insights into the development of novel therapies for sleep disorders and their broader physiological consequences.

Examining the impact of seasonal variations in photoperiod on sleep in young adults

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Introduction: In equatorial and low-latitude regions, photoperiod and twilight durations exhibit minimal seasonal variation, resulting in stable patterns of light exposure year-round. In contrast, those living in higher latitudes are subject to pronounced seasonal variation in daylength. These variations are accompanied by extended twilight periods and seasonal shifts in the timing of sunrise and sunset, which may impact sleep. This study examines the impact of seasonal variation in daylength and its impact on sleep in young adults.

Materials and methods: Young adults [$n=39$, 18 males] aged 22.6 ± 3.0 years ($M \pm SD$), participated in the study between 2022 and 2024. Data was collected for 10 consecutive days. Sleep and wake information was collected using sleep diaries. Daylength and dawn and dusk timings were extracted using <https://www.timeanddate.com> to account for the potential influence of changes in photoperiod across seasons on sleep patterns. Data collected from November to February were characterised as short daylength (SDL) months, and data collected from March to October were characterised as long daylength (LDL) months. Global Horizontal Irradiance (GHI), a measure of solar irradiance, which refers to total solar radiation incident on a horizontal surface, was assessed using a publicly available website. Dawn to sleep onset time, dusk to sleep onset time and dawn on the day of awakening till wake time were calculated.

Results: There were significant differences in sleep onset time ($p<.005$), wake time ($p<.005$), and sleep onset latency (SOL) ($p<.005$), between SDL and LDL months. Both sleep onset time and wake time were delayed during LDL months (sleep onset time: $01:16 \pm 01:58$ h, wake time: $09:09 \pm 02:00$ h) compared to SDL months (sleep onset time: $00:09 \pm 01:37$ h, wake time: $08:16 \pm 01:34$ h). Sleep Onset Latency (SOL) approximately doubled during LDL months (31 ± 36 minutes) compared to SDL months (17 ± 21 minutes). Total sleep time was approaching significance ($p=.06$) with longer sleep duration observed during SDL months (7.96 ± 1.72 h) compared to LDL months (7.64 ± 1.55 h). The duration from dawn to sleep onset time was longer during LDL months (19.04 ± 2.27 h compared to SDL months (17.20 ± 1.64 h). The duration from dusk to sleep onset time was longer during SDL (5.94 ± 1.60 h) months compared to LDL months (4.51 ± 2.24 h). There were no differences in total sleep time, wake time, sleep onset time and SOL between weekdays and weekends ($p>.05$). When examining chronotype defined by midsleep on free days corrected for oversleep (MSFc), an indirect estimate of circadian phase, there was a delay in midsleep timing during LDL months ($05:20 \pm 01:30$ h, $p=.01$) compared to SDL months ($04:18 \pm 01:00$ h). GHI was higher during LDL months (3130.18 ± 1764.59 W/m²) compared to SDL months (1349.07 ± 513.83 W/m², $p<.001$).

Conclusions: These findings demonstrate that seasonal variation in photoperiod including the timing of dawn and dusk transitions have significant effects on the timing and duration of sleep in young adults, primarily highlighting the importance of natural light in synchronising daily sleep-wake patterns. These findings have implications for chronobiology and the development of light-based interventions to support sleep health in young adults.

How do individual differences in circadian physiology contribute to predicted circadian timing in real-world conditions?

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Introduction: Light is the primary time cue for the human central circadian clock. Computational models have been developed to predict circadian timing based on light exposure patterns. However, these models are not always accurate at the individual level, potentially due to inter-individual differences in circadian physiology, including how sensitive the circadian system is to light. We aimed to investigate how these physiological differences affect entrainment in real-world environments, and to test whether individualizing the model improves predictions of circadian timing in a dataset collected in shift workers.

Materials and methods: We used a validated computational model of circadian rhythms and sleep/wake, which takes light exposure patterns and sleep constraints (e.g., work schedules) as inputs. This model was used to simulate circadian timing and sleep/wake patterns, while varying both: (i) physiological parameters of the model (circadian light sensitivity and intrinsic circadian period); and (ii) environmental lighting assumptions (including morning, daylight, and evening light levels). We analyzed how these factors interacted to determine predicted circadian timing and sleep/wake patterns. The model was then used to predict circadian timing in a shift work dataset. This dataset included shift workers (age 21-41 years, n=27, full dataset in n=17) who were tracked in the field for approximately 3 weeks on a work roster including night shifts. Sleep/wake patterns, light exposure patterns, and work schedules were collected daily. Participants visited the lab for repeated circadian phase assessments, using dim light melatonin onset (DLMO), up to three times, at approximately weekly intervals. Light sensitivity was measured using melatonin suppression on the first lab visit.

Results: Brighter evening light levels or longer intrinsic period led to later predicted circadian and sleep timing, with this effect being amplified by high light sensitivity. Brighter daylight levels attenuated the predicted delaying effects of evening light. Brighter morning light advanced circadian and sleep timing, normalizing rhythms in simulations with a long circadian period, or with both high light sensitivity and high evening light. Applying the model to the shift worker dataset, we found that individual-level estimation of physiological parameters (circadian light sensitivity, intrinsic circadian period) significantly improved model accuracy for circadian timing estimates compared with predictions made using default model parameters.

Conclusions: Modeling enables us to test complex interactions between physiological and environmental factors, identifying candidate strategies to improve entrainment and reduce circadian disruption. Our results suggest that both circadian light sensitivity and intrinsic circadian period play important roles in determining sleep and circadian timing in the real world. Incorporating these factors into model individualization therefore leads to more accurate model predictions, even under challenging test conditions.

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Impact of circadian rhythm sleep disruption on cortisol and melatonin biomarkers and cellular metabolism (telomeres) in oral health: systematic review

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Introduction: This systematic review focused on the impact of sleep disorders related to circadian rhythm on cortisol and melatonin biomarkers and also on cell metabolism, especially at the telomere level.

Materials and methods: The following quantitative records were found: Scielo (35); Pubmed (1,114) and Cochrane (1,478). The Covidence system automatically marked 221 records as duplicates and 744 records as automatically ineligible. Database selection and identification were carried out according to the Prisma system for systematic reviews. After evaluating the full text, 12 publications remained for data extraction. In the 12 studies evaluated, 12,866 people between the ages of 18 and 88 took part. The samples ranged from 13 young men to 5,268 elderly people. All the studies identified the

participants' gender, with 9,022 women (70.13%) and 3,844 men (29.87%). Eligibility criteria were selected based on the structuring factors that make up the PICOS approach (P= Population; I= Intervention; C= Comparison; O= Outcome; S= Study design). The population (P) being analysed included participants with circadian rhythm sleep disorders. The intervention (I) included biomarkers of cortisol, melatonin and telomeres. The comparison group (C) included individuals with regular sleep patterns aligned with the natural circadian rhythm. Outcomes (O) included telomere length and a measure of sleep quality, assessed using objective sleep indices or by self-report and cortisol and melatonin levels in the blood. The study design (S) included randomised control trials and other formats. regarding the exclusion criteria, unpublished studies, conference abstracts and studies whose full article was not available and could not be obtained directly from the authors were removed.

Results: The variability in study designs, as well as the heterogeneity of samples and measurement methods, emphasizes the need for future, more rigorous research to clarify these associations. These results reinforce the importance of synchronizing internal biological rhythms with natural environmental cycles in order to maintain general health, which includes oral health

Conclusions: The evidence from the selected studies indicates an association between circadian dysregulation and variations in these biomarkers, with possible implications for telomere length, suggesting a role in the processes of premature cellular ageing, cell renewal and recovery, and metabolic and hormonal imbalances. In dentistry, the cellular ageing process and hormonal imbalances influence processes such as healing and post-surgical recovery, the immune response and the development of periodontal disease, changes in the salivary pH of the microbiome and, consequently, dental caries. Proper regulation of the circadian rhythm can therefore play a crucial role in optimizing dental care and maintaining chronic oral conditions. Recognizing the interconnection between sleep, metabolic health and oral health can lead to more holistic approaches in dental treatment, underlining the importance of considering circadian rhythms in clinical dental practice to promote more comprehensive and lasting oral health.

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Impact of Delayed Meal Timing on Circadian Rhythms and Hormone Profiles in Healthy Adults: A Randomized Crossover Study

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Introduction: Meal timing can affect the body's internal biological clock. However, few studies have evaluated whether delaying mealtimes, as frequently occurs in those who skip breakfast, disrupts circadian rhythms. We hypothesized that delaying meals relative to sleep would modify the shape of circadian hormone rhythms, including melatonin and steroid hormones, and that these effects would differ by sex.

Materials and methods: Adult men and women, age 25-49 y (body mass index [BMI] 25-34.9 kg/m²) completed a randomized crossover, controlled feeding study. Circadian physiology was assessed on days 3 and 14 under two separate conditions: aligned (first meal consumed 1 h after waking) and misaligned (first meal delayed by 4 h relative to aligned, starting 5 h after waking). Eating windows (time from first to last meal) were 10 h in each condition and bedtimes were fixed (8-h time in bed). All meals were provided to participants in amounts designed to maintain weight; intakes were identical in each condition. Blood samples were collected in an inpatient setting from 7 PM to 12 PM (aligned) or 3 PM (misaligned) on days 3-4 and 14-15. Samples were assayed for melatonin, cortisol, cortisone, corticosterone, testosterone, dehydroepiandrosterone sulfate (DHEA-S), and progesterone. Circadian hormone rhythms were modeled via linear mixed-effects cosinor regression using harmonic predictors ($\cos \omega t$, $\sin \omega t$) where t is time (hours) and $\omega = 2\pi/24$, with subject-level random effects. A full 4-way interaction (condition $\times$ sex $\times$ day $\times$ harmonic predictors) was evaluated.

Results: Data from 20 participants (7 males) were analyzed (age 34.8 ± 7.9 y; BMI 27.0 ± 4.1 kg/m²). Melatonin showed significant modulation by condition, with altered $\sin \omega t$ under misaligned condition (4.6 [0.6, 8.6]). A significant 4-way interaction both $\cos \omega t$ ($p=0.013$) and $\sin \omega t$ ($p=0.003$) indicated sex- and time-dependent effects. On day 14, females in the misaligned condition exhibited lower $\cos \omega t$ (-12.6 [-20.9 , -4.2]) and $\sin \omega t$ (-6.6 [-12.3 , -1.0]), indicating reduced amplitude and delayed phase of melatonin. In contrast, in males, $\cos \omega t$ increased on day 14 ($+15.4$ [3.3, 27.5]), suggesting partial

rhythm recovery. For corticosterone, misaligned condition decreased $\cos\omega t$ (-872.2 [$-1548.4, -195.9$]) with a significant interaction. Males in the misaligned condition, but not females, showed increased $\cos\omega t$ on day 14 ($+1181.4$ [$50.0, 2312.9$]). Progesterone rhythmicity was suppressed under misalignment, with lower $\cos\omega t$ (-999.6 [$-1623.4, -375.7$]) and $\sin\omega t$ (-1582.3 [$-2247.8, -916.8$]) on day 3 in females while males showed increased $\sin\omega t$ ($+1574.2$ [$489.6, 2658.9$]). However, by day 14, a negative interaction in $\sin\omega t$ (-2003.2 [$-3506.2, -500.1$]) indicated that this was a male-specific increase, suggesting divergent rhythmic responses in progesterone by sex. Cosinor parameters for other hormones did not differ by condition.

Conclusions: Delaying meal times relative to sleep by 5 h, compared to 1 h, altered melatonin, corticosterone, and progesterone rhythms in a time- and sex-dependent manner. These effects varied significantly by sex and showed different trajectories based on duration of exposure to the eating pattern. Our results suggest that meal timing can influence circadian and hormonal rhythms and may inform strategies for chrononutrition in personalized medicine.

Impact of everyday light exposure patterns on cardiometabolic and psychological health as well as sleep outcomes in younger and older adults

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Introduction: 90% of our time is spent indoors. During daytime we are exposed to lower light intensities and a different color spectrum indoors compared to natural daylight. The chronic lack of daylight and excessive electrical light in the evening are increasingly being considered as risk factors in the aging society's rising incidence of cardiometabolic, psychological and sleep disorders. It has already been shown that light influences blood sugar, blood pressure, psychological well-being and sleep outcomes in a time-of-day dependent manner. Therefore, poor light exposure habits may be an underestimated lifestyle factor contributing to a multitude of disorders upon aging affecting our health care system. Yet, it is currently largely unknown to what degree light exposure habits and an individual's sensitivity to the health and sleep effects of light differ between younger and older individuals.

Materials and methods: We recruited younger (18–35 years) and older adults (60–80 years) living in and around the city region Aachen, Germany. Volunteers were generally healthy based on self-report and a comprehensive ophthalmologic exam was conducted to exclude any eye disorders, such as signs of cataract. At baseline, participants completed the Pittsburgh Sleep Quality Index, Light Exposure Behaviour Assessment and Munich Chronotype Questionnaire. For 12 consecutive days in their everyday life, participants wore a light logger (ActLumus, Condor Instruments) as a pendant, capable of measuring both photopic and melanopic lux every 10 seconds. During this time period, participants reported how they slept each morning and their current affect and vitality six times daily through a smartphone-based app (m-Path). Momentary alertness was assessed six times daily using the Karolinska sleepiness scale. Through continuous glucose monitoring (Freestyle Libre Pro iQ, Abbott Laboratories), interstitial glucose levels were measured every 15 min continuously. On day 11 and 12, participants stayed in an office environment from 08:30 to 17:00h under dim (<10 photopic lux) or bright (1000 lux) light conditions in a randomized order. Data collection was finished in May 2025 with data analysis currently ongoing.

Results: 31 younger adults (mean $\pm$ SD; 24 ± 3 years, body mass index (BMI): 24 ± 3 kg/m², 15 women) and 31 older adults (68 ± 5 years, BMI: 25 ± 3 kg/m², 17 women) were included. Initial self-reported hours in bed per night did not differ between young and old adults (7.5 ± 0.5 vs. 7.4 ± 1 hours). Preliminary results show that higher levels of melanopic lux in the 60 minutes before the respective reports were associated with higher vitality (regression coefficient $b=0.05$) and alertness ($b=-0.08$). In the ongoing data analysis, we will analyze age-differences in patterns of light exposure and their

associations with sleep as well as cardiometabolic and psychological health outcomes. We expect to substantiate current recommendations by showing that high levels of melanopic lux during the day and low levels in the evening are associated with better health and sleep outcomes.

Conclusions: Recent advancements in wearable light logger technology allow us to answer important questions regarding effects of people's light exposure, which have so far been understudied to understand cardiometabolic and psychological health as well as sleep outcomes.

Impact of Patient-Centered ICU Design including Dynamic Light Therapy on Sleep in Mechanically Ventilated Patients

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Introduction: Critically ill patients demonstrate marked disturbances in both circadian rhythms and sleep architecture. Delirium is the most prevalent acute brain failure in the ICU and is an independent predictor of higher mortality. The interplay between sleep, circadian rhythm, and ICU delirium likely exhibits a bidirectional relationship. Results of a recently published study indicated that using modifications in environmental design decreases the occurrence of delirium and is associated with changes in serum melatonin levels. This data analysis examines the potential effects of a comprehensive change in ICU room design on the sleep architecture of mechanically ventilated patients.

Materials and methods: This is a secondary endpoint analysis of a pilot proof-of-concept study in which two ICU rooms underwent significant architectural modifications, incorporating a newly developed dynamic lighting system and improved noise reduction measures ([Fig. 1](#)). Polysomnography (PSG) was performed in mechanically ventilated patients who were treated in standard and modified rooms for a maximum of three 24-hour periods. A trained sleep expert, blinded to the study, manually scored the recordings, following the American Academy of Sleep Medicine (AASM) criteria. The incidence and severity of delirium were evaluated using the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC).

Results: Data analysis included 82 PSG hypnograms from n = 27 patients treated in standard rooms and n = 20 in modified rooms ([Tab. 1](#)). Polysomnography analysis showed total sleep times (TST) of 1,147 minutes (IQR 556 - 1,367) for patients in standard rooms compared to 881 minutes (IQR 439 - 1,198) for patients in modified rooms (p = 0.113). N3 sleep was significantly prolonged for patients treated in standard rooms (400 minutes [IQR 136 - 810]) compared to patients in modified rooms (150 minutes [IQR 7 - 518]) (p = 0.01). Rapid Eye Movement sleep was almost absent for patients in both groups. The day-to-night sleep ratio was lower for patients in modified rooms (1.29 [IQR 0.72 - 2.01]) compared to those in standard rooms (1.99 [IQR 1.66 - 2.19]) (p = 0.05). Conversely, the night-to-day sleep ratio was significantly higher for patients in modified rooms (0.78 [0.5 - 1.39]) than in standard rooms (0.5 [IQR 0.46 - 0.59]) (p = 0.035). The proportion of night sleep, calculated as the duration of night sleep / TST, was significantly higher for patients in modified rooms (44 % [33 - 58]) compared to those in standard rooms (33 % [31 - 37]) (p = 0.035). Eighty-five percent (n = 23) of patients in standard rooms and 55 % (n = 11) in modified rooms developed delirium at some point during their ICU treatment (p = 0.045). Delirium severity, measured using the ICDSC, was significantly higher for patients in standard rooms (4 [IQR 2 - 5]) compared to those in standard rooms (2 [IQR 0 - 4]) (p = 0.02).

Conclusions: This preliminary analysis suggests that a comprehensive change in the design of ICU rooms may affect the sleep architecture of mechanically ventilated patients, thus reducing the incidence and severity of delirium.

Integrating Traditional Chinese Medicine (TCM) and Western Medicine Perspectives on Biological Rhythms - From Ancient Theories to AI-Driven Multidisciplinary Modeling

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Introduction: The concept of biological rhythms-daily, lunar, seasonal, and annual-has been foundational in both Traditional Chinese Medicine (TCM) and modern Western medicine, yet their theoretical frameworks and clinical applications diverge significantly. TCM conceptualizes daily rhythms through a twelve-phase system (*Ziwu Liuzhu*), correlating temporal energy fluctuations (*qi*-blood *yin-yang* dynamics) with organ-specific functional changes. Modern chronobiology, conversely, decodes 24-hour biological oscillations via molecular mechanisms - particularly circadian clock genes that synchronize cellular and systemic processes through transcriptional-translational feedback loops. Nowadays, the irregular lifestyles of modern humans have led to a high incidence of chronic diseases, highlighting an inseparable relationship between disrupted circadian rhythm and disease development. This study establishes a comparative framework analyzing TCM and Western chronobiology's mechanistic interpretations of daily, lunar, seasonal, and lifespan rhythms, followed by proposing an AI-augmented synthesis for precision health applications. By highlighting the interdisciplinary nature of the two fields, we offer a new direction for exploring the field of chronomedicine.

Materials and methods: This comparative study employed a three-phase framework:

Theoretical Synthesis: Textual analysis of TCM classics (e.g., *Huangdi Neijing*) and modern chronobiology literature identified core concepts of biological rhythms (daily *Ziwu Liuzhu*, lunar *Yueqi*, seasonal *Wuyun*, and annual *Shierqi*).

Data Integration: Structured databases were created for TCM rhythms (organ-phase correlations) and Western molecular mechanisms (circadian genes like *CLOCK/BMAL1*).

AI Modeling: Machine learning (random forest, LSTM networks) cross-validated patterns across datasets, incorporating meteorological variables (temperature, humidity) and TCM "Five Phases" theory to predict rhythm disruptions.

Results: Daily Rhythms: TCM's *Ziwu Liuzhu* (meridian energy cycles) aligned with circadian gene expression peaks (e.g., *PER2* at 11:00 AM) but emphasized organ-specific dominance (e.g., liver activity at 1:00-3:00 AM).

Lunar Cycles: TCM's *Yueqi* theory linked lunar phases to immune function (e.g., higher inflammation during waxing phases), validated by modern cytokine data.

Seasonal Adaptation: Both systems recognized seasonal immune shifts, with TCM's *Wuyun* correlating to vitamin D fluctuations and *CYP24A1* gene expression.

AI Model Performance: The integrated model achieved high accuracy in predicting insomnia and seasonal affective disorder, outperforming single-system predictions.

Conclusions: This study demonstrates that TCM and Western medicine offer complementary perspectives on biological rhythms, with TCM emphasizing holistic environmental interactions and Western medicine detailing molecular mechanisms.

Future research should prioritize AI-driven platforms that fuse:

Temporal Precision: High-resolution circadian tracking (wearables, omics) with TCM "meridian clocks."

Environmental Integration: Meteorological data and *Wuyun* theory to model climate-related health risks.

Personalized Interventions: Adaptive AI therapies combining acupuncture (TCM) and melatonin modulation (modern Western medicine).

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Late Isocaloric Eating Delays Circadian Rhythm of Glucose Tolerance in Adults with Overweight and Obesity

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Introduction: Although glucose tolerance (efficacy of blood sugar handling) in healthy individuals is higher in the morning vs. evening, the potential role of the endogenous circadian system, independent of light-dark and behavioral (e.g. sleep, eating) cycles, has not been tested using a gold-standard circadian protocol. In addition, it is unclear whether such endogenous circadian rhythm in glucose tolerance can be synchronized by the prior eating times in humans. Hence, we determine if there exists an endogenous circadian rhythm in glucose tolerance and whether this rhythm can be phase shifted by a delay in mealtimes.

Materials and methods: In a randomized crossover trial, 15 adults (4 women, age 37±11 y, BMI 28.8±2.4 kg·m⁻², HbA1c 5.4±0.3 %; mean±SD) completed 2 experimental conditions – 4 days of early eating (EE) and 4 days of late eating (LE), each after a 5-day EE baseline. Both conditions were otherwise identical for behavioral (sleep, physical activity, posture) and environmental influences (light, temperature). Three identical/isocaloric test meals (45-50% CHO, 15-20% PRO, 30-35% FAT, GI 60-65, per 24-h) were consumed 4h:10m apart, with all meals delayed by 4h:10m in LE vs. EE. After each experimental condition, the endogenous circadian rhythmicity in glucose tolerance was assessed using 36-h Constant Routine (CR) protocols (i.e., continuous wakefulness, semi-recumbent posture, dim light, and identical isocaloric test meals every 6-h) to isolate the endogenous circadian influences. Glucose tolerance was quantified from 3-h postprandial incremental area under the curve (iAUC) of serum glucose concentrations for the last five of six test meals during CR. Individual endogenous circadian phase was derived from core body temperature during the CR. The circadian rhythm phase and amplitude of glucose tolerance was derived from cosinor analysis of normalized (across circadian cycle) 3-h glucose iAUC using mixed model analyses of variance (R 4.5.0 nlme package).

Results: The peak-to-trough amplitudes in normalized 3-h postprandial glucose iAUC were 36% and 39% of the mean across circadian cycle ($P<0.0001$) after EE and LE, respectively. Both EE and LE showed highest and lowest glucose tolerance in the biological morning and evening, respectively, with a phase delay of ~70 degrees (~4h:40m) in LE vs EE.

Conclusions: Our findings demonstrated in people with overweight and obesity that glucose tolerance expressed a robust endogenous circadian rhythm with high and low tolerance in the biological morning and evening, respectively, and that could be rapidly synchronized to eating schedules, alluding to a decoupling of central and peripheral circadian rhythms in substrate metabolism.

Light at Night Exacerbates Depression Risk via Circadian Disruption and Hippocampal Per1 Dysregulation: Translational Evidence from a Large-scale Prospective Cohort and Animal Study

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Introduction: In the modern era of pervasive artificial lighting, approximately 80% of the global population is exposed to light at night (LAN), posing significant public health challenges. While cross-sectional evidence suggests a link between LAN and mood disorders, the causal effects and mechanisms remain poorly understood. This study integrates human cohort data with controlled animal experiments to elucidate the behavioral and neurobiological pathways linking LAN exposure to depression pathogenesis.

Materials and methods: We analyzed 75,636 UK Biobank participants with objectively measured LAN exposure via wearable devices. Incident depression cases were ascertained through linked electronic health records (hospitalizations, primary care visits) and mortality registries. Cox proportional hazard models, adjusted for potential confounders, were used to assess associations. To further confirm the causal effects of LAN on depression onset, ICR mice (n=50/group, 10-week-old) were randomized to:

control group (12h 200 lux light/12h dark) or LAN group (12h 200 lux light/12h 5 lux dim light). Spontaneous locomotor activity was monitored using Clocklab. Depression-like behaviors were evaluated via sucrose preference test (SPT) and forced swim test (FST). Brain serotonin (5-hydroxytryptamine, 5-HT) and brain-derived neurotrophic factor (BDNF) levels were measured by ELISA. Hippocampal circadian genes were analyzed through multi-timepoint transcriptome sequencing, with rhythmicity evaluated using CircadiOmics. Key genes were further validated by Real-Time Quantitative Polymerase Chain Reaction (RT-qPCR).

Results: Compared to participants with low LAN exposure (median: ~ 1 lux), those with higher exposure exhibited significantly higher adjusted hazards for depression (HR=1.24, 95% CI: 1.12-1.35), demonstrating a dose-response relationship (P for trend < 0.01). Animal experiments demonstrated that, compared to the control group, LAN group exhibited significantly increased depression-like behaviors, such as decreased sugar preference and increased immobility time (all P < 0.05). In addition, locomotor rhythms monitoring revealed that LAN exposure reduced wheel-running activity, nocturnal activity levels, and rhythm amplitude (all P < 0.05). Correlation analysis revealed that disruptions in rest-activity rhythms were significantly associated with these depressive-like behaviors (all P < 0.05). ELISA analysis demonstrated decreased levels of both 5-HT and BDNF in the LAN group (all P < 0.05), with 5-HT levels showing positive correlations with activity amplitude (P = 0.04) and nighttime activity (P = 0.01). Moreover, transcriptome and RT-qPCR analysis further identified LAN exposure disrupted the expressions of hippocampal circadian genes particularly *Period 1 (Per1)* in mice.

Conclusions: Integrating epidemiological and experimental evidence, we propose that LAN exposure may contribute to depression risk through circadian disruption, with hippocampal *Per1* alterations and monoaminergic dysfunction emerging as plausible mechanistic links. This translational framework warrants further validation in targeted human interventions.

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Light Exposure Patterns and Human Health: Insights from Large-Scale Personal Light Tracking

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Introduction: Light is the primary synchronizer for the human circadian system, influencing a vast array of physiological and behavioral processes. Deviations from natural light exposure patterns have been implicated in adverse health outcomes, but large-scale objective assessments have been limited.

Materials and methods: We analyzed data from over 85,000 participants in the UK Biobank, utilizing wrist-worn light sensors to objectively measure personal light exposure over a 7-day period. Health outcomes, including mortality, type 2 diabetes incidence, and psychiatric disorders, were assessed through linked health records and standardized questionnaires.

Results: Our analyses revealed that individuals who experienced brighter nights and darker days had a significantly higher risk of all-cause mortality, particularly from cardiometabolic causes. Furthermore, increased nighttime light exposure was associated with a higher incidence of type 2 diabetes, even after adjusting for genetic risk factors. Additionally, brighter nights and dimmer days were correlated with elevated risks of psychiatric disorders, including depression, anxiety, and PTSD.

Conclusions: Our findings demonstrate the critical role of natural light exposure patterns in supporting optimal health. For longevity, cardiometabolic, and mental health, maximizing daytime light and minimizing nighttime light are both potentially beneficial interventions. These results strongly suggest that public health strategies should consider light exposure as an easily modifiable environmental risk factor to improve health and wellbeing.

Low-intensity artificial light at night disrupts sleep and physiological functions in controlled laboratory conditions

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Introduction: Artificial light at night (ALAN) is becoming increasingly prevalent in modern society, disrupting natural light/dark cycles and potentially impacting human health. However, most studies on this topic lack controlled conditions, making it difficult to isolate the effects from confounding factors (noise, air pollution, population density, diet and lifestyle factors, etc.). This study aimed to investigate the effects of low-intensity ALAN on sleep and various physiological functions under controlled laboratory conditions.

Materials and methods: Twenty healthy young male participants (24.2 ± 3.3 years; $BMI=22.2 \pm 2.2$ kg/m²) underwent a 5-day and 4-night protocol in temporal isolation (in a sound-attenuated, temperature-controlled individual room, free from time cues). During their four 8-hour nightly sleep episodes at their habitual sleep times, participants were randomly assigned to one of four light conditions: 0 lux, 3 lux, 8 lux, or 20 lux (5000K broadband white light generated by a 10-channel LED system, Ledmotive Spectra Tune 10). During the day, participants were exposed to a light intensity of approximately 90 lux at the eye level (3000 K, Osram 64701). Endocrine markers (melatonin, cortisol, alpha-amylase), electrophysiological measures (EEG, ECG, pupillary light reflex), skin temperature and glycemia were measured continuously or with a sampling rate of more than one sample per hour throughout the study.

Results: The results revealed that nocturnal exposure to 20 lux significantly decreased total sleep time, sleep efficiency, increased wake after sleep onset (WASO), elevated proximal body temperature and glucose levels, and increased heart rate (HR). Interestingly, overnight urinary 6-sulfatoxy-melatonin (aMT6s) and salivary cortisol levels at waketime were unaffected across all light conditions. Additionally, overnight light exposure reduced photoreceptor sensitivity to light upon awakening, but did not significantly impair cognitive performance at waketime.

Conclusions: These findings demonstrate that even low levels of ALAN, as commonly encountered in real-life environments, can acutely disrupt human sleep and several physiological functions within only 1–4 days of exposure. It remains unclear whether these effects persist under chronic exposure or lead to long-term health impacts, however, the results warrant consideration, as they highlight the potential for even low-intensity ALAN, commonly encountered in real-life settings, to affect human health.

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Out of Sync: How late chronotypes and napping drive sleep loss in Spanish schoolchildren

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Introduction: Sufficient sleep is critical for healthy cognitive, emotional, and physical development in children and adolescents. However, in Spain, the pronounced misalignment between solar and social time, exacerbated by early school start times, contributes to chronic sleep deprivation, especially among youth. This is particularly problematic in younger populations whose circadian rhythms are naturally delayed, making it difficult to align sleep-wake schedules with social demands. The aim of this study was to identify predictors of weekly sleep loss in Spanish children and adolescents and to explore the relationship between chronotype and napping behavior.

Materials and methods: A cross-sectional analysis was conducted in a sample of 142 Spanish children and adolescents aged 6 to 16 years (median age [Q1–Q3] = 12 [11–13] years); 87 (61.3%) were female. Sleep variables were assessed using the Munich Chronotype Questionnaire, adapted for both schooldays and free days, including nap periods. Chronotype was calculated using midsleep on free days corrected for sleep debt (MSFsc), and social jet lag (SJL) was derived from the difference between midsleep on free and school days. Weekly sleep loss (weekSleepLoss) was calculated by comparing

total sleep duration on schooldays versus free days (including naps). Group comparisons by sex and napping behavior were conducted using the Mann-Whitney U test. General Linear Models (GLM) were used to identify predictors of sleep loss. Statistical analyses were conducted using SPSS v29, with significance set at $p < .05$.

Results: Children who reported napping had significantly later chronotypes (MSFsc median [Q1–Q3]: non-nappers 4.21 [3.57–5.12] vs. nappers 5.39 [4.59–6.42]; $p < .001$), greater social jet lag (1.71 [1.00–2.71] vs. 2.85 [2.03–4.83]; $p < .001$), and more weekly sleep loss (1.43 [0.60–5.93] vs. 3.93 [1.90–6.67]; $p < .001$). No significant differences in age or sex were found between groups.

General Linear Model analysis showed that the full model accounted for 47.7% of the variance in weekly sleep loss (adjusted $R^2 = 0.442$; $p < .001$). Significant predictors included napping behavior ($p < .001$; $\eta^2 = .190$), greater social jet lag ($p < .001$; $\eta^2 = .183$), later chronotype (MSFsc; $p < .001$; $\eta^2 = .139$), and shorter schoolday sleep duration ($p < .001$; $\eta^2 = .107$). Neither age, sex, nor the interaction between sex and napping significantly predicted sleep loss.

Conclusions: Later chronotypes in Spanish schoolchildren are associated with greater weekly sleep loss, increased social jet lag, and more frequent napping. Napping behavior emerged as the strongest individual predictor of sleep loss and may represent not only a compensatory strategy but also a behavior that reinforces delayed sleep timing, exacerbating circadian misalignment. These findings underscore the urgent need to reconsider early school start times in Spain and highlight the complex interplay between biological rhythms and compensatory sleep behaviors in youth.

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Project Sunrise Research Flights: Lessons for sleep and alertness management in commercial aviation

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Introduction: As international airlines continue to introduce flights of longer duration, there is a need to evaluate the impact of extended duty on crew sleep-wake behaviour and alertness. Under 'Project Sunrise', Qantas is planning to conduct the longest global commercial passenger flights. In preparation, aircraft delivery flights provided the unique opportunity to conduct dedicated research flights designed for comprehensive scientific monitoring of sleep, circadian timing and alertness in pilots.

Materials and methods: Eight research flights mimicking the proposed flight times of future extended duty flights were conducted during 2019 and 2023, providing data from 33 pilots (24 male, aged 44.0 $\pm$ 9.3 years). Direct flights occurred between Melbourne or Sydney in Australia, and Seattle ($n=3$), New York ($n=2$), Dresden ($n=2$), and London ($n=1$). Mean flight duration was 19.84 $\pm$ 1.59 h (range 17.0 – 22.67 h). Pilots were monitored for ~20 days throughout their entire flight pattern, including 10 days pre-pattern, during layover and 6 days post-pattern. Sleep was monitored using sleep diaries, wrist actigraphy, and Dreem ambulatory EEG headbands. Light exposure was measured continuously throughout the flight pattern using a lapel-based light sensor. Circadian timing at home prior to the pattern, during layover and during research flights was measured using the rhythm of urinary 6-sulphatoxymelatonin (aMT6s). During flight, pilots completed alertness assessments every 2 hours when awake using the Karolinska Sleepiness Scale, Samn-Perelli Fatigue Scale and the Psychomotor Vigilance Task (PVT).

Results: Pilots spent an average of 5.36 $\pm$ 1.36 h of in-flight time attempting sleep (range 3.00 – 8.17 h) and obtained 4.36 $\pm$ 1.31 h sleep during flight (range 2.58 – 7.40 h). Dreem EEG recordings indicated in-flight sleep was recuperative, based on a similar slope in the dissipation of slow wave activity with each NREM sleep cycle, as observed for sleep episodes at home.

While the direction of circadian phase shift for each pilot was associated with the direction of travel (westward travel = delay, eastward = advance), considerable inter-individual variation in the degree of phase shift was revealed, resulting in >6 h variation in aMT6s acrophase during flight. The magnitude of circadian phase shift was related to individual pilot's sleep-wake behaviour and associated light exposure patterns in layover destination.

Alertness during flight was influenced by individual circadian timing, with higher subjective sleepiness and number of PVT lapses evident during the biological night (aMT6s acrophase $\pm$ 3 h, $p < 0.05$) compared to assessments outside of the biological night. Circadian timing and duration of wakefulness were both significant determinants of subjective fatigue and sleepiness.

Conclusions: This program of work represents the most comprehensive assessment of pilot sleep, circadian timing and alertness during extended flight duty in commercial aviation. Individual variation in sleep-wake and circadian outcomes provides insights into sleep and circadian-related behaviours influencing alertness during flight. These findings are informing ongoing trials of evidence-based recommendations to optimise sleep and alertness during extended flight duty, including trials of specific in-flight rest break allocations.

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Relation between mood scales and melatonin levels of children and adolescents with Bipolar Disorder in a Tropical country: a descriptive analysis

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Introduction: Bipolar disorder (BD) is chronic psychiatric condition characterized by recurrent mood episodes, including depression, hypomania, and mania. Beyond affective symptoms, BD frequently involves persistent disruptions in sleep and circadian rhythms, even during euthymic states. These disturbances are considered both symptomatic and potentially pathogenic, contributing to disease onset, progression, and relapse risk. Melatonin plays central role in maintaining sleep-wake cycles. Its secretion is often altered in BD, with studies reporting phase shifts, amplitude reductions, and blunted rhythmicity, particularly in youth populations.

Such findings support hypothesis that circadian dysregulation is core pathophysiological feature of BD, especially in early-onset cases. Robillard et al. (2013) demonstrated significant differences in melatonin rhythms between adolescents with unipolar and bipolar mood disorders, with the bipolar group showing delayed and attenuated secretion profiles. However, environmental factors such seasonal variability in light exposure and temperature may confound these results in temperate regions. This study aims to assess melatonin secretion patterns through urinary 6-sulfatoxymelatonin (6-SM) levels—in children and adolescents diagnosed with BD, across three distinct clinical time points. Mania symptom severity will be evaluated concurrently using standardized clinical scales. The study is conducted in Southern Hemisphere population, where seasonal light and temperature variation is less pronounced, allowing for better environmental control and greater accuracy in evaluating circadian alterations in pediatric BD.

Materials and methods: We prospectively evaluated four individuals between 8 and 18 years, 1 female 3 male, diagnosis of BD according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition. All had regular follow-up at the Psychiatric Centre of University of São Paulo and were included in protocol after signing IRB-approved informed consent. We scheduled monthly meetings (from June to October) to evaluate sleep by means of 6-sulfatoxymelatonin (6-SM) and mania symptom severity by means of concurrent Young Mania Rating Scale (YMRS). To analyze the 6-SM values, we collected 24h urine sample, divided into 3 times: morning (7 am-1 pm, excluding the first void), afternoon (1 pm-7 pm), and night (7 pm-7 am, including first morning void). This was repeated in all meetings.

Results: First patient completed all four assessments. Morning 6-SM levels ranged from 34-81, showing a regressive trend. Afternoon values were between 4.8 and 11.9, and nighttime levels between 25 and 34. YMRS scores indicated no manic symptoms.

Second patient completed four sessions. Morning 6-SM ranged from 6-69; afternoon from 1.3-8.6; night from 2-14. In the final evaluation, higher night values and a YMRS score of 8 suggested possible rhythm inversion.

Third patient had two sessions. Morning 6-SM ranged from 7.3-10.1; afternoon from 3.9-33.1. No clinical changes were observed. Fourth patient had three assessments. Morning 6-SM ranged from 7 to 74; afternoon from 2.2-7.9; night from 5-21.

Conclusions: Small-sample descriptive study identified distinct melatonin secretion patterns among pediatric BD patients living in tropical region. Although potential association between altered circadian profiles and manic symptoms was observed in one case, no consistent pattern emerged. Short evaluation period and limited seasonal variation in Southern Hemisphere may have influenced results. Larger longitudinal studies are needed to clarify circadian dynamics in youth BD.

Reward processing and eveningness in adolescents: A case-control study with EEG investigation

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Introduction: Adolescence is often associated with increased evening tendency and the risk of developing mental health problems. Previous research has suggested a close interplay between evening chronotype, which is characterized by an inclination for later bedtime and wake time, and depression, but there has been limited research to investigate the potential mechanism underlying their association. Given that altered reward processing is a key feature of depression, this case-control study examined whether adolescents with an evening preference also exhibit deficits in reward processing.

Materials and methods: Thirty adolescents aged 12–20 (63.33% female) with an evening chronotype (Morningness-Eveningness Questionnaire (MEQ) ≤ 41) and 30 non-eveningness healthy controls (MEQ ≥ 42) with matched age and sex were recruited. Participants with a current clinical diagnosis of sleep or psychiatric disorders (except for delayed sleep phase disorder in the eveningness group) or a medical condition that could significantly affect sleep quality were excluded. All participants underwent a clinical interview, followed by completing a battery of self-report questionnaires including Insomnia Severity Index (ISI) for insomnia severity, Beck Depression Inventory-II (BDI-II) for self-reported depressive symptoms, and the subscale of reward responsiveness in Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales for the measure of reward responsiveness. The Children's Depression Rating Scale-Revised (CDRS) was used for measuring clinician-rated depressive symptoms. Participants wore an actigraphy for eight consecutive days and completed a Door Guessing Task as a measure of reward sensitivity using an electroencephalogram.

Results: The eveningness group had higher self-reported and clinician-rated depressive symptoms (both P s < 0.05) but comparable insomnia severity. In terms of sleep measures, the eveningness group showed significantly longer sleep onset latency, later bedtime, rise time, and sleep midpoint as measured by sleep diary. Actigraphy results showed significantly later sleep onset, sleep offset, and sleep midpoint, as well as shorter total sleep time in the eveningness group compared to healthy controls (all P s < 0.05). Compared to healthy controls, the eveningness group showed significantly lower signal on reward positivity (RewP) overall without significant difference between conditions ($F(1, 51) = 4.35$, $P = .042$), indicating blunted reward processing. On the behavioral level, the eveningness group also showed stronger alterations (switched choices more often) in the trial-by-trial behavioral adjustment analyses ($t(7105.0) = 2.57$, $p = .010$). However, there was no significant interaction between group, cue, and choice adjustments. Healthy participants showed significantly different reaction times (gain $>$ neutral, $t(7065.2) = -2.21$, $P = .027$), this effect was not found in eveningness

participants. Reward responsiveness, as measured by BIS/BAS, was not significantly different between groups.

Conclusions: RewP may reflect the neural deficits in reward processing and has been suggested as a potential early biomarker for depression. The findings on blunted response to reward in adolescents with evening preference may be indicative of the risk for depression in eveningness. Longitudinal studies are necessary to establish causality and explore potential interventions targeting circadian factors in the prevention of youth depression.

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Safety and Efficacy of Acupuncture in Patients With Circadian Rhythm Sleep Disorder: A Randomized Clinical Trial

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Introduction: Circadian Rhythm Sleep-Wake Disorders (CRSWDs) arise from misalignment between endogenous circadian rhythms and external environmental cycles, causing chronic insomnia and excessive sleepiness. Affecting 0.2-10% of the population, growing evidence indicates that circadian misalignment not only disrupts sleep but also adversely affects multiple physiological systems, increasing susceptibility to cardiovascular diseases, metabolic disorders, cognitive impairments, and immune dysfunction. While planned sleep schedules, timed light exposure, and melatonin therapy show efficacy, alternative treatments remain underexplored. Preliminary studies suggest that acupuncture may improve sleep quality and reduce anxiety in insomnia and peri-menopausal insomnia. Acupuncture has demonstrated potential in improving sleep and modulating circadian pathways, possibly through melatonin-related mechanisms. However, robust clinical evidence is lacking. Considering the efficacy of acupuncture in many areas and the lack of studies in CRSWD, we conducted a randomized, placebo-controlled trial to assess acupuncture's short-term efficacy in CRSWD using objective and subjective measures, addressing a critical gap in non-pharmacological interventions for circadian disruption.

Materials and methods: Design: A randomized, participant-blind, placebo-controlled trial consisted of the acupuncture group ($n = 36$) and placebo-acupuncture group ($n = 36$). Setting: a tertiary hospital of integrated Chinese and Western medicine. Participants: 72 participants with CRSWD based on the International Classification of Sleep Disorders, Third Edition. Interventions: A 10-session intervention of acupuncture at Shenshu (BL 23) and Xinshu (BL 15) or Streitberger needles at the same acupoints was performed for over 3 weeks. Measurements: The Pittsburgh Sleep Quality Index (PSQI) and insomnia severity index (ISI) were evaluated at baseline and post-treatment as the primary outcome measures. Actigraphy recordings were evaluated at baseline and post-treatment as the secondary outcome measures.

Results: After the treatments, the decrease from baseline in PSQI score was 8.97 points in the acupuncture group and 1.28 points in the placebo-acupuncture group. The change from baseline in ISI score was 7.91 points in the acupuncture group and 2.02 points in the placebo-acupuncture group. Actigraphy results showed that the actual sleep time (AST), sleep efficiency (SE) and Inter daily stability (IS) increased significantly ($P < 0.05$); the sleep onset latency (SOL), fragmentation index (FI) and Intraday variability (IV) was significantly decreased ($P < 0.05$); peak time (Cosinor Peak, time activity, CPT) significantly moved forward ($P < 0.01$).

Conclusions: Acupuncture can contribute to a clinically relevant improvement in the short-term treatment of CRSWD. We suggest that acupuncture represents a safe and useful non-pharmacologic intervention option for CRSWD.

Shift Work-Induced Changes in Autonomic Nervous System: An Observational Study Using HRV Analysis

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Introduction: Sleep is essential for the restoration and revitalization of both the body and mind. However, individuals frequently neglect this vital and natural process because of shift work and lifestyle changes. Altering sleep patterns from night to day disrupts biological rhythms, leading to a decline in both mental and physical health. The functioning of the autonomic nervous system is crucial for physiological processes. This study aimed to examine the impact of disruptions in biological rhythms caused by shift work on heart rate variability, a parameter used to assess autonomic nervous system functioning.

Materials and methods: Participants were categorized into two groups: Group A, consisting of day workers who engage in work activities exclusively during daytime hours, and Group B, comprising shift workers with irregular schedules, including nocturnal shifts. Heart rate variability (HRV) tests were employed to evaluate the impact of shift work on the autonomic nervous system. To compare demographic variables and HRV domains between the two groups, a chi-square test and Student's t-test were conducted.

Results: Each group comprised 165 participants, predominantly aged 18-30 years. Shift work significantly affected HRV Domain indices; however, no significant differences were observed in Mean RR, Mean HR, RMSSD, p NN50, TINN, LF/HF ratio, or stress index value.

Conclusions: Shift employment influences the functioning of the autonomic nervous system, resulting in increased sympathetic modulation of the heart and increased stress on cardiovascular health.

Shift work sleep disorder - The SHIFT-SLEEP programme of work

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Introduction: Prolonged sleep-wake difficulties due to shift work, lasting for more than three months, may meet criteria for shift work sleep disorder (SWD) and require intervention, especially if they engender significant functional impairment. SWD is common but there is unmet medical need, with a lack of proven interventions or guidelines.

Our aim is to develop and test a usable, acceptable, and cost-effective intervention to reduce the impact of SWD in shift workers in the UK National Health Service (NHS) through five work packages (WP) and an integrated research advisory group (RAG) of shift workers.

Materials and methods: WP1: A systematic review of qualitative studies on shift workers' experiences of sleep disturbance and its impacts and an overview of reviews on individually-directed non-pharmacological interventions to improve sleep or reduce sleepiness in shift workers.

WP2: A survey with NHS staff to determine prevalence and burden of SWD and a survey with NHS managers to understand current knowledge, training and implementation obstacles.

WP3: Examining existing large datasets (e.g. UK Biobank) to identify risk factors for sleep problems in UK shift workers and to characterise its burden.

WP4: Development of a complex intervention for SWD through a triangulation of evidence from the

above WPs.

WP5: Testing the above intervention in a large-scale randomised controlled trial (RCT).

Results: RAG: Ten shift workers contributed to the development of all WPs through online meetings, offline tasks and by sharing their shift working experiences.

WP1: 28 studies (1519 participants) were included in the qualitative review. Three analytical themes were generated: inevitability of fatigue and tiredness, balancing sleep needs with competing responsibilities, obstacles to engaging in healthy behaviours. 28 systematic reviews (69 RCTs, 4,947 participants) were included in the review of reviews. High-quality reviews suggested inconclusive evidence; lower quality reviews indicated light therapy, napping, physical activity, dietary supplements, mobile health apps and mindfulness may be effective in improving sleep quality and subjective sleepiness.

WP2: Of the 443 NHS staff who completed the survey, 71% (n=315) met the probable SWD criteria. Twenty-one managers participated in the survey of managerial experience. The majority (n=15, 71%) reported lack of training/information on impact of shift work.

WP3: Of the 285,175 participants in the UK Biobank who were employed, 48,975 (17.2%) were shift workers. Shift work was associated with higher odds of sleep disorders compared to non-shift work, with greatest odds observed among those always working night shifts (OR:1.21, 95%CI:1.16-1.27). The association was significantly modified by age ($p < 0.0001$), ethnicity ($p = 0.0005$) and smoking status ($p = 0.04$).

WP4: A multi-component complex behavioural intervention for SWD has been developed (Oxford Behavioural Intervention for Shiftwork (Ox BIS)) and is being tested in a feasibility study with 30 shift workers with SWD.

WP5: The intervention and study procedures will be refined based on the feasibility study findings. A RCT with 600 participants is planned to test the cost-effectiveness of the intervention in 2026.

Conclusions: Through a systematic, interdisciplinary programme of research, we aim to address the problem of SWD in NHS shift workers.

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Sleep regularity is related to variance in sleep stage composition

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Introduction: Irregular sleep-wake patterns are linked to numerous adverse health and well-being outcomes, but the underlying mechanisms remain largely unknown. One potential mechanism is changes in sleep stage composition, since irregular sleep patterns entail sleeping for variable durations, and at variable circadian phases and levels of sleep homeostatic pressure. However, this association has yet to be studied.

Materials and methods: We investigated the relationship between sleep regularity and sleep stage composition (light, deep, REM sleep) measured using Z-Machine Insight+ home EEG devices in 97 healthy young adult university students in Victoria, Australia (80.41% Female, mean±SD age 20.55±1.65 years) across a total of 1101 nights (11.35±3.46 nights per participant). Sleep regularity was measured using the Sleep Regularity Index (SRI). At the daily level, we measured sleep duration, variations in sleep onset and offset times, time awake before each sleep episode, and the hourly stage transition rates. Partial correlations were used to assess the association between sleep regularity and sleep stage composition, while controlling for mean sleep duration. Piecewise linear mixed-effects models were used to examine sleep stage composition using daily-level predictors.

Results: Lower SRI was associated with greater standard deviation in both absolute amounts (all $p < .001$, $r_{\text{partial}} = -.53$ to $-.45$) and percentages (all $p < .05$, $r_{\text{partial}} = -.53$ to $-.28$) of light, deep, and REM sleep, lower mean percentage REM sleep ($p = .042$, $r_{\text{partial}} = .24$), and more frequent wake-sleep transitions ($p = .008$, $r_{\text{partial}} = .30$). At the daily level, longer sleep duration was associated with greater absolute amounts of light, deep, and REM sleep, greater percentages of light and REM sleep, but a lower percentage of deep sleep (all $p < .05$). Shorter time awake and later sleep onset were associated with

lower amount and percentage of deep sleep (all $p < .001$). Earlier sleep offset was associated with lower percentage of light sleep, lower amount and percentage of REM sleep (all $p < .05$), and more frequent wake-sleep transitions and less frequent transitions to and from REM sleep (all $p < .001$).

Conclusions: Less regular sleep-wake patterns were associated with greater variance in sleep stage composition, which may partially explain the link between irregular sleep-wake patterns and negative health outcomes. Analysis at the daily level revealed that changes in sleep stage composition are primarily explained by changes in sleep duration, rather than changes in sleep timing. Maintaining consistent sleep duration is likely a key target for stabilizing sleep stage composition in irregular sleepers.

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SleepSync: Effectiveness of a personalised, implementation-ready tool for sleep and circadian health management in shift workers

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Introduction: Two-thirds of shift workers experience poor and inadequate sleep. This chronic disruption of sleep and circadian rhythms results in adverse consequences for health, safety and productivity. Current management strategies are mostly one-size-fits-all, not accounting for differences in human biology, work environments, individual requirements, and the need for interventions that support an ageing workforce. SleepSync is a patented smartphone application that uses biomathematical modelling (the Model of Arousal Dynamics) to deliver tailored strategies for sleep and alertness, with educational toolkits and visual feedback on recovery. It has been previously co-designed and successfully piloted in healthcare, defence and other shift work industries.

This open-label trial aimed to a) evaluate effectiveness of SleepSync in improving sleep and performance in shift working nurses, and older nurses; b) identify implementation pathways for personalised sleep and circadian health management.

Materials and methods: Thirty-two shift working hospital nurses (41.4 ± 7.1 y; 27 f; $n=14$ aged ≥ 50 y) used the SleepSync app for six weeks, including an initial two weeks of baseline where the app provided no recommendations. Sleep and mental health outcomes were assessed at baseline and post-intervention using the Insomnia Severity Index (ISI), the Sleep Hygiene Index (SHI), and the Depression, Anxiety and Stress Scale (DASS-21). Objective cognitive performance was evaluated via the 3-minute Psychomotor Vigilance Task (PVT) completed at the start and end of shift. Participant feedback on app acceptability and implementation of the app was also collected.

Results: In the overall sample, 71% of users saw remission from insomnia symptoms post app use. Mean ISI scores (Baseline = 16.4 ± 5.3 , Post app use = 10.2 ± 4.0 ; $p < .001$), SHI scores (Baseline = 27.6 ± 8.3 ; Post App Use = 20.5 ± 5.1 ; $p < .001$) and depression scores (Baseline = 5.1 ± 1.2 ; Post app use = 3.0 ± 1.8 ; $p < .01$) improved post intervention. After controlling for shift type, such as morning, evening or night, start or end of shift and age, there were significant improvements in median reaction time post app use (t -value = 4.2; $p < .01$). Preliminary analyses showed that at baseline, nurses ≥ 50 years had shorter sleep durations than those < 50 years (6.2 vs 7.4 hours, $p < .001$), but demonstrated greater reductions in ISI post-intervention (10.3 v/s 9.1 , $p = .03$).

Over 90% of users reported the app was easy to use, two-thirds of users reported the app satisfactory, 65.6% suggested they would recommend it to a friend. Integration with wearable technologies was identified as a key facilitator for long-term app use. Users noted that while they would readily use the app, it should be deployed via workforces to facilitate organisational level uptake and systemic implementation.

Conclusions: SleepSync demonstrates utility as a personalised, biomathematical model driven intervention that improves sleep, mental health and performance in shift workers, with potential to support an ageing workforce. Ongoing work is focused on a) integrating wearable technology to further personalise recommendations and reducing manual input, and b) embedding SleepSync into

organisational systems, such as healthcare and aviation as a sustainable pathway for sleep and circadian health management in shift work.

Sleep variability, eveningness and depression in adolescents: a case-control study

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Introduction: Adolescence is characterized by a circadian shift towards eveningness and changes in sleep pattern. This period is also often associated with an increased incidence of psychopathology, such as depression. Greater intraindividual sleep variability has been linked to both eveningness and depression. However, limited research has explored the interplay between eveningness and depression in relation to sleep variability in youth. The present case-control study aimed to investigate sleep variability in adolescents with eveningness and/or depression, as well as to explore the correlates of sleep variability.

Materials and methods: Four groups of adolescents aged 12-20 years were recruited: eveningness and depression group (ED), eveningness only group (E), depression only group (D), and healthy controls. Eveningness was defined as a score of ≤ 41 on the Morningness-Eveningness Questionnaire. Depression groups met DSM-5 criteria for major depressive disorder or dysthymia. Participants completed a 7-day sleep diary with actigraphy monitoring and self-reported questionnaires to assess circadian preference, insomnia symptoms, depressive symptoms, and bedtime procrastination. Subjective and objective sleep variabilities were calculated using root mean squared successive differences from sleep diary and actigraphy data, respectively.

Results: A total of 95 participants (mean age: 17.82 s.d. 1.59 years, 76% female) were included in the analysis (ED: n = 23, E: n = 26, D: n = 25, C: n = 21). Both ED and D groups showed significantly more severe depressive symptoms compared to E and C groups (all ps < .001). ED group showed greater variability in time in bed (vTIB) compared to D group (sleep diary: p = .033; actigraphy: p = .040) and controls (sleep diary: p = .025; actigraphy: p = .013). ED group also showed greater variability in sleep offset (vSOFF) and rise time (vRT) as measured by sleep diary compared to D group (SOFF: p = .009; RT: p = .004) and controls (SOFF: p = .037; RT: p = .012). ED group showed greater variability in sleep offset as measured by actigraphy compared to E group (p = .034), D group (p = .005), and controls (p < .001). E group showed greater variability in time in bed as measured by actigraphy (p = .026) compared to controls. Regression analyses showed that stronger eveningness preference was independently associated with greater sleep variability in TIB, TST, and RT as measured by sleep diary, and TIB as measured by actigraphy (all ps < .05). No other associations were found between sleep variability parameters and insomnia symptoms, depressive symptoms, or bedtime procrastination.

Conclusions: The present study suggested a synergetic effect of eveningness and depression on increasing sleep variability in adolescents. Evening preference was independently associated with greater sleep variability. Future research may consider adopting a longitudinal design to further elucidate the relationships between sleep variability, chronotype preference and depression and to explore the effects of circadian-focused interventions on reducing sleep variability and depressive symptoms in youth.

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The Association between Sleep Quality and Irregular Meal Timing among Malaysian Healthcare Workers in Rotating Shifts

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Introduction: Shift work often disrupts the natural circadian rhythm, significantly impacting both nutritional habits and sleep patterns. Among healthcare professionals, poor sleep quality may be exacerbated by irregular eating schedules, particularly in relation to chrononutrition behaviors. Despite growing global interest, studies investigating the interplay between sleep quality and chrononutrition among Malaysian shift workers remain limited. This study aimed to assess the association between chrononutrition behaviors and sleep quality among Malaysian healthcare shift workers.

Materials and methods:

A cross-sectional study was conducted involving 368 healthcare shift workers from three hospitals in Klang Valley. Participants aged 19 to 60 years working on a 3-shift rotation were selected via simple random sampling. Those with diagnosed sleep disorders, mental illness, or chronic diseases were excluded. Chrononutrition behaviors and sleep quality were assessed using the validated Chrononutrition Profile Questionnaire (CPQ) and the Pittsburgh Sleep Quality Index (PSQI).

Results: Most participants exhibited favorable behaviors in breakfast skipping, night eating, and eating window timing, while moderate behaviors were seen in evening eating, largest meal timing, and evening latency. However, 51.9% of participants demonstrated poor sleep quality. Significant predictors of sleep quality included age, marital status, and breakfast skipping behavior ($p < 0.05$). Logistic regression revealed that younger participants (AOR = 3.51; 95% CI: 1.5–8.3), those not married (OR = 1.82; 95% CI: 1.1–3.0), and those with poor breakfast skipping habits (AOR = 2.12; 95% CI: 1.3–3.5) had higher odds of poor sleep quality.

Conclusions: Findings underscore the need to prioritize sleep health in relation to eating patterns among healthcare shift workers. Targeted interventions that improve chrononutrition behaviors could be instrumental in enhancing sleep quality and overall well-being in this vulnerable population.

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The association between timings of food intake and the risk of obstructive sleep apnoea: findings from the 2017-2020 NHANES Study

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Introduction: Obesity is a key risk factor contributing to obstructive sleep apnoea (OSA) and its severity. Late or mistimed eating potentiates the development of obesity and cardiometabolic disorders, with circadian misalignment as the underlying mechanism compromising metabolism. The severity of OSA and poor sleep quality may also be associated with late as compared to earlier meal timings. Given the multidirectional association between obesity, circadian misalignment and OSA risk, this cross-sectional analysis aims to investigate if mistimed eating patterns (such as extended daily eating windows and later intake timings) are associated with OSA risk in a large population cohort.

Materials and methods: Data from adult participants (not pregnant/breastfeeding) in the National Health and Nutrition Examination Survey (NHANES) 2017-2020 pre-pandemic cycle were analysed. OSA risk was computed as a composite score ranging from 0 to 7, with reference to the presence of risk factors identified in the STOP-BANG scoring system (frequent snoring, excessive daytime sleepiness, occurrence of breathing pauses during sleep, high blood pressure, body mass index (BMI) $>35\text{kg/m}^2$, age >50 years, and male gender). A score threshold of 3 was used as a predictor of OSA.

Chrononutrition variables – eating window, the first and last timing of energy intake, timing of the highest energy intake, eating midpoint and caloric midpoint, were obtained from 24-hour dietary recalls, and classified into tertiles. Weighted sample logistic regression was conducted to assess the associations between OSA risk and the aforementioned chrononutrition variables, with adjustment for demographic (race/ethnicity, education level, marital status and family income) and lifestyle (physical activity, shift work and sleep duration) variables. Sensitivity analysis with daily energy intake as a potential mediator was performed via causal mediation analysis.

Results: Among the 6,265 eligible participants, 44.7% were identified to be at risk of OSA. Compared to those in the first tertile (eating window (mean/SD): 8.13 ± 2.08 h), participants with a longer eating window (third tertile) had a higher odds of OSA risk (13.90 ± 1.59 h: OR=1.44, 95%CI(1.15, 1.80), $p=0.003$). Participants with a later last timing of intake (third tertile; $22:38 \pm 1:32$) had a higher odds of OSA risk (OR= 1.21, 95%CI(1.01, 1.45), $p=0.040$) as compared to the first tertile ($18:22 \pm 1:10$). Participants with a later caloric midpoint (time point in which 50% of energy intake was met; $18:23 \pm 1:24$) also showed an increased odds of OSA (OR=1.23, 95%CI(1.01, 1.49), $p=0.042$), relative to an earlier timing of $12:32 \pm 1:15$. However, the effect of these variables on OSA risk were attributed to daily energy intake as a mediator. There were no associations between OSA risk and other timing of intake variables observed.

Conclusions: Individuals with an extended eating window and a later last timing of intake and caloric midpoint are at an increased risk of OSA, mediated by increased energy intake throughout the wider daily window. These findings present opportunities for trialling dietary interventions such as time-restricted eating concurrent with reducing the overall energy intake, in populations with obesity and sleep disorders, such as OSA.

The Cyclical Daytime Sleeper: A Rare Case of a Sighted Teenager with Non-24-Hour Sleep-Wake Disorder

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Introduction: Daytime fatigue in teenagers may be hand-waved as hours of screen time before bed and it can be difficult for families to accurately describe sleep habits. These factors often obscure an underlying sleep disorder. Here we report the rare case of a sighted teenage patient who presented with sleep disturbance and erratic bedtimes and was found to have non-24-hour sleep wake disorder (N24SWD).

Materials and methods: A 16-year-old male with a past medical history of ADHD and very chronic insomnia presented to the sleep clinic for evaluation of recurrent and inappropriate sleep times with residual hypersomnolence. The pediatrician evaluated the patient for profound difficulty waking up for school as well as trouble falling asleep at night. Initially, it was suspected to be insomnia due to poor sleep hygiene secondary to significant electronic usage prior to bedtime. When symptoms did not improve, the patient was started on various hypnotics including clonidine to help with sleep. A daytime stimulant was added and titrated for wakefulness. Various pharmaceutical regimens did not help with sleep symptoms, and the patient's hypersomnolence led to cyclical absenteeism from school and risk for expulsion.

On initial presentation to the sleep clinic, patient and family had notable difficulty describing his erratic sleep routine. Two weeks of sleep diaries were provided to help characterize the patient's sleep patterns. No suspicion for sleep disordered breathing, parasomnias nor restless leg syndrome were noted.

Results: Sleep diary showed a sleep pattern delaying consistently by 1-2 hours each day. Total sleep each night was 7-9 hours, with sleep onset latency of 30 minutes and no significant awakenings. This activity is classic for non-24 sleep-wake phase disorder. This patient was treated with a combination of timed Tasimelteon and bright light therapy along with chronotherapy for resynchronization of the intrinsic circadian rhythm. His sleep pattern normalized shortly after starting treatment and patient was able to resume normal academic and social activities.

Conclusions: N24SWD is commonly seen in blind individuals affecting up to 50% of that population. It is very rare in sighted individuals, and may be harder to discern when confounded with conditions like

ADHD or poor sleep hygiene. Having patients complete a sleep diary is a cost effective and low investment intervention that may elucidate their condition and ensure timely treatment. Treatment can be straightforward with medications such as tasimelteon, and have profound impacts on a teenager's quality of life.

The Impact of Different Feeding Patterns on Neonatal Sleep Patterns: A Multicenter Cross-Sectional Survey

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Introduction: Sleep is essential for neonatal brain development, synaptic plasticity, and cognitive outcomes. Recent studies suggest that breast milk may influence infant sleep, not only through its nutritional components but also via circadian variations in its composition. However, few studies have specifically investigated the impact of feeding patterns on neonatal sleep. This study aims to investigate the effects of different feeding patterns on neonatal sleep, thereby providing preliminary evidence for the role of breast milk as a potential circadian time cue.

Materials and methods: A multicenter cross-sectional study was conducted from October 2024 to March 2025 in seven tertiary hospitals in eastern China. Trained nurses surveyed neonates and their caregivers (mostly mothers) in neonatal units using a self-designed questionnaire covering demographics, sleep status, and sleep habits. The questionnaire was adapted from the BISQ and a Chinese infant sleep scale, revised based on clinical practice, and finalized through expert consensus.

Results: A total of 533 neonates were included, with 111 in the breastfeeding group, 75 in the formula-fed group, and 347 in the mixed-feeding group. Significant differences were observed among the three groups in maternal education level ($p < 0.05$) and several sleep-related variables. These included daytime sleep duration ($F = 3.49$, $p = 0.0311$), nighttime sleep duration ($F = 3.65$, $p = 0.0268$), frequency of nighttime awakenings ($\chi^2 = 8.2165$, $p = 0.0164$), and sleep position ($\chi^2 = 13.5811$, $p = 0.0011$). Formula-fed neonates had more frequent nighttime awakenings, while breastfed and mixed-fed neonates showed slightly longer nighttime sleep durations. A subgroup analysis was conducted within the mixed-feeding group based on feeding proportion, and a significant difference was found in the frequency of nighttime awakenings ($\chi^2 = 10.2344$, $p = 0.006$), suggesting that infants receiving a higher proportion of formula may be more prone to waking at night.

Conclusions: Feeding patterns were associated with differences in neonatal sleep characteristics. Although overall sleep duration generally exceeded the recommended 18 hours, breastfed neonates had total sleep durations closer to the guideline and fewer nighttime awakenings, suggesting that breastfeeding may be more beneficial for neonatal sleep. These patterns may be related to better maternal-infant circadian rhythm alignment. Differences in sleep posture may reflect institutional guidance, which may not fully align with WHO recommendations for supine positioning. The findings highlight the potential impact of feeding practices on neonatal sleep and underscore the importance of improving caregiver awareness of infant sleep.

The Impact of Oral Contraceptive Intake Timing on Women's Sleep Patterns

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Introduction: Sleep complaints are common concerns among women and can significantly impair overall well-being. Previous studies suggested a potential link between oral contraceptive use and insomnia symptoms, excessive daytime sleepiness and poor sleep quality in women of reproductive age. However, the direction of this association is unclear, with some studies suggesting that contraceptives might improve sleep, while others point out that it may worsen it. A possible explanation may rely on the real-life patterns of use, and the timing of contraceptive ingestion may play

a role in these effects. This study aimed at investigating whether the time oral contraceptives are taken influences sleep quality in women of reproductive age.

Materials and methods: Women aged 18 and older who consistently used oral contraceptives were invited to participate in an online survey. Recruitment was conducted via email and social media. Exclusion criteria included irregular contraceptive use (including changes in contraceptive use pattern in the last 3 months), users of non-oral contraceptives (such as intrauterine devices), pregnant, breastfeeding and postmenopausal women, night-shifts workers, individuals taking medications affecting sleep, and individuals with psychiatric or uncontrolled clinical conditions. The questionnaire collected demographic information and sleep-related outcomes, including chronotype (Morningness-Eveningness Questionnaire short version – MEQs), sleep quality (Pittsburgh Sleep Quality Index – PSQI), daytime sleepiness (Epworth Sleepiness Scale – ESS), and insomnia symptoms (Insomnia Severity Index – ISI). Based on self-reported contraceptive intake times, participants were divided into three groups: morning (4:00–10:00 AM), midday (11:00 AM–2:00 PM), and evening (7:00 PM–1:00 AM). Categorical variables were examined with Fisher's exact test, while continuous variables were analyzed using the General Linear Model. Analyses were performed using Jamovi software, with p-values <0.05 considered as statistically significant.

Results: Out of 705 respondents, 439 met the inclusion criteria. Of these, 71 reported taking contraceptives in the morning, 54 at midday, and 321 in the evening. The average participant age was 26.17 ± 6.68 years. Most were single, white, had completed high school, earned between four and five minimum wages, had a eutrophic BMI, and used combined oral contraceptives. Demographic variables did not significantly differ across intake timing groups. The majority of participants had an intermediate chronotype (72.2%), mild insomnia symptoms at IGI (78.5%), excessive daytime sleepiness at ESS (54.5%), and poor sleep quality at PSQI (64.8%). No statistically significant associations were found between the timing of contraceptive use and chronotype ($p=0.06$), insomnia severity ($p=0.361$), daytime sleepiness ($p=0.085$), or sleep quality ($p=0.98$).

Conclusions: The findings indicate that the timing of oral contraceptive intake does not significantly affect sleep parameters. Although being an observational study based on subjective self-report sleep outcomes, this research contributes to a relatively underexplored area of women's health. Further studies are required, including randomized controlled trials, to further investigate the effects of contraceptives on the sleep pattern of women with reproductive age.

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The Impact of Shift Work on Eating Patterns and Glucose Levels in Medical Interns: An Observational Study

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Introduction: Shift work, particularly night shifts, is an established disruptor of circadian rhythms and is linked to adverse metabolic outcomes, including impaired glucose regulation. Medical interns represent a population at heightened risk due to long and irregular working hours. Understanding the interplay between shift schedules, eating behaviours, and glycemic control is critical for informing preventive strategies in this vulnerable group.

Materials and methods: We conducted a prospective observational study among medical interns from various departments at a large training hospital in Singapore. Participants were monitored over two weeks during regular day shifts and night shifts. Eating patterns were assessed by real-time photographic dietary logging via a mobile application. Each participant wore a continuous glucose monitoring (CGM) device for two weeks, enabling detailed analysis of interstitial glucose fluctuations. Primary endpoints included changes in meal timing, meal frequency, macronutrient distribution, and mean glucose. Statistical analysis was conducted using four time windows (evening: 17h–23h, night 23h–5h, morning: 5h–11h, afternoon: 11h–17h) and shift type (day shift, night shift) as factors in repeated measures ANOVA.

Results: A total of 61 interns (mean age 24.6 ± 1.0 years; 61% female) contributed data from 416 day shifts and 190 night shifts. Night shifts were associated with a significant shift in meal timing. While overall meal frequency was not different (2.4 ± 0.8 meals/day shift vs 2.6 ± 1.1 meals/night shift),

fewer meals were taken in the evening preceding a night shift (0.74 ± 0.5) compared to a dayshift (0.96 ± 0.4 meals, $p = 0.02$), and more meals were taken during the night (0.47 ± 0.5 meals/night shift vs. 0.05 ± 0.1 meals/day shift, $p < 0.001$) and morning period (0.69 ± 0.4 meals/night shift vs. 0.55 ± 0.4 meals/day shift, $p = 0.043$). Increased meals at night more often contained proteins, carbohydrates, and processed snacks, while meals less often contained fruit/vegetables during the evening. CGM data revealed a similar shift towards higher mean glucose levels during the nights (night shift: 88.3 ± 1.4 mg/dL vs. day shift: 82.8 ± 1.2 mg/dL, $p < 0.001$) and lower mean glucose levels in the afternoon following a night shift (night shift: 88.5 ± 1.6 mg/dL vs. day shift: 97.5 ± 1.2 mg/dL, $p < 0.001$).

Conclusions: Among medical interns, night shifts substantially alter eating behaviours, showing a redistribution of meal timing and a shift in macronutrient content toward more energy dense and processed food with lower fruit and vegetable intake. These behavioral changes were accompanied by shift in glycemic control, with higher night-time glucose levels and lower glucose during the afternoon post-night shift compared to day shifts. These findings underscore the need for targeted nutritional and organizational interventions to mitigate the adverse metabolic impact of shift work in healthcare professionals.

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The impact of working nights or rotating shifts on sleep – A cross-sectional survey

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Introduction: Shift work although common in several sectors pose significant risks to the health of shift workers due to disruption of healthy sleep-wake schedules and may lead to shift work sleep disorder (SWD). Prevalence of SWD has been estimated around 27% globally, however, there are no prevalence studies in the United Kingdom. Our aim is to determine the prevalence and impact of SWD in the National Health Service (NHS) shift workers; to identify the associated health burden of SWD in this population; to describe interventions and support they have used to help with their sleep, its effectiveness, and the obstacles to their use.

Materials and methods: A cross-sectional survey (mix of validated questionnaires and bespoke questions) was developed through multiple meetings with a research advisory group comprising of ten shift workers. Survey items include: demographics, shift working pattern, SWD, physical and mental health, work productivity, interventions/support tried for sleep difficulties and its effectiveness. A participant who was employed by the NHS, worked shifts that involve working after 6pm or before 7am (i.e. non-standard hours) and worked non-standard hours for a minimum of 3 months was eligible to take part.

The study was conducted at two NHS Trusts between April and June 2025.

Results: Of the 534 who attempted the survey, 458 (86%) met eligibility criteria. 443 (97%) participants completed the survey. The mean age was 36.1 ± 10.7 years (range: 19-71). The majority of participants were female ($n=366$, 83%); registered nurses ($n=218$, 49%); and worked rotating shifts ($n=286$, 65%). Shift work duration varied from 3 months to 44 years.

Based on the SWDI, 315 (71%) met criteria for probable SWD. The proportion of probable SWD was statistically significantly higher in: females ($p=0.04$); higher NHS pay bands (5 and above) ($p=0.01$); shift work duration of more than 5 years ($p=0.01$); Registered Nurses and Midwives ($p=0.03$); the presence of a long-term health condition ($p=0.047$).

Participants with probable SWD had (i) lower EQ-5D-5L utility ($p<.001$) and VAS scores ($p<.001$) indicating poorer HRQoL, (ii) a higher proportion of likely depression ($p<.001$) and likely anxiety ($p<.001$) (iii) greater presenteeism (impairment while working) ($p<0.001$), higher overall work impairment/productivity loss ($p=0.001$) and greater activity impairment ($p<0.001$) due to their sleep problems.

The most common strategies tried by participants for their sleep problems were caffeine ($n=216$), naps

(n=206), changes in diet (n=167), change in physical activity and exercise (n=152) and over the counter sleeping aids (n=131). The majority of the participants indicated that these strategies were slightly or moderately effective. The majority (n=406, 92%) did not seek/receive support for their sleep difficulties.

Lack of awareness about available sources of support (n=155), busy schedule/time constraints (n=153) and long waiting times for appointments (n=152) were the most commonly chosen obstacles for seeking support.

Conclusions: The prevalence of SWD appears to be high in NHS shift workers. This has an adverse impact on their health and work productivity. Information collected on strategies used and their effectiveness will inform development of a new intervention for SWD.

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The influence of chronotype on physical activity and sleep in community-dwelling older adults

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Introduction: Chronotype refers to an individual's natural tendency to sleep or be alert at specific times over a 24-hour period. It is widely known that different chronotypes exhibit diverse patterns of wake and sleep. However, it is less clear how having an earlier or later chronotype differentially impacts daytime activity levels, sleep, and circadian stability, particularly in older adults with objective early cognitive impairment. This study investigates how the midpoint of sleep—a reliable continuous measure of chronotype—is associated with measures of physical activity and sleep in older adults with early cognitive impairment.

Materials and methods: This analysis utilized cross-sectional data from two clinical trials with a combined sample of 196 older adults ages 50-85 with objective early cognitive impairment, defined as performance on cognitive testing measuring at least one standard deviation below age-matched normative values. Participants wore a GENEActiv accelerometer for an average of 23.5 ± 6.76 days (range: 8-37). All analyses were conducted in R (version 4.4.2), and raw accelerometry data were processed with GGIR (version 3.2-6).

Sleep midpoint was calculated as the time halfway between sleep onset and wakeup measured relative to midnight, and served as an indicator of chronotype. Daytime physical activity measures included average acceleration (milli-gravity) and accumulated time (hours) in inactivity, light physical activity, and moderate physical activity. Sleep was assessed with sleep duration (hours), which is accumulated nocturnal sleep within the sleep window. Stability of sleep-wake patterns between days was assessed with the circadian marker interdaily stability (derived with R package nparACT version 0.8).

Multivariable linear regression analyses were conducted to test for associations between sleep midpoint and activity/sleep measures. Exploratory mediation analyses were conducted *post hoc* to investigate mechanistic pathways through which sleep midpoint may impact sleep duration. Outliers beyond ± 3 standard deviations were removed from analyses. All models were adjusted for the covariates of age and sex.

Results: Sleep midpoint was significantly associated with daytime hours accumulated in inactivity ($b=0.32$, $p<0.001$) as well as daytime average acceleration ($b=-1.33$, $p=0.026$), indicating that participants with earlier sleep midpoints spent less time inactive and had higher average activity levels. Sleep midpoint was not associated with light ($p=0.57$) or moderate physical activity ($p=0.19$). Sleep midpoint was negatively associated with sleep duration ($b=-0.16$, $p=0.015$) and interdaily stability ($b=-0.02$, $p=0.003$), such that participants with earlier sleep midpoints had a longer sleep duration and more

stable sleep-wake patterns. *Post hoc* exploratory mediation analyses revealed statistically significant indirect effects of sleep midpoint on sleep duration via time accumulated in inactivity (Total Indirect Effect $b = -0.17$, $p < 0.001$).

Conclusions: In older adults with early cognitive impairment, earlier chronotypes were more active, slept for a longer duration, and had more stable sleep-wake rhythms compared to later chronotypes. The relationship between earlier chronotype and longer sleep duration was mediated by less daytime inactivity. As sleep and circadian dysfunction are an early risk factor for neurodegenerative diseases, older adults should leverage individualized lifestyle modifications to sleep midpoint and daytime activity based on their chronotype to improve sleep/circadian quality and reduce individual risk for cognitive decline.

The role of light in predicting circadian phase shifts in shift workers

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Introduction: Shift workers exhibit substantial individual variability in circadian response to shift work. This variability remains poorly understood. Light exposure, a critical environmental cue for circadian phase shifts, has been shown to account for this individual variability in circadian timing following night shifts. This study aims to explore the predictive role of light exposure for circadian timing across diverse roster patterns.

Materials and methods: In an ongoing study, shift workers ($n = 40$, age 37.26 ± 9.02 years, 19 females) were monitored during a usual 6-day roster. Roster patterns included consecutive night shifts, consecutive early morning shifts, early morning-to-night rotations and night-to-early-morning rotations. Participants completed daily sleep diaries and wore a wrist activity monitor to assess sleep-wake timing, and a lapel-worn light sensor for continuous measurement of light exposure. Circadian phase was assessed on the first and last day of roster via 6-sulphatoxymelatonin (aMT6s) acrophase (peak) in urine. The phase-shifting effect of light was quantified as the mean difference in light exposure levels between the phase advance (3-7 hours after acrophase) and phase delay zones (3-7 hours before acrophase) of the circadian phase response curve to light across 6 days. Phase advance/delay zones were adjusted each day to account for individual phase shift per day.

Results: Preliminary analyses revealed substantial individual variability in the magnitude and direction of phase shifts across roster patterns (mean magnitude of phase shifts = 1.77 ± 1.60 h; range = -6.57 to $+4.92$ h). For example, following consecutive night shifts, phase shifts varied from -5.53 h to $+4.92$ h (mean = -1.11 ± 2.57 h). 10 participants exhibited a phase delay and three exhibited a phase advance. Following consecutive morning shifts, phase shifts varied from -2.38 h to $+3.22$ h (mean = $+0.80 \pm 1.31$ h). Seven participants exhibited a phase advance and two exhibited a phase delay. The degree of phase shift in either direction was significantly associated with the difference in light exposure between the advance and delay zone across the 6 days ($\beta = 0.001$, $p = .0004$, $R^2 = .29$). Including diurnal preference in the model improved explanatory power, with the multiple regression accounting for 43% of the variance in phase shifts (adjusted $R^2 = .40$). Further analyses will examine whether the predictive power of light exposure varies across different roster types.

Conclusions: Preliminary findings highlight substantial individual variability in circadian phase responses to various roster patterns. This variability was shown to be partly explained by differences in light exposure during the critical periods of the human circadian phase response curve to light. These results support the predictive role of light exposure in understanding circadian phase shifts across different roster patterns. This research is important for improving the prediction of circadian timing to inform personalised interventions for shift workers.

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The role of plasma Melatonin levels in regulating systemic inflammation in patients with Obstructive Sleep Apnea Syndrome

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Introduction: To assess the relationships between Melatonin and Obstructive Sleep Apnea Syndrome (OSAS). Melatonin, a neurohormone nocturnally produced by the pineal gland in the brain plays a crucial role in regulating the sleep-wake cycle. Melatonin has antioxidant, anti-inflammatory properties, and may be involved on glucose homeostasis related to insulin resistance and lipid metabolism.

Materials and methods: We conducted a retrospective cross-sectional study of 63 cases diagnosed with OSAS mean aged 54.74 ± 10.95 year-old, of which 40 was smokers and 23 nonsmokers. Demographic, anthropometric (Body Mass Index-BMI, neck and abdominal circumference), pack-years smoking, blood pressure, fasting lipid panels that includes: Triglycerides (TG), Total Cholesterol (TC), Low Density Lipoprotein cholesterol (LDLc), High Density Lipoprotein cholesterol (HDLc), Very Low Density Lipoprotein (VLDL) cholesterol, nonHigh-Density Lipoprotein (nonHDL) cholesterol, glycemia, leukocytes, thrombocytes, C Reactive Protein (CRP), albumin, uric acid, urea and creatinine were assessed. Melatonin and its metabolite, 6-hydroxymelatonin (a marker of plasma melatonin level) were determined through overnight urinary levels, by Liquid Chromatography Mass Spectrometry (LC-MS/MS) method and expressed in nmol/L. As a measure of insulin resistance, the Triglycerides Glucose (TyG) index was calculated as the natural logarithm (Ln) of plasma glucose and TG using the formula: $\text{Ln}(\text{TG} [\text{mg/dL}] \times \text{glucose} [\text{mg/dL}] / 2)$. Atherosclerotic cardiovascular disease (ASCVD) risk was assessed according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines. All the participants in the study completed the Epworth Sleepiness Scale (ESS) questionnaire and underwent Cardiorespiratory Polygraphy, in accordance with the established guidelines of the American Academy of Sleep Medicine. The scientific research program was conducted in accordance with the norms of ethics in effect: protection of personal data; use the biological samples for the intended purpose; and informed consent of the subjects. Statistical analysis included Spearman correlations tests, one-way ANOVA test, and two-tailed *t* test. A *p* value < 0.05 was considered statistical significant.

Results: The mean values of Melatonin was significantly higher in study group (smokers and nonsmokers) and in smokers ($p=0.0006$; $p=0.0003$). Apnea Hypopnea Index (AHI), Oxygen Desaturation Index (ODI), Pulse variance Index, TyG index, ASCVD risk were statistically significant higher in smokers versus nonsmokers ($p=0.02$; $p=0.001$; $p=0.008$; $p=0.03$; $p=0.04$). The average value of AHI in smokers and nonsmokers patients was 43.49 ± 19.76 , respectively 47.10 ± 21.60 in smokers and 35.90 ± 12.33 in nonsmokers. In study group (smokers and nonsmokers) statistically significant correlations were found between Melatonin and ODI ($r=-0.39$; $p=0.001$), AHI ($r=-0.27$; $p=0.02$), Lowest Desaturation% ($r=0.27$; $p=0.02$); Melatonin and TC ($r=0.30$; $p=0.01$), TG ($r=0.25$; $p=0.04$), LDLc ($r=0.28$; $p=0.02$), nonHDLc ($r=0.24$; $p=0.05$), while in smokers study group, between Melatonin and ODI ($r=-0.30$; $p=0.05$), TyG index ($r=0.37$; $p=0.01$), VLDL ($r=0.44$; $p=0.003$), LDLc/HDLc ratio ($r=0.34$; $p=0.02$); AHI and ASCVD risk ($r=0.34$; $p=0.03$), BMI ($r=0.34$; $p=0.03$).

Conclusions: In OSAS patients, Melatonin may have predictive value for disease severity and, should consider screening in patients with OSAS. Melatonin has a time-dependent regulation on glucose, lipid homeostasis, and body weight, and can be considered in the treatment of patients with OSAS.

Acknowledgments: Thanks!

Timed Blue-Light Intervention Enhances Alertness and Reduces Clinical Errors in ICU Night-Shift Nurses

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Introduction: Night-shift intensive care unit (ICU) nurses frequently suffer from circadian misalignment, resulting in elevated melatonin secretion, increased sleepiness, psychological stress, and reduced cognitive performance-factors associated with heightened risk of medical errors. To evaluate the efficacy of a timed blue-light intervention in mitigating circadian disruption and enhancing alertness, mood, and vigilance in ICU night-shift nurses.

Materials and methods: A quasi-experimental crossover design was implemented involving 22 ICU nurses. Participants were randomized to either wear blue-light emitting eyewear (460 nm, 1500 lux) for 20 minutes at 00:00, 02:00, and 04:00 during two consecutive night shifts, or remain under standard ambient lighting. After a one-month washout, subjects crossed over to the alternate condition. Key outcome measures included salivary melatonin levels, Karolinska Sleepiness Scale (KSS), Depression Anxiety Stress Scale (DASS-21), and 10-minute Psychomotor Vigilance Task (PVT), assessed before, during, and after each shift.

Results: Compared with the control condition, blue-light exposure suppressed melatonin levels by over 30%, decreased subjective sleepiness and stress scores by at least 20%, and improved PVT reaction time and accuracy by 15% and 10%, respectively. These effects were consistent across the crossover phases.

Conclusions: Timed blue-light exposure via eyewear is an effective, low-cost, non-pharmacological intervention to improve cognitive alertness, mood, and vigilance among ICU night-shift nurses, with potential to reduce clinical errors and enhance patient safety.

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Use of Apple Watch to Optimize Light Therapy and Reduce Circadian Misalignment for Night Shift Workers

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Introduction: Circadian misalignment, a primary etiology of mood, fatigue, and performance deficits in approximately 80% of shift workers, can be alleviated with targeted light interventions. However, general "light at night" interventions do not account for shift workers' variable circadian phases. Recently, our lab validated Apple Watch (AW) as a noninvasive means of predicting circadian timing (i.e. dim light melatonin onset, DLMO). Here, we extend this by examining the clinical utility of AW in informing circadian interventions. We hypothesized the AW-informed group would result in higher rates of circadian alignment following treatment vs the control (non-personalized) group. We also compared the magnitude of phase shifts between these interventions.

Materials and methods: Night shift workers (N=60) were randomly assigned to either the AW or control group, and DLMO was measured before and after treatment. AW data (accelerometer and heart rate) was collected over 2 weeks and processed through a biomathematical model of the human circadian system to produce estimated DLMOs. Light-dark schedules were then created from the corresponding phase response curves and implemented with light boxes and blue-blocker glasses (at-home or in-lab) to induce phase shifts. Participants in the control group followed a non-personalized light-dark schedule (light from 18:00 and 21:00; light avoidance from 04:00 and 10:00). Circadian alignment was operationalized as DLMO between 02:00 and 14:00, and a relative risk ratio was used to compare the rate of circadian alignment between the two groups.

Results: AW-Informed schedules resulted in a 64.7% increase in circadian-aligned subjects whereas Control resulted in a 40% decrease in circadian-aligned subjects ($p = .013$). Percent of subjects aligned post-treatment was 3.1 times higher in the AW group (62.2%) compared to the control group (20.0%). AW-Informed phase-delay schedules achieved average delays of 2.0 hours $\pm$ 4.7 SD, whereas control phase-delay schedules advanced subjects an average of 0.7 hours $\pm$ 3.7 SD ($p = .040$). The risk of

erroneously inducing circadian misalignment is 3.3 times greater using control schedules (13.3%) than AW-informed schedules (4.4%).

Conclusions: Personalized light-dark schedules made with wearables data are much more effective at correcting circadian misalignment. In fact, non-personalized "light at night" schedules may be *harmful* by further misaligning night shift workers. Consumer-based wearables are already commonplace and thus make this personalized circadian medicine solution highly scalable. In the future we aim to identify facilitators and barriers of implementing personalized circadian medicine in the real world.

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Validation of the Bergen Shift Work Sleep Questionnaire in workers under split shift or early morning shift

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Introduction: The Bergen Shift Work Sleep Questionnaire (BSWSQ) was developed explicitly to assess sleep difficulties related to day, evening, and night shifts, as well as rest days. The BSWSQ is a unique questionnaire addressing sleep in relation to several types of shifts. Although this questionnaire possesses adequate psychometric properties, it does not capture sleep difficulties related to early morning or split shifts. These types of atypical schedules are frequent among school support staff, precarious, female-dominated jobs, and may have potential harmful effects on sleep and occupational health. To support future investigation of these impacts, this study aimed to validate an adaptation of the BSWSQ for early morning and split shifts and to examine the presence and stability of the two constructs (Insomnia/wakefulness and Sleepiness) within these shifts. The study also assesses discriminant and convergent validity.

Materials and methods: A total of 3,510 participants (94% women; 51.5% aged 45 years or older), including school daycare staff and specialized education technicians in direct student care, in the province of Quebec, Canada, were recruited and completed an online survey. The survey comprised several self-reported questionnaires: the BSWSQ – which includes 6 items targeting insomnia and sleepiness symptoms across four subscales (split, early morning, continued day shift, and rest days) – the Hospital Anxiety Depression Scale, and the Epworth Sleepiness Scale.

Results: A multilevel confirmatory factor analysis was conducted to model both stable between-person differences and within-person fluctuations in Insomnia/wakefulness and Sleepiness symptoms across work shifts, as supported by intraclass correlations (ICCs) ranging from .68 to .78. The model specified that Insomnia/wakefulness was measured by items 1 to 3 of the BSWSQ and Sleepiness by items 4 to 6 at both levels. Results demonstrated that the two-factor model (Insomnia/wakefulness and Sleepiness) held across levels, with strong fit indices and reliability metrics at both the within- and between-person levels. The metric invariant model demonstrated excellent fit to the data: robust CFI = .972, robust TLI = .952, robust RMSEA = .063, and SRMR = .038 (within) and .047 (between). Standardized loadings ranged from .609 to .768 for Insomnia/wake items and from .741 to .805 for Sleepiness items, indicating strong measurement consistency across contexts (day, morning, split) at both levels. The average Cronbach's alpha coefficient was of .851.

Conclusions: These results suggest that the two-factor structure provides an excellent approximation of the observed covariance matrices at both levels. Moreover, findings support the structural distinctiveness and reliability of both constructs (Insomnia/wakefulness; Sleepiness) at each level and indicate strong internal consistency across work shifts. Metric invariance across levels (within- vs. between persons) and scalar invariance across contexts (different work shifts), were also supported, confirming stable measurement properties. The psychometric strategy used strengthens the theoretical and applied value of the BSWSQ in occupational contexts, where sleep symptoms are intrinsically nested within individuals yet vary based on work demands. This advancement better aligns the instrument with its foundational purpose. Assessing the impact on sleep of two understudied types of atypical schedules will enrich the understanding of occupational health issues experienced by marginalized and precarious groups of workers.

Validation of the self-rating version of the Scale for Symptom Severity of Circadian Rhythm Sleep-Wake Disorders

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Introduction: There is no validated severity rating scale for intrinsic circadian rhythm sleep-wake disorders (CRSDWs), including delayed sleep-wake phase disorder (DSWPD). We developed "the Scale for Symptom Severity of Circadian Rhythm Sleep-Wake Disorders," which has relatively good reliability and validity. We adapted it into a self-rating version, and this study aimed to examine its reliability and validity.

Materials and methods: The self-rating version of the Scale for Symptom Severity of Circadian Rhythm Sleep-Wake Disorders is described in Japanese and consists of 12 items with 4 or 6 anchor points, with a total score range of 0 to 40. It includes items such as problems with sleep onset and offset at the desired times the patients defined, social adaptation, morning or daytime symptoms in physical and neuropsychiatric areas, deviations from 24-hour regularity such as free-running, irregular patterns, and variations in awakening time, over the past one week. Twenty-three patients with DSWPD, diagnosed according to the International Classification of Sleep Disorders, 3rd edition, who visited the Department of Psychiatry at Fujita Health University Hospital, were included in this study. Any ongoing treatments or comorbidities were allowed for inclusion. At any point during the patients' treatment course, patients were asked to rate their own symptoms using this questionnaire. Simultaneously, the structured interview version of the scale was administered independently by two physicians, with these scorings kept hidden from the patients. Additionally, the following assessments were conducted: the Clinical Global Impression of Illness Severity (CGI-S) by the physician in charge, and the Morningness-Eveningness Questionnaire (MEQ), Munich Chronotype Questionnaire (MCTQ), and subjective complaints regarding quality of life assessed using a Likert scale, by the patients. The study was approved by the Ethics Committee of Fujita Health University, and all participants provided written informed consent.

Results: Twenty-three patients with DSWPD were included in the analysis. The Cronbach's alpha coefficient was 0.7617. Spearman's rank correlation coefficients between the total score of the self-rating scale and each measure were as follows: 0.8395 and 0.7782 for the structured interview version of the scale (for two raters), 0.6187 for CGI-S, -0.6366 for subjective complaints by Likert scale, -0.5104 for MEQ, and 0.6359 for MSFsc (MCTQ); all these correlations were statistically significant.

Conclusions: The data in this study suggested that this self-rating version of the scale has relatively good internal consistency and criterion validity. Because the number of samples was small, it would be preferable to confirm the findings with a larger sample size, as well as to examine the response to symptom changes using longitudinal data.

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Wearable-device-measured light at light exposure and Irritable bowel syndrome risk

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Introduction: Irritable bowel syndrome (IBS) affects approximately 7–21% of the global population. Circadian rhythm disruption (CRD) is increasingly recognized as a contributing factor in gastrointestinal

disorders. Light at night (LAN), a common feature of modern environments, is a primary external cue for circadian misalignment. However, the relationship between LAN exposure and IBS risk remains unclear. This study aimed to investigate whether objectively measured LAN exposure is associated with incident IBS.

Materials and methods: We analyzed data from 67,590 UK Biobank participants (mean age: 62.7 years; 59.2% female), excluding baseline shift workers. LAN exposure was measured via wrist-worn accelerometers. IBS cases were identified through linked health records. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for IBS risk across LAN levels, adjusting for demographic, lifestyle, metabolic, psychiatric, and sleep-related covariates. Additionally, a series of sensitivity analyses were conducted to validate the main results.

Results: Over a median follow-up of 7.0 years (466,674 person-years), 820 incident IBS cases were recorded. A non-linear association was observed: IBS risk began to rise above an average nighttime LAN level of 175 lux. Participants exposed to >175 lux had a higher risk of IBS (HR = 1.35; 95% CI: 1.05–1.73) compared to those with lower exposure. Findings remained robust in multiple sensitivity analyses: excluding early IBS cases (within 1 or 2 years), using non-imputed data, restricting the sample to participants with ≥6 days of valid accelerometer wear, adjusting for the month of accelerometer measurement, and excluding individuals with high nighttime activity levels. All results remained significant ($P < 0.05$), confirming the robustness of the association.

Conclusions: Among older adults, higher LAN exposure was associated with an elevated risk of incident IBS. LAN exposure may serve as a novel and robust predictor of IBS risk, warranting further investigation.

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Wearable Ring-Based Algorithm for Chronotype Estimation from Passive Physiological Data

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Introduction: Chronotype, an individual's preference for sleep-wake timing, influences cognitive function, metabolic health, and overall well-being. Traditional assessments, such as the Morningness-Eveningness Questionnaire (MEQ), rely on self-reports susceptible to recall bias. Advances in wearable technology enable the passive collection of physiological and behavioral data, offering a more objective alternative. This study proposes an algorithm leveraging sleep, physical activity, and distal skin temperature data from a wearable ring to estimate chronotypes unobtrusively. The MEQ score served as the reference standard for algorithm training and testing.

Materials and methods: Eighty-three healthy participants (46 women; Age, mean $\pm$ SD: 36.5 $\pm$ 7.8 years) consented to participate in the study and provided Oura Ring data. This data was collected over an 8-month period preceding their response to the study questionnaire, resulting in a total of approximately 13000 days of data across all subjects. Each participant contributed a median of 180 days of data to the dataset. Chronotype was estimated using a final dataset comprised of 90 calendar days, derived by rolling a window with a one-month step size across each participant's available data. The participants included 7 evening types (MEQ score $\leq$ 41), 27 morning types (MEQ score $\geq$ 59), and 49 classified as intermediate chronotypes (MEQ score 42–58).

Results: Data preprocessing included filtering for sleep sessions lasting longer than three hours and recorded within one hour of the user's most frequent timezone. Participants with at least 30 valid sleep sessions within the 90-day period were included in the analysis. Periods, when the ring was not worn were excluded, and physical activity and skin temperature data were synchronized with retained sleep instances. Handcrafted features were extracted from sleep, physical activity, and skin temperature data. Sleep features included median bedtime, wake time, and the standard deviation of sleep midpoint, reflecting sleep timing and regularity. Activity patterns were characterized by identifying the 10 most active and 5 least active consecutive hours, extracting their average activity levels, times of occurrence,

relative amplitude, acrophase, and maximum activity level. Similarly, for temperature, the 5 highest and 5 lowest consecutive hours were identified, and their average temperatures, times of occurrence, relative amplitude, acrophase, maximum and minimum temperatures, and temperature range were extracted. A linear regression model was employed, with group k-fold cross-validation used to assess generalizability. The model achieved a mean absolute error of 4.79 in MEQ score estimation and explained 67% of the variance in estimating MEQ scores from the extracted features ($R^2 = .67$).

Conclusions: These preliminary findings support the feasibility of estimating chronotypes using wearable ring data, offering an unobtrusive alternative to traditional questionnaire-based assessments. The algorithm demonstrated promising accuracy in predicting MEQ scores, suggesting its potential application in personalized health and behavioral interventions. Future studies should validate the algorithm in larger and more diverse populations to enhance its generalizability and applicability.

What would you do to reduce jetlag and when? Survey of a convenience sample of undergraduate students and implications for public education

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Introduction: Jetlag is circadian disruption caused by rapid travel over time zones. Evidence-based interventions include appropriately timed light-dark exposure, aligned schedules of sleep-wake, and judicious use of caffeine, melatonin, and other pharmacological sleep aids. Although 9.4 billion people flew in 2024, use of evidence-based strategies appears modest. This may be due to limited public understanding of circadian rhythms.

Materials and methods: We assessed applied knowledge by asking a convenience sample what strategies they would use to reduce jetlag, and when they would apply these. Eligible participants were enrolled in an introductory elective subject on sleep and circadian rhythms at the University of Sydney during 2021 to 2025. Students came from all university faculties and are typical of undergraduates in terms of gender (two-thirds female) and visa status (half international). Surveys were administered before learning about jetlag, but after learning about circadian rhythms.

Results: Of N=5,938 participants (60% response, 63% female, mean age 20.3, SD 2.4 years), the majority (87%) reported experience of jetlag and international flight (91%). 10% had flown internationally but not experienced jetlag, whilst 1% had experienced jetlag without international travel. When asked how much they were bothered by jetlag, 22% indicated “not at all”, 37% “a little”, 20% “moderately”, 14% “quite a bit”, 5% “extremely”, and 1% “can’t remember”.

Presented with 21 strategies, the top 3 selected for use before flight were: going to bed earlier/later than usual (67%), staying well-hydrated (66%), and avoiding alcohol (51%). Use earplugs/headphones (80%), stay well-hydrated (74%), and take naps (74%) were most common for during flight. Most frequently selected for after flight were go outdoors for sunlight (74%), stay well-hydrated (66%), and exercise (52%). A median of 7 strategies were endorsed per time point.

Across time points, participants selected: alter sleep time (94%), nap (91%), alter sleep duration (91%), take melatonin (61%), use over-the-counter sleep aids (53%), take prescribed sleep medications (48%), eat lighter/heavier meals (71%), eat healthier foods than normal (68%), take vitamins or supplements (61%), drink caffeinated beverages (69%), avoid caffeinated beverages (74%), stay well-hydrated (90%), do yoga or stretching exercises (65%), meditate or do relaxation exercises (64%), exercise (74%), drink alcohol (40%), avoid alcohol (72%), go outdoors for sunlight (85%), use earplugs/headphones to block noise (86%), wear compression stockings for circulation (57%), or use a jetlag app (50%).

The greater the impact from jetlag, the greater the number of strategies endorsed for during ($\rho=0.11$, $p<0.001$) and after flight ($\rho=0.06$, $p<0.001$), but not before travel ($\rho=0.02$, $p=0.264$). Those who reported greater jetlag impact also endorsed booking strategies more often ($p<0.05$), such as picking a

flight that arrived at a certain time (73%), choosing a direct flight (58%), picking a preferred seat (46%), and choosing to travel in premium cabins (25%).

Conclusions: Most participants selected evidence-based strategies to mitigate jetlag, although many strategies were chosen to enhance comfort or wellbeing. Results suggest high motivation to counteract travel fatigue, which presents opportunities to improve use of anti-jetlag strategies. Research to evaluate changes in behaviour after education on jetlag is needed.

Within-subject variation in circadian timing in shift workers repeating the same shift pattern

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Introduction: While inter-individual variation in circadian response to shift work has been demonstrated, the within-individual variation in circadian timing when shift workers repeat the same shift pattern is unknown. Light is a key factor influencing individual circadian timing. This study aims to examine the consistency in circadian timing between two repeated occasions of the same shift pattern and the role of light exposure in explaining within-individual variability in circadian timing among shift workers.

Materials and methods: In an ongoing study, shift workers ($n=25$, age 39.12 ± 11.50 years, 10 females) from multiple industries were monitored during two replications of their usual shift patterns (8-10 days), separated by at least 6 weeks. Shift patterns included consecutive night shifts, consecutive early morning shifts, and early-morning-to-night rotations. Participants completed daily sleep diaries and wore a wrist activity monitor to measure sleep-wake timing, and a lapel-worn light sensor for continuous measurement of light exposure. Circadian phase was assessed at the end of each shift pattern via 6-sulphatoxymelatonin (aMT6s) acrophase (peak) in urine. A light consistency index (LCI) was calculated as the percentage of time for which light was above or below a threshold of 70[TS1] melanopic lux at corresponding parts of the work roster, to examine the consistency of light exposure patterns between the two occasions of the same shift pattern. The difference in average light exposure between the two occasions in the phase-advance (90-degree bin after acrophase) and phase-delay zones (90-degree bin before acrophase) of the circadian phase response curve to light was calculated.

Results: Analyses revealed moderate consistency in aMT6s acrophase between the two occasions of the same shift pattern (within-subject correlation: $r = 0.59$, $p < .001$), although substantial within-individual differences remained (mean difference = 2.38 ± 1.56 h; range = 0.14–5.46 h). Consistency in circadian timing was significantly associated with a higher light consistency index prior to circadian assessment ($\beta = -0.09$, $p = .02$, $R^2 = .22$). Aligning LCI to individual acrophase improved its ability to predict differences in acrophase ($\beta = -0.08$, $p = .0003$, $R^2 = .45$). Individuals with greater variation in acrophase had greater difference in light within the phase advance and delay zones. Linear regression revealed within-individual variation in acrophase was associated with differences in average light level in the advance ($\beta = 1.99$, $p = .02$) and delay ($\beta = 3.75$, $p = .00002$) zones between the two occasions ($R^2 = .56$).

Conclusions: Findings highlight within-individual variability in circadian phase in shift workers, despite following identical shift patterns. This indicates that circadian timing in workers cannot be assumed from a single measurement. This variability was explained by differences in light exposure, highlighting the value of light exposure for predicting circadian timing amongst shift workers. The ability to use light to improve circadian prediction has implications for informing personalised interventions in this population.

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Work ability and health-related productivity loss by chronotype: Results from population-based panel study

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Introduction: Chronotype, representing individual variation in circadian preference, has been increasingly linked to occupational health outcomes. Most previous studies have focused on clinical health parameters or general productivity, and rarely considered diverse occupational settings. This study aimed to investigate the association between chronotype and two key occupational health outcomes—work ability (WA) and health-related productivity loss (HRPL)—using longitudinal panel data in a large working population.

Materials and methods: Data were obtained from the Korean Work, Sleep, and Health Study, a population-based panel survey conducted from 2022 to 2024. The study included 10,065 wage-earning participants aged 19–70 years. Chronotype was assessed using the reduced Morningness-Eveningness Questionnaire and categorized as morning, intermediate, or evening type. WA was measured using the Work Ability Index and dichotomized into “poor” vs. “not poor.” HRPL was calculated as a percentage using the Work Productivity and Activity Impairment questionnaire. Generalized estimating equation models were applied to estimate odds ratios (ORs) for poor WA and mean differences in HRPL, adjusting for gender, age and occupation. Subgroup analysis was conducted based on gender, age, occupation type, and shift work status.

Results: Compared to morning types, evening chronotypes had significantly higher odds of poor WA (OR: 2.291, 95% confidence interval [CI]: 1.717–3.058) and greater HRPL (mean difference: 5.362 percentage points, 95% CI: 3.902–6.822). Intermediate types also showed elevated odds of poor WA (OR: 1.390, 95% CI: 1.097–1.762) and higher HRPL (mean difference: 4.925 percentage points, 95% CI: 3.932–5.918), though to a lesser extent than evening types. Subgroup analyses demonstrated that the association among chronotype, WA, and HRPL remained consistent across demographic and occupational groups. However, these relationships were more pronounced among men, younger workers, and white-collar employees. Notably, among the shift workers, the evening types showed no significant differences in ORs for poor WA or HRPL compared to the morning types.

Conclusions: Chronotype significantly influences WA and HRPL, with evening types experiencing the poorest outcomes due to circadian misalignment. These findings suggest the importance of considering chronotype in workplace health interventions. Strategies such as flexible schedules and sleep health programs may mitigate productivity losses and enhance employee well-being, improving long-term workforce sustainability and reducing health inequities.

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Dental

Analysis of Chest and Abdominal Respiratory Movements Prior to Masticatory Muscle Activity During Sleep in sleep bruxism subjects

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Introduction: Previous studies have reported a slight decrease in blood oxygen saturation prior to the occurrence of rhythmic masticatory muscle activity (RMMA) in individuals with sleep bruxism (SB). Furthermore, it has been shown that the use of mandibular advancement devices can reduce the

frequency of RMMA episodes. These findings suggest that increased upper airway resistance may play a role in the generation of RMMA. As upper airway resistance increases, the body must exert greater respiratory effort to maintain adequate ventilation. Therefore, the aim of this study was to investigate whether respiratory effort increases prior to RMMA onset. To this end, we quantitatively assessed the phase difference of chest and abdominal respiratory movements during quiet sleep period and the period immediately preceding RMMA episodes. In addition, we analyzed non-specific masticatory muscle activity (NSMMA) in the same manner and compared the results with those of RMMA.

Materials and methods: Polysomnographic (PSG) recordings were conducted on healthy volunteers in their 20s. Ten participants (4 males and 6 females; mean age: 23.1 ± 1.19 years; BMI: 19.6 ± 1.7 kg/m²; RMMA index: 5.61 ± 1.57 episodes/hour) were selected based on the criteria of having an apnea-hypopnea index (AHI) ≤ 5 and an RMMA index ≥ 4 episodes/hour.

For the evaluation of RMMA and NSMMA, we extracted 20 second segments immediately preceding each episode. Any segments that contained masseter muscle activity or apnea/hypopnea events were excluded from the analysis. In total, 236 RMMA segments and 326 NSMMA segments were included. For quiet sleep period, 236 artifact-free 20 second segments without masseter activity or arousals were selected. In each segment, chest and abdominal respiratory waveforms were plotted on X and Y axes to create Lissajous figures. The perpendicular distance from the resulting curve to its Lissajous line was calculated every 0.1 seconds along the Y-axis. The average of these distances was defined as the Respiratory Phase Difference Index (RPDI). For each subject, the median RPDI values were calculated across RMMA, NSMMA, and quiet sleep conditions. Statistical comparisons were performed using the Friedman test. When significant differences were observed, post-hoc pairwise comparisons were conducted using the Wilcoxon signed-rank test with Bonferroni correction.

Results: RPDI values were significantly higher in the 20 second segments preceding RMMA compared to those during quiet sleep periods ($P = 0.0059$). Similarly, RPDI values prior to NSMMA episodes were significantly elevated compared to those during quiet sleep periods ($P = 0.0059$). However, no significant difference was found between the RPDI values between RMMA and NSMMA episodes ($P = 0.3926$).

Conclusions: The present study demonstrated that both RMMA and NSMMA are preceded by a significant increase in chest and abdominal phase difference when compared to quiet sleep period, indicating the presence of respiratory effort prior to the onset of these muscle activities. Although RMMA and NSMMA represent distinct forms of masticatory muscle activity, both appear to be preceded by similar respiratory dynamics. These findings suggest that respiratory effort may be a common physiological background mechanism underlying the occurrence of sleep-related masticatory muscle activity.

Artificial Intelligence in the Management of Obstructive Sleep Apnea: Innovations and Challenges

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent and underdiagnosed disorder that significantly impacts cardiovascular health, cognitive function, and overall quality of life. Traditional diagnostic and treatment pathways for OSA—such as polysomnography and CPAP therapy—face challenges related to accessibility, cost, patient adherence, and clinical resource constraints. In this context, **artificial intelligence (AI)** emerges as a transformative tool with the potential to revolutionize every stage of OSA management.

From automating early screening in primary care and dental settings to enhancing the accuracy of diagnostic algorithms and optimizing personalized treatment plans, AI is reshaping how clinicians approach this complex condition. Yet, while AI-driven solutions offer tremendous promise, they also raise important questions around data privacy, algorithm transparency, clinical validation, and integration into existing care models.

This review explores the **current innovations, applications, and limitations** of AI in OSA management, emphasizing both the clinical potential and the ethical, technical, and operational challenges that must be addressed to realize its full impact.

Materials and methods: This review was conducted through a comprehensive search of peer-reviewed literature and clinical studies published between 2015 and 2025, focusing on the application of artificial intelligence (AI) in the diagnosis and management of Obstructive Sleep Apnea (OSA). Databases

searched included PubMed, Scopus, and IEEE Xplore using keywords such as "artificial intelligence," "machine learning," "sleep apnea," "OSA screening," and "AI diagnosis."

Included studies were selected based on relevance to AI-driven innovations in early screening, diagnostic accuracy, treatment personalization, and long-term management of OSA. Articles addressing ethical, technical, and integration challenges of AI in clinical practice were also reviewed to provide a balanced perspective.

The findings were categorized into thematic areas: (1) AI in screening and early detection; (2) AI-supported diagnostic tools; (3) AI-guided treatment planning; and (4) system-level challenges including data privacy, algorithm bias, and implementation barriers. The review aims to synthesize current knowledge and identify gaps for future research.

Results: AI applications in OSA management showed promising outcomes across four areas:

1. **Screening** – AI tools effectively identified at-risk individuals using health records, questionnaires, and wearable data.
2. **Diagnosis** – Machine learning models improved accuracy in detecting sleep events and apnea severity.
3. **Treatment** – AI helped personalize therapies by predicting CPAP adherence and matching patients to alternatives.
4. **Challenges** – Key barriers include limited clinical validation, data privacy concerns, and poor integration into care systems.

Overall, AI shows strong potential but requires further refinement for routine clinical use.

Conclusions: Artificial intelligence is reshaping the landscape of obstructive sleep apnea management by enhancing screening, diagnosis, and personalized treatment. While early results are promising, widespread clinical adoption remains limited by challenges in validation, data security, and system integration. Continued research and cross-disciplinary collaboration are essential to fully realize AI's potential in improving OSA care.

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Breath, Bite, and Bedtime: Sleep's Impact on Kids' Oral Health

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Introduction: Background: Sleep-Disordered Breathing (SDB) in children affects both airway function and oral health, with often-overlooked links to dental caries.

Objectives: This poster outlines the mechanisms connecting SDB to increased caries risk in children by examining key contributing factors and how myoline treatment can be helpful in treatment.

Materials and methods: Methods: We synthesize current understanding of SDB's physiological and behavioral impacts, like mouth breathing and poor sleep, and their direct/indirect effects on oral health.

Results: Results: SDB frequently causes xerostomia (dry mouth) due to mouth breathing, reducing salivary protection. Associated gastroesophageal reflux (GERD) often lowers salivary pH, fostering an acidic oral environment that promotes enamel erosion and sensitivity. Poor sleep quality leads to inconsistent oral hygiene and disrupted eating, escalating caries risk. Nighttime snacking or sugary drinks for comfort further exacerbates problems. SDB is also linked to bruxism.

Conclusions: Conclusions: Early dental recognition of these SDB-related oral signs is crucial for timely diagnosis and multidisciplinary interventions including myoline therapy to mitigate oral health complications.

Changes Of The Protocols And The Extensions In The General Dentistry After Dental Sleep Medicine Emerging As An Individual Branch

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Introduction: Dental Sleep Medicine is the most important and individual branch in the field of Dentistry which enables A Dentist to treat Obstructive Sleep Apnea to provide general health and wellbeing to the patient. The most important aspect here is if we focus on the iceberg of sleep disorders only 5% of the disease is visible and 30% of the life will be spent in sleep that is why the highest amount of focus should be done on sleep disorders.

After Dental Sleep Medicine evolved as an individual branch a lot of research was done which resulted some changes in the protocol of some treatments of the general dentistry to make the patient away from the risk of Obstructive Sleep Apnea. The reason is that the previous protocols do boost the risk of Obstructive Sleep Apnea. Now it is the duty of A Dentist to know about these changes and the extensions.

Materials and methods: Edentulous UPPP, followed by the posterior obturator, orthodontic for the 4 4 Xtn anterior central wedge detection of the tongue for narrow posterior nasal aperture home block for habits remove the cause for infants change the housing bottle

Results: OSA can be treated more successfully

Conclusions: •In view of the positive Health Benefits over the long run, the small pains and efforts to be tolerated now for them are much worthy. and •IT IS A Wiser THING TO SPEND SMALLER POCKET IN ADVANCE RATHER THAN TO SPEND BAGS IN URGENCY

Acknowledgments: DR brain Palmer

Clinical Innovation in Dental Sleep: A Serial Device Approach to Mandibular Advancement Device

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Introduction: Mandibular advancement devices (MADs) are a validated treatment for primary snoring and mild to moderate obstructive sleep apnea (OSA). While titratable MADs are standard, many patients find them uncomfortable or difficult to use. This abstract presents a novel, stepwise, non-adjustable MAD protocol — Sleep Buddy — which uses a custom-fabricated series of three mandibular advancement devices to progressively advance the mandible over time, without mechanical adjustment.

Results

Preliminary results indicate high patient compliance, low side-effect incidence (e.g., TMJ discomfort, salivation), and strong subjective improvements in snoring reduction and sleep quality. Patients reported the staged advancement to be intuitive and less intimidating than conventional titratable devices. Follow-up with home sleep testing (HST) in a subset of users demonstrated reductions in snoring index and AHI.

Conclusion

A non-adjustable, staged MAD protocol may represent a simplified and patient-friendly alternative to traditional titratable devices. This system has the potential to expand access to MAD therapy via streamlined digital workflows and lower complexity, particularly in telehealth-driven models. Further study is warranted to assess long-term outcomes and scalability.

Disclosures

The author is the inventor of the Sleep Buddy device and holds a patent for the design. No commercial sales have yet occurred. This abstract is intended to present the clinical concept and early user feedback.

Materials and methods: Forms of bisacryl or nylon have both been used.

Results: Results are patient comfort. There's ease in wearing the appliance so the compliance rate is higher. Because patients can be scanned or use an at home impression kit, Sleep Buddy can be offered through physicians or dentists.

Conclusions: See above:

The appliances are custom made with a starting point of a half molar forward. That approach with the encouraged nasal breathing by the connector being in the anterior, has been shown to be very kind to the TMJs, a big concern with traditional MADs. This incremental, premade approach makes it super

easy for patients and prescribing doctors for follow up appointments. This system can be used easily in telehealth driven models and easily streamlined in digital workflows.

Acknowledgments: Dr. Mary Ann Childs, DMD,RPh is an independent clinical researcher/ sleep innovation consultant. She is the inventor and patent holder of Sleep Buddy. The abstract is submitted to share clinical innovation in Mandibular Advancement Device therapy under development.

Clinical Outcomes for the Treatment of Mild-to-Severe Obstructive Sleep Apnea with Non-Permanent Maxillary Expansion and Mandibular Advancement/Expansion Oral Appliances: A Retrospective Analysis of Real World Data

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Introduction: Both dental expansion and mandibular advancement oral appliances are important clinical approaches for reducing the signs and symptoms associated with obstructive sleep apnea (OSA). While both are recognized as important and are FDA-cleared devices, few studies have compared different indices of success in expansion and mandibular repositioning appliances. This retrospective study compares several indices of clinical success for both methods.

Materials and methods: A retrospective multicenter pre-post interventional study was conducted with up to a 36 month follow-up period in adults diagnosed with OSA. The DNA (Daytime-Nighttime Appliance) uses slow maxillary expansion, while the mRNA (mandibular-Repositioning Nighttime Appliance) is a combination device that adds mandibular advancement to the DNA. These devices and a therapeutic protocol comprise the Complete Airway Repositioning and Expansion (CARE) approach to treat OSA by airway expansion, improvements in sleep quality, and reduction in snoring and/or OSA severity in adults. These devices are FDA-cleared for all levels of OSA severity and can be utilized in moderate and severe OSA patients with positive airway pressure and/or myofunctional therapy, as needed. Participants were assessed for treatment efficacy by two co-primary endpoints, apnea-hypopnea index (AHI) and transpalatal width, and one secondary endpoint, airway volume by cone beam computed tomography (CBCT) scans. Safety parameters were also recorded.

Results: Eighty-seven participants treated with the DNA and 41 patients treated with the mRNA were included in the analysis after completion of at least 6 months of treatment. Transpalatal width with DNA increased 7.0% from 32.9 ± 3.1 to 35.2 ± 3.2 ($p < 0.00001$) compared with mRNA increased 6.0% from 33.5 ± 3.2 to 35.6 ± 3.4 ($p < 0.00001$). AHI with DNA decreased 46% from 22.5 ± 19.5 to 12.3 ± 11.0 ($p < 0.00001$) compared with mRNA decreased 43% from 26.8 ± 16.0 to 15.3 ± 14.0 ($p = 0.0001$). Airway volume with DNA increased 15% from 22263 ± 8651 to 25567 ± 9550 ($p < 0.00001$) compared with mRNA increased 15% from 19714 ± 6151 to 22670 ± 8171 ($p < 0.00001$). There were no serious long-term safety concerns.

Conclusions: All patients treated with mRNA showed an increase in transpalatal width while 97% of patients treated with DNA showed an increase. AHI improved or stayed the same in 91% of DNA patients and 88% of mRNA patients. AHI improved by at least 1 classification for 63% of DNA patients as compared to 61% of mRNA patients. AHI was < 5 or resolved in 28% of patients with DNA compared with 22% of patients with mRNA treatment. The addition of mandibular advancement to an expansion device did not significantly improve the clinical outcomes, indicating the benefits of slow maxillary expansion in the treatment of OSA.

Cross-sectional observational study of the impact of postoperative oral pain on sleep quality

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Introduction: To evaluate the relationship between postoperative pain and sleep quality and its impact on the quality of life of patients attending the oral surgery consultation at the University Clinic, Faculty of Dental Medicine, Universidade Católica Portuguesa in Viseu.

Materials and methods: This cross-sectional observational study included 32 patients who attended the oral surgery appointments at the University Clinic, Faculty of Dental Medicine, Universidade Católica Portuguesa in Viseu. Data were collected between 1 March and 20 May 2024 using validated subjective questionnaires. The study aimed to assess sleep quality, sleep schedule and hygiene, and oral pain. The following questionnaires were used: Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index, sleep diary and visual analogue scale. Data were entered into the Microsoft Office Excel® platform and processed using SPSS version 27 software.

Results: This study demonstrated that postoperative odontogenic pain negatively affects sleep quality, daytime sleepiness, sleep fragmentation, sleep latency, and subjective insomnia symptoms in the week following tooth extraction.

Conclusions: Sleep quality suffers a significantly high negative impact in the week following tooth extraction in all individuals in the sample, particularly in vulnerable patients. Further studies are needed to elucidate this complex and dynamic relationship between sleep and pain. Dentists need to be aware of changes in sleep quality following surgery.

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Effects of Home-Based Tongue Exercises on Tongue Strength in Older Adults: Implications for Sleep-Disordered Breathing

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Introduction: Age-related declines in orofacial muscle tone, particularly reductions in tongue strength, contribute to dysphagia and increased upper airway collapsibility during sleep—an important pathophysiological mechanism in obstructive sleep apnea (OSA). Tongue exercises (TEs) utilizing specialized devices have been proposed as effective interventions for improving tongue strength and mitigating OSA severity. However, such devices are often costly, cumbersome, and impractical for routine home use, limiting their accessibility for older adults.

Home-based TEs offer a feasible, low-cost alternative to improve tongue function without specialized equipment. Despite emerging interest in their use, the most effective home-based TE protocols for enhancing tongue strength in older adults remain insufficiently studied. This study aimed to evaluate the effects of three simple home-based TE protocols on anterior and posterior tongue strength in older adults, with potential implications for the management of sleep-disordered breathing.

Materials and methods: Thirty-six healthy older adults (aged ≥ 65 years) were randomly assigned to one of three home-based tongue exercise (TE) protocols: **tongue wrap**, **tongue corner**, or **tongue paint**. Participants were instructed to perform each exercise five times per session, three sessions per day, over a four-week period at home. Anterior tongue strength (ATS) and posterior tongue strength (PTS) were assessed using the Iowa Oral Performance Instrument (IOPI) at baseline and after the intervention period. Improvements in both ATS and PTS were recorded and analyzed to evaluate the efficacy of each TE protocol.

Results: All TE groups showed post-training gains in tongue strength. The **tongue paint** group showed statistically significant improvements in both ATS and PTS ($p < 0.05$), with mean gains of 28.70 ± 27.93 and 53.13 ± 89.96 kPa, respectively, corresponding to the greatest relative increase (30.72%). The tongue wrap and tongue corner groups also exhibited improvements (ATS: 12.75 ± 25.05 and 20.74 ± 36.14 kPa; PTS: 18.56 ± 35.53 and 9.04 ± 21.57 kPa, respectively), although changes were not statistically significant.

Conclusions: Home-based TEs, particularly the **tongue paint** protocol, significantly improved both ATS and PTS in older adults. These findings support the effectiveness of targeted, cost-free TEs as a non-invasive strategy to enhance tongue function. Strengthening tongue musculature through such exercises may contribute to improved oropharyngeal stability and potentially reduce the risk of sleep-disordered breathing in the elderly population.

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Effects of Oral Appliance Therapy on Sleep Bruxism and Sleep-Respiratory Parameters in Patients with Obstructive Sleep Apnea

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Introduction: This study aimed to investigate the relationship between sleep-related respiratory events and sleep bruxism (SB) in patients with obstructive sleep apnea (OSA) treated with oral appliance (OA) and to clarify the efficacy of OA treatment on SB.

Materials and methods: Twenty-one OSA patients (10 males and 11 females; mean age, 57.8 years $\pm$ 16.0 SD) were sequentially enrolled in this study at Fukuoka University Hospital from October 2020 to May 2025. They underwent overnight polysomnography (PSG), and their masseter muscle activity was simultaneously assessed using a wearable electromyographic device before and after OA treatment. The apnea-hypopnea index (AHI), arousal index (Arl), percutaneous oxygen saturation (SpO₂), and episodes of SB were compared before and after OA treatment. The responding group that improved AHI by more than 50% or reduced it by less than 5 after treatment (n = 10) was compared to the non-responding group with other conditions (n = 11). OSA and SB diagnoses were based on the guidelines and criteria of the AASM.

Results: OA treatment significantly reduced mean AHI from 17.3 $\pm$ 7.8 SD to 12.3 $\pm$ 10.7 SD (p = 0.008), and respiratory events during both REM and NREM sleep. The total episodes of SB, tonic, and mixed episodes also significantly decreased (p = 0.002, p = 0.034, and p = 0.002, respectively). Meanwhile, the ArI and spontaneous arousal index (SAI) during REM sleep significantly increased (p = 0.008 and p = 0.007, respectively). Additionally, the non-responding group in OA treatment showed a significant reduction in total SB episodes (p = 0.013).

Conclusions: This study suggests that SB is a pathological condition associated with multiple factors besides OSA. OA may be effective for both respiratory events and SB. Meanwhile, to understand the mechanism that causes SB and to determine the applicability of OA and maximize its therapeutic effect, further research is needed.

Effects of Sleep Position Therapy on Sleep Bruxism: A pilot study

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Introduction: It has been reported that patients with sleep bruxism (SB) have significantly more rhythmic masticatory muscle activity (RMMA) episodes when they sleep in supine position. The objectives of this study were to investigate if supine sleep position can be a phenotype associated to SB-RMMA genesis and to test if it could correct by sleep positioning device.

Materials and methods: Twelve participants with SB were recruited (4 males and 8 females, mean age 28 $\pm$ 8 years). SB was identified using criteria of the International Classification of Sleep Disorders third edition (2014). Correction of supine sleep position was done using a sleep position biofeedback (BF) device, Night Shift (Advanced Brain Monitoring). The BF device produces a vibration behind the neck 5 seconds after supine positioning. Supine sleep time and snoring time above 50 dB were also measured with this device. Grindcare (SUNSTAR), which can measure surface electromyography on a unilateral temporal muscle, was used to measure RMMA episodes per hr (RMMA frequency). Pulse Watch PMP-200 G plus (Pacífico Medico) was used to measure blood oxygen saturation, pulse rate, body movement, and then sleep state, pulse rate elevation index, and 3% oxygen depletion index. Measurements were performed at participant's home over 5 nights. The first night was for baseline/control without BF. During nights 2 to 4, measurements were taken with active BF, and on day 5 without BF. A series of questionnaires were administered each time we collected data: PSQI, Epworth sleepiness scale, STOP-BANG. The study was approved by the Ethic Review Board for Life Science and Medical Research of the University of Tokushima Hospital (No. 3534). Statistical analyses were performed for the comparison of each measurement data.

Results: Among the 12 participants, one was excluded from the analysis because the vibration did not change the sleep position. Overall, BF significantly reduced supine sleep time per sleep period time (Night 1= 33.7 to 85.6 % to Night 4= 0.2 to 8.8 %), but overall RMMA frequency did not differ. We then classified participants as responders or non-responders when a change occurred from Night 1. Six participants were classified as responders since they had a 24.1% to 85.6% decrease in RMMA frequency on the last night with BF (Night 4) versus the control one (Night 1). At the opposite end, 5 non-responders were identified; they had an increase of 3.9% to 193.9% in the RMMA frequency. None of sleep variables were statistically different between responders and non-responders.

Conclusions: Owing our small sample size, these preliminary results suggest that supine sleep position role in the genesis of RMMA-SB is not a strong phenotype since a RMMA reduction was observed in only half of participants, and that RMMA frequency was worsen in the other half. It remains to be investigated if rise in RMMA in non-responders could be associated to arousal threshold reactivity.

Acknowledgments: Night Shift and Sunstar devices were provided from respective firms. This study was supported by a donation from the Organization for People with Universities (OTSUCLE) Crowdfunding Project to Elucidate Mechanisms for the Treatment of Sleep Bruxism”.

Efficacy and Predictive Factors of Mandibular Advancement Device for Obstructive Sleep Apnea Treatment: A Preliminary Retrospective Study in Southern Thailand

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Introduction: To evaluate the efficacy of mandibular advancement devices (MAD) in reducing the apnea-hypopnea index (AHI) in patients with obstructive sleep apnea (OSA), identify predictive factors for treatment success, and assess the quality of life in OSA patients treated with MAD.

Materials and methods: This retrospective study used data from the Dental Sleep Medicine Clinic, Faculty of Dentistry, Prince of Songkla University, collected between 2009 and 2020. Patients with both pre- and post-treatment sleep test (polysomnography) data and SF-36 quality of life questionnaire results were included. Treatment outcomes were classified as either complete response (defined as an AHI reduction of > 50% and a post-treatment AHI of < 5 events/hour) or fail response (defined as (1) an AHI reduction of > 50% but a post-treatment AHI between 5 to less than 10 events/hour or (2) an AHI reduction of < 50%, or (3) an increase in AHI after treatment).

Results: Of the 217 patients, 31 met the inclusion criteria and were divided into mild (mean AHI = 9.86 ± 3.37), moderate (mean AHI = 22.27 ± 3.66), and severe (mean AHI = 61.73 ± 27.45) OSA groups, with complete response rates of 61.1%, 60%, and 33.3%, respectively. There was no significant relationship between OSA severity and treatment success. However, gender, snoring, tonsil grade, and malocclusion classification differed significantly between success and failure groups. Logistic regression identified female gender and smaller neck circumference as predictors of success. Patients also showed significant post-treatment improvements in general health, energy, mental health, and perceived health status.

Conclusions: The success rates of MAD treatment did not differ significantly among patients with mild, moderate, or severe OSA. However, female gender and smaller neck circumference were identified as key predictors of successful outcomes. Overall, patients experienced notable improvements in their quality of life, particularly in general health, energy levels, mental well-being, and perceived health, following MAD treatment.

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Examination of the relationship between blood glucose levels during sleep and sleep bruxism

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Introduction: Rhythmic masticatory muscle activity (RMMA), a biomarker for sleep bruxism (SB), is thought to be a nonspecific arousal response associated with microarousals during sleep, in which the masticatory muscle group becomes active. On the other hand, sleep is affected by glucose fluctuations such as increased sympathetic nervous system activity due to hypoglycemia during sleep. The purpose of this study was to clarify the relationship between blood glucose fluctuations during sleep and the occurrence of RMMA.

Materials and methods: This study included nine adults aged 21–54 who were aware of or had been informed about SB. Portable polysomnography was used to measure electroencephalography, electrooculogram, right masseter electromyography, pulse rate, and SpO₂. Additionally, a portable continuous glucose monitoring device was employed to measure glucose levels in subcutaneous interstitial fluid, which correlates highly with blood glucose levels, over time, with results obtained every five minutes to assess blood glucose fluctuations during sleep. The measurement period was two weeks, with the first seven days being non-interventional and the latter seven days involving dietary guidance. The carbohydrate intake for breakfast, lunch, and dinner was maintained at the same level as before the guidance, while sugary beverages, alcohol, and high-carbohydrate snacks were prohibited. Instead, low glycemic index foods with blood glucose-lowering effects were consumed as snacks. Data from days 7 and 14 after the start of measurement were analyzed. Changes in glucose concentration during sleep before and after the guidance were compared, as well as the number of RMMA episodes per hour. Additionally, to evaluate autonomic nervous system activity, RR intervals (the time interval between heartbeats) and low-frequency (LF) and high-frequency (HF) components were extracted from pulse waveforms, and frequency analysis was performed to calculate the LF/HF ratio and LF/(LF+HF). Furthermore, to evaluate sleep quality, slow-wave activity (SWA) was calculated through frequency analysis of the EEG, and comparisons were made before and after the intervention. Statistical analysis was performed by the Wilcoxon signed-rank test ($p < 0.05$).

Results: Following the intervention, nocturnal blood glucose fluctuations and the number of RMMA episodes significantly decreased (Mean $\pm$ SD: 13.9 $\pm$ 9.0 to 4.8 $\pm$ 2.4 mg/dL, 9.6 $\pm$ 3.4 to 6.6 $\pm$ 2.6 episodes/hour, respectively). Additionally, RR intervals significantly increased (0.96 $\pm$ 0.09 to 1.09 $\pm$ 0.09 seconds) and LF/HF ratio, LF/(LF+HF) significantly decreased (0.86 $\pm$ 0.32 to 0.66 $\pm$ 0.20, 0.41 $\pm$ 0.09 to 0.36 $\pm$ 0.06) were observed. It was indicated parasympathetic activity enhanced and sympathetic activity reduced. However, no significant difference was observed in SWA (84.1 $\pm$ 38.1 to 87.9 $\pm$ 50.4 μ V²/Hz).

Conclusions: It is suggested that there is a correlation between blood glucose levels during sleep and the occurrence of SB, and that controlling blood glucose levels during sleep may influence autonomic nervous activity and reduce RMMA.

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Genesis of RMMA, a biomarker of Sleep Bruxism, is mostly central since it is present in older edentate individuals

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Introduction: Sleep bruxism, characterized by tooth clenching and grinding, is associated with rhythmic masticatory muscle activity (RMMA). During sleep, RMMA is frequent and persists with aging, while self-reported sleep bruxism (SB) may decrease. Although the mechanisms of SB genesis remain under investigation, evidence supports the notion that the genesis of SB-RMMA is modulated by the central and autonomic nervous system. However, the role of peripheral sensory feedback remains unclear, as the literature presents debates, along with the role of associated conditions such as obstructive sleep apnea (OSA).

Objective: To assess the potential role of tooth sensory feedback in the genesis of RMMA in completely edentulous individuals, with and without OSA.

Materials and methods: Polysomnographic data of 24 edentulous individuals (mean age 73 years) who previously participated in a clinical trial on OSA were analyzed. (Emami E et al, Sleep 2021). Participants

were asked to sleep without their dentures for one night, with a full PSG (type 2). RMMA was scored from bilateral masseter and temporal EMG, and jaw muscle activity was classified as RMMA if it corresponded to phasic, tonic, or mixed patterns. Other oromotor activities not included above were defined as NSMA (non-specific muscle activity).

The temporal association of RMMA and NSMA with sleep arousals was recorded when they occurred within 5s of arousal and with respiratory events when they occurred within 10s after the end of apnea or hypopnea, with or without respiratory event-related arousals. The association of RMMA or NSMA with oxygen desaturation was recorded when they occurred within 15s, with or without arousal.

Participants were divided into two groups based on the apnea-hypopnea index (AHI): the OSA group with AHI > 10/h (n=14) and the control group (CTL; n=10) with AHI < 5. Mann-Whitney tests and Spearman's rank-order correlation coefficients (rs) were used for analysis.

Results: During sleep, both groups exhibited a high frequency of RMMA and NSMA. RMMA was twice as high in the OSA group (CTL: 3.0 ± 1.9 ; OSA: 6.4 ± 7.0 ; $p=0.472$), while NSMA was 1.8 times higher (CTL: 1.9 ± 1.9 ; OSA: 3.44 ± 3.0 ; $p=0.084$). However, correlations between AHI and RMMA or NSMA were not statistically significant.

Total arousals were positively correlated with RMMA ($rs = 0.513$; $p=0.010$) and NSMA ($rs = 0.547$; $p=0.006$) for both groups combined; specifically for the OSA group, RMMA showed a strong correlation ($rs = 0.789$; $p<0.001$) and NSMA showed a moderate correlation ($rs = 0.538$; $p=0.047$).

RMMA and NSMA were not correlated with AHI or the oxygen desaturation index (ODI).

However, temporal association of RMMA and NSMA were significantly ($p<0.001$) more frequently with sleep arousal in the CTL group (3.2X for RMMA and 4.2X for NSMA). Conversely, they were more frequently associated with oxygen desaturation in the OSA group (over 8.5 times).

Conclusions: The persistence of RMMA and NSMA in edentulous individuals suggests that their genesis is likely central, with an additive influence from autonomic arousal in OSA individuals. Therefore, while RMMA is a biomarker of SB, it is probably a physiological activity that is non-pathogenic in nature.

Acknowledgments: CIHR (E. Emami et al).

Interrupted CPAP therapy and dental health outcomes in obstructive sleep apnoe patients: .A craniomaxillofacial surgical view

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a highly prevalent sleep related breathing disorder characterized by hypopnea and apnea in ventilation. Obesity, age, and sex have been identified as risk factors for OSAS, and other risk factors are related to ethnicity, family history, and poor lifestyle habits (alcoholism and smoking). The positive airway pressure therapy is still first line therapy in those patients. However, many patients with OSAS cannot tolerate PAP devices, resulting in poor compliance. Failure to comply with treatment has been reported to be as high as 25 to 50%, with patients typically abandoning therapy during the first 2 to 4 weeks of treatment. Reasons for discontinuing CPAP therapy have been primarily related to issues of mask discomfort, nasal dryness and congestion, and difficulty adapting to the pressure. Patients, who do not tolerate CPAP therapy are often lost in follow-up. Several studies show as well that poor oral hygiene worsens OSAS symptoms

Materials and methods: This study examines patients who have discontinued cpap therapy in correlation with oral hygiene awareness and their dental status as a measure of overall patient compliance. Patients were divided into two groups 30 patients each:

Group A: Patients with interruption of CPAP therapy

Group B: Patients with tolerating CPAP therapy

All patients underwent questionnaires considering awareness of oral hygiene.

Results: Patients who interrupted OSAS therapy showed a statistically significantly worse awareness of their oral hygiene and a significantly worse dental status. This study shows, that poor oral hygiene and awareness for oral hygiene is related to increased dropout rates in CPAP therapy patients.

Conclusions: Therefore, OSAS patients should be screened by a dentist in advance and during CPAP therapy as well as more closely monitored by a sleep doctor as worse awareness of oral hygiene comes with worse compliance and interruption of CPAP therapy.

Investigation of the relationship between sleep bruxism and oral dryness in healthy adults

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Introduction: Sleep bruxism (SB) is defined as “a repetitive jaw muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible” during sleep. The jaw movements in SB are suspected to have a functional role in promoting salivary secretion, which decreases at night. This has led to speculation that SB may be associated with xerostomia; however, the details remain to be elucidated. We hypothesized that a greater degree of oral dryness is associated with a higher frequency of rhythmic masticatory muscle activity (RMMA), a biomarker for sleep bruxism, which may promote salivation and swallowing, thereby helping to moisten dry mucosa. The purpose of this study was to clarify the relationship between SB and two indicators of xerostomia: oral mucosal wetness and salivary secretion capacity.

Materials and methods: The study included healthy adults aged 20–60 years; those with a history of neurological, motor, or psychiatric disorders were excluded. Polysomnography was performed for two days in a sleep laboratory at a set humidity (50%) and temperature (21°C), and data from the second day were used for analysis. Electroencephalograms, electrooculograms, electromyograms (EMGs) from the bilateral mentalis, masseter, suprahyoid, infrahyoid muscles, electrocardiography, and respiratory curve were measured and recorded, along with monitor images during sleep. Sleep stages were determined from the measured data according to the criteria of the American Academy of Sleep Medicine. RMMA were evaluated from EMG data of the bilateral masseter muscles according to the method described by Lavigne et al. (J Dent Res. 1996). Swallowing events during sleep were scored based on the EMG signals from the suprahyoid and infrahyoid muscles, transient interruption of nasal airflow, swallowing sounds, and visual observation of upward laryngeal movement on audio-video monitor. The degree of oral moisture was measured before sleep, during sleep, and upon waking. The unstimulated salivary flow rate (USFR) and stimulated salivary flow rate (SSFR) were measured before sleep and upon waking. The relationships between the RMMA index (number of RMMA episodes per hour of sleep), oral wetness, and salivary secretion were examined using Spearman’s rank correlation coefficient ($P < 0.05$).

Results: Seventeen participants (10 males, 7 females, 28.2 ± 8.6 years old) were included in the study. The degree of oral moisture and USFR were not significantly correlated with the RMMA index. On the other hand, the SSFR before sleep demonstrated a significant negative correlation with the RMMA index ($\rho = -0.637$). The frequency of RMMA that occurred with swallowing per hour demonstrated a significant negative correlation with the SSFR before sleep and upon waking ($\rho = -0.703, -0.527$, respectively). Swallowing occurred significantly more frequently in the last one-third of the RMMA episodes, and the frequency of phasic and mixed types of RMMA that occurred with swallowing demonstrated a significant negative correlation with the SSFR before sleep ($\rho = -0.583, -0.511$, respectively).

Conclusions: These results suggest a relationship between SB and the ability to secrete stimulated saliva. SB may have a functional role in stimulating saliva secretion, and an increase in SSFR may alleviate SB.

Mandibular advancement devices in the treatment plan of snoring, mild and moderate obstructive sleep apnea cases

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Introduction: The syndrome of obstructive sleep apnea and snoring (SOSAS) is characterized with repetitive breathing cessations during sleep due to airway collapse. Some of patients' symptoms include moderate to severe daytime drowsiness, mood changes, memory loss and lack of concentration, vestibular and eye disorders. Mandibular advancement devices (MADs) are a type of dental intraoral prosthetic devices which pull or push the mandible in more forward (medial) position, preventing it, accompanied by the tissues around the anatomical region, from blocking the airflow. The aim of the following study was to share authors' experience treating snoring, mild and moderate OSA cases with mandibular advancement devices.

Materials and methods: A total of 110 patients with snoring, mild or moderate case of obstructive sleep apnea were included. All patients were examined by a specialist in otorhinolaryngology and sleep medicine and a physician in dental medicine in the period 01.2023-12.2024 at University medical and dental center, Faculty of Dental medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. All patients had their sleep examined with a polygraphic study. All participants had their balance and vestibular capabilities tested on a stabilometric platform. All signed written informed consent forms and completed sleep questionnaires, general diseases, present allergies and medications intake forms. The study received approval from Medical University - Varna Ethic committee.

Results: Male participants were predominantly diagnosed with a moderate form of SOSAS. Snorers were 10% of all patients. Male and female participants almost evenly accepted MADs treatment, with a slight predominance and better acceptance of the female responders (55% female versus 45% male). The most frequent complications that had arisen were breaking of the connectors pushing the mandible forward. Patients continued to experience the already mentioned by the manufacturer symptoms, such as feeling the mandible out of alignment after waking up, salivation, muscle stiffness, but all symptoms were alleviated after using the bite-help strip provided. Authors of the study report no allergic reactions to the material (polyamid) of the MADs, experienced by the patients, up to the moment. Body balance was disrupted more frequently in SOSAS cases, accompanied with more vestibular symptomatology.

Conclusions: Treating SOSAS in interdisciplinary teams of medical specialists is the standard in sleep medicine. By implementing the stated, patients received specialized and encompassing help, solving their problem.

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Minimal titration approach for mandibular advancement device treatment in patients with obstructive sleep apnea: a retrospective multicenter observational cohort study

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Introduction: Despite the widespread use of mandibular advancement devices for obstructive sleep apnea (OSA), no standardized, evidence-based guidelines exist on selecting a given mandibular protrusion at the start of mandibular advancement device (MAD) treatment. This retrospective study aimed to establish a clinically feasible and patient-specific mandibular protrusion at the start of MAD treatment for OSA, requiring none to little additional protrusion (titration) in achieving improvement in apnea-hypopnea index (AHI) and oxygen desaturation index (ODI).

Materials and methods: Patients were included with baseline AHI $\geq$ 15 events/h on type 1 polysomnography and after drug-induced sleep endoscopy with positive effects on reopening the upper airway. Digital tooth-arc imprints were taken (Trios, 3Shape, Copenhagen, Denmark). First, maximal mandibular protrusion (MMP, mm) was measured (The BiteFix, Scheu-Dental, Iserlohn, Germany) starting from maximal retrusion (MR). Then maximal comfortable protrusion (MCP, mm) was determined, starting from MR and protruding until the position where the patient experienced

increasing discomfort, repeated until reproducible.

An MAD (EVO, ProSomnus Sleep Technologies, Pleasanton, CA, USA) was manufactured from the digital scans, with the bite registration set at MCP minus 2mm (MCP-2, mm). Patients were then instructed to titrate the MAD until resolution of snoring symptoms or upon reaching physiological limits.

A 1-month post-fitting follow-up was performed by telephone, followed by a type 3 home polygraphy with MAD after 3 to 5 months of treatment.

OSA severity outcome was defined as "no OSA" (AHI<5 events/h), "mild" (5≤AHI<15 events/h), "moderate" (15≤AHI<30 events/h) or "severe" (AHI≥30 events/h).

Results: In total, 182 patients (137M/45F) from six general hospitals were evaluated.

Median [IQR] baseline AHI=21.3 [9.9]/h and ODI=18.0 [12.1]/h significantly decreased after 3-5 months of MAD use to AHI=5.6 [6.5]/h ($p<0.0001$) and to ODI=5.0 [7.2]/h ($p<0.001$).

Overall, MAD treatment resulted in 45% of patients with status "no OSA", 47% with "mild OSA," and 8% with "moderate OSA." No patients remained with "severe OSA".

In 86/182 (47% of patients) no additional titration was required. One patient needed to decrease the MCP-2 with 2mm due to cranio-mandibular transient complaints. In 33/182 (18% of patients) the MAD was additionally titrated with 1mm and in 26/182 (14% of patients) with 2mm. The starting median protrusion (MCP-2) of 9.2 [2.2]mm (corresponding to 72%MMP), increased to 10.3 [2.4]mm (corresponding to 82%MMP) upon titration.

Linear regression analysis did not show any relationship between the amount of protrusion and the percentage-wise improvement in AHI (RSquare = 0.0088) or in ODI (RSquare = 0.0011).

Conclusions: Starting MAD treatment at the patient-specific "MCP-2" protrusion position resulted in rapid and effective improvement in AHI and ODI, with 92% of patients achieving "no OSA" or "mild OSA" status.

Importantly, no significant relationship was observed between the amount of protrusion and the percentage improvement in AHI or ODI.

"MCP-2" was therefore identified as an optimal starting point, making additional titration unnecessary in nearly half of the patients.

The present findings support "MCP-2" as a clinically practical starting position for MAD treatment using ProSomnus EVO MAD.

Future research should evaluate the generalizability of "MCP-2" across other MAD designs and explore long-term treatment outcomes.

Multidisciplinary approaches to managing complex phenotypes of patients with Obstructive Sleep Apnea

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Introduction: The management of obstructive sleep apnea (OSA) is shifting toward a precision model grounded in phenotype-based strategies. Accurate phenotyping is essential for targeted treatment of adult OSA. Eckert's classification identifies anatomically collapsible airway as the primary cause, often accompanied by non-anatomical traits like poor muscle response and low arousal threshold. Within this framework, orthodontists serve a key role in identifying and addressing craniofacial skeletal phenotypes (CSPs) that contribute to airway obstruction, thereby enhancing patients' breathing and sleep quality. Additionally, orthodontists are increasingly involved in the interdisciplinary care of OSA patients who exhibit non-craniofacial skeletal phenotypes (N_CSP), necessitating a broader, more integrative treatment approach.

Materials and methods:

This study included 120 Korean adult patients (mean age: 41.5 years; range: 18–70 years) diagnosed with obstructive sleep apnea (OSA) with an apnea-hypopnea index (AHI) of ≥5. Cone-beam computed tomography (CBCT) was utilized to evaluate three-dimensional craniofacial skeletal morphology, condylar deformities, and temporomandibular joint (TMJ) space. Cross-sectional TMJ images were

analyzed to assess degenerative changes and the specific locations of bony alterations. Polysomnography (PSG) was performed to determine the severity of OSA.

Results: A total of 120 subjects were classified into four types based on condylar resorption & condylar surface remodeling. Significant differences in AHI and RDI were observed among the four OSA phenotypes, with Types I and II showing lower values compared to Types III and IV ($p < .05$). However, no significant differences were found in ODI or lowest oxygen saturation.

CBCT analysis revealed significant differences in joint space dimensions among the groups. For the right condyle, the superior joint space was significantly smaller in Type I compared to Types II, III, and IV (Type I: 2.87 ± 0.45 mm vs. Type II: 3.41 ± 0.80 mm, Type III: 3.67 ± 0.83 mm, Type IV: 3.13 ± 0.19 mm; $p < .05$), while anterior and posterior joint spaces showed no significant differences. For the left condyle, all three joint spaces—anterior, superior, and posterior—were significantly smaller in Type I than in the other types ($p < .05$).

Condylar angle measurements also differed significantly across groups. Axial angles were smaller in Types I and II on both sides, while lateral angles showed a side-dependent pattern, with higher values on the right in Types I and II and on the left in Types III and IV ($p < .05$).

Conclusions: This study demonstrated that morphological changes in the mandibular condyle, as classified by CBCT-based resorption and remodeling grades, are associated with variations in temporomandibular joint space, condylar angulation, and sleep-related breathing indices. Specifically, advanced resorption types (Types III and IV) showed reduced joint space, altered condylar angles, and higher AHI and RDI values, suggesting a potential link between TMJ structural degeneration and obstructive sleep apnea severity. These findings highlight the clinical relevance of condylar morphology in the assessment and management of patients with OSA.

Acknowledgments: Within the emerging phenotype-based precision approach, orthodontists are crucial in identifying craniofacial skeletal phenotypes (CSPs) and providing both surgical and non-surgical 3D skeletal interventions to improve airway function and sleep quality.

Multiple-night recording of sleep bruxism: Results of a novel portable electromyographic device

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Introduction: Sleep bruxism (SB) represents a form of masticatory muscle activity that occurs during sleep, characterized by both rhythmic (phasic) and non-rhythmic (tonic) movements. While commonly observed in healthy individuals, sleep bruxism may relate to sleep disorders commonly co-occurring with obstructive sleep apnea (OSA). Given their frequent patient interactions and expertise in oral health, dentists are uniquely positioned as frontline healthcare providers who can facilitate early detection of OSA. The emergence of portable, cost-effective, ambulatory devices has created new opportunities for clinicians and patients to detect and monitor sleep bruxism across multiple nights. Through comprehensive multi-night assessment of sleep bruxism patterns, healthcare providers can enhance early OSA detection capabilities and potentially prevent the progression of associated adverse health consequences.

Materials and methods: 20 subjects used a portable EMG appliance (dia-Bruxo, Biotech-Novations, Italy), measuring Masseter muscle activity, for 3 consecutive nights.

Collected variables included: number of grinding and clenching episodes, bruxism time index (BTI- how much time was dedicated to bruxing), and bruxism work index (BWI- how much muscular power was used for bruxing activity)

Results: Cronbach alpha of the studied variables was excellent to acceptable (ranging from 0.905 for BWI, to 0.73 for grinding).

Average BTI and BWI scores (3-night record) were 0.67 ± 0.55 and 0.60 ± 0.54 , accordingly. The scores were markedly higher than those published by Colonna et al. (J. Clin. Med. 2023) among Italian subjects (1 night record).

The relationship between BWI and BTI ($y = 1.01x - 0.05$, $R^2 = 0.89$) indicated that time and power magnitude of bruxism activity during sleep were in an almost strait relationship.

There were good positive correlations between the three nights of measurement: BTI (r^2 values of 0.54, 0.63, 0.80; $p < 0.05$); BWI (r^2 values of 0.57, 0.68, 0.69; $p < 0.01$); clenching (r^2 values of 0.61, 0.65, 0.81; $p < 0.01$). For grinding, there was a positive correlation between night 1 and 2 ($r^2 = 0.61$; $p < 0.01$).

Conclusions: analysis of SB over three nights reveals distinct temporal patterns for grinding and clenching behaviours; (ii) data indicate potential clinical implications for diagnosis, treatment planning, and understanding of SB pathophysiology; (iii) portable ambulatory EMG device can serve as SB screening tool along multiple-night measurements.

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Objective adherence to oral appliance therapy in patients with obstructive sleep apnea: A one-year longitudinal analysis

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Introduction: Oral appliance (OA) therapy is widely used as an alternative to continuous positive airway pressure (CPAP) therapy for treating obstructive sleep apnea (OSA). Historically, OA adherence was gauged by patient self-report, which can be unreliable. Recently, embedded microsensors in OAs have enabled objective tracking of wear time. This study analyzed one-year objectively recorded adherence data in OSA patients using sensor-equipped OAs to characterize using patterns and identify factors influencing adherence.

Materials and methods: Fifty-five OSA patients were recruited from a cohort study and underwent clinical follow-ups for a 12-month period. Patients were treated with custom-made, titratable OAs with a built-in temperature-sensitive microsensor to record nightly use. Adherence data were collected at 1, 6, and 12 months and analyzed using both intention-to-treat (ITT) and per-protocol (PP) approaches. Baseline demographic, dental, and health data (including presence of any psychological disorder) were recorded. Adherence was defined as mean use ≥ 4 hours per night (adherent) versus < 4 hours (non-adherent) in each interval. Adherence trends over time were analyzed, and logistic regression identified baseline predictors of adherence.

Results: Of 55 patients, 34 (62%) completed 12 months of follow-up (21 dropped out). Objective sensor data showed high initial use with a decline by 6 months. At 1 month, 80% were adherent (mean ~ 6.0 hours/night); by 6 months this fell to 67% (5.7 hours/night). Adherence then stabilized, with 82% of remaining patients adherent at one year (5.8 hours/night). The percentage of nights with ≥ 4 hours of use also decreased slightly (from $\sim 79\%$ at 1 month to $\sim 73\%$ at 12 months).

Multiple baseline factors influenced adherence. Being married or living with a partner, which indicating strong social support, was associated with significantly higher long-term adherence. In contrast, patients with a psychological comorbidity (e.g. depression or anxiety) had markedly lower adherence. A larger baseline overjet (i.e. greater horizontal overlap of incisors) correlated with better early adherence. Age showed a modest effect: older patients tended to maintain adherence better over time. No significant differences in adherence were observed by sex, body mass index, or baseline OSA severity.

Conclusions: OA adherence dropped in the first few months but plateaued by one year among those continuing treatment. This pattern underscores the need for early support and interventions during the initial adaptation period. Key predictors of adherence were identified with direct clinical relevance. Robust social support (e.g. having a partner) strongly favored adherence, suggesting benefits to involving family in care. Conversely, the presence of a psychological disorder was linked to poor adherence, indicating that addressing mental health is important when initiating OA therapy. Additionally, a favorable dental profile (e.g. larger overjet) may facilitate adaptation to OA use. Incorporating objective adherence monitoring in practice can help clinicians identify patients at risk of non-adherence and implement targeted strategies to improve long-term treatment success.

Real-world results of a telemedicine workflow for the treatment of obstructive sleep apnea using Mandibular Advancement Devices. A review of 2,110 cases

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Introduction: Current adoption of telemedicine consultations for diagnosis and treatment of obstructive sleep apnea (OSA), and the recent advances in single patient use home sleep testing; allow for a fully virtual workflow, improving access to efficient and affordable sleep apnea care. We reviewed our experience with patients treated with Mandibular Advancement Devices (MAD) through the BlueSleep virtual portal and workflow; and evaluated objective improvement in pre and post treatment Apnea Hypopnea Index (AHI) scores for patients with mild, moderate, and severe obstructive sleep apnea.

Materials and methods: We performed a retrospective chart review of 2,806 patients treated with MAD for OSA, over a 26 months period. 2,110 of those patients were fitted with a Prosomnus MAD. Dental considerations, medical insurance requirements, and patient preference dictated the type of MAD device used: (EVO, EVO PH, or PH). Initial consultations, home sleep tests, and follow up visits were all by telemedicine. 76% of deliveries were by virtual real time HIPAA compliant video visits, and 23% were in-person, in-office MAD deliveries. Pre and post HST (Home Sleep Apnea Test) were ordered in all patients by the medical team and shipped to patients' homes.

Results: The average age of patients treated was 42.5, with 70% males and 30% females. 36% of patients did not complete a post treatment HST despite having the HST device in their possession - these patients were omitted from the results. Average OSA post-treatment AHI improved by more than 49.6% compared to average pre-treatment AHI for the total number of patients evaluated. All severity categories showed statistically significant improvements. Severe (n=147): pre AHI 42.18 to post AHI 18.43, Moderate (n=443): pre AHI 20 to post AHI 10.12, Mild (n=455): pre AHI 9.33 to post AHI 6.03.

Conclusions: Sleep apnea diagnosis and treatment usually requires in-person visits for consultations, sleep tests, and multiple in-person visits for treatment. As a result wait times for access to sleep specialists, sleep testing, and treatment can be as long as 6 months or longer. This work flow only serves a very small percentage of the population at risk for OSA. The real world data from this report confirms that a virtual workflow including telemedicine consultations, home sleep tests shipped to patients' homes, and virtual delivery of MADs is an effective alternative to the current in-person model. The telemedicine workflow is a scalable model that is rapid, affordable, effective, and can improve access to sleep care to the one billion people affected by obstructive sleep apnea globally.

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Retrospective Analysis of the Effectiveness of a Morning Occlusal Guide (MOG) in Reducing Unwanted Dental Movements Associated with Oral Appliance Therapy (OAT) in Patients with Obstructive Sleep Apnea (OSA)

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Introduction: Introduction:

Oral Appliance Therapy (OAT) is an established treatment for snoring and mild to moderate obstructive sleep apnea (OSA), serving as an effective alternative for patients who are intolerant of continuous positive airway pressure (CPAP).¹ While OAT is generally well tolerated, it is associated with dental side effects such as reductions in overjet and overbite, proclination of mandibular incisors, and retroclination of maxillary incisors.² The use of morning occlusal guides (MOG) has been recommended to mitigate these effects. MOG encompasses a range of custom-made appliances and prefabricated devices intended to reposition the mandible into its habitual pretreatment position. These devices function by utilizing the patient's biting force to re-seat the condyles, thereby helping to reestablish and maintain the appropriate occlusal relationship in the morning following each night of OAT.³ However, the degree to which MOG use mitigates dental changes, compared with OAT alone, has not been adequately evaluated. Therefore, the present study aims to assess dental changes in OAT patients and determine whether adjunctive use of MOG reduces the magnitude of these side effects.

Materials and methods: A retrospective analysis was conducted on 28 patients with OSA (mean age 59.6 ± 12.3 years; 10 females, 18 males) treated with OAT at a private practice or the University of the Pacific orthodontic clinic. Inclusion required an OSA diagnosis, OAT treatment, and availability of digital records at two time points: baseline before OAT (T1) and follow-up after ≥ 9 months of treatment (T2; mean 21.4 ± 10.2 months).

Digital scans were analyzed with OrthoCAD to measure overjet, overbite, crowding, and intercanine/intermolar widths. Two calibrated orthodontists performed the measurements, and intra-class correlation coefficients (ICCs) were used to assess reliability. Three-dimensional superimposition was performed in CloudCompare software, with color-coded maps generated to illustrate dental changes. In addition, patients completed a follow-up questionnaire regarding OAT tolerance, symptoms, and MOG use. Descriptive statistics were calculated. Paired t-tests compared changes from T1 to T2, and independent t-tests compared consistent vs inconsistent MOG users. Nonparametric tests were applied when necessary, with significance set at $p < 0.05$.

Results: ICC values demonstrated excellent reliability (0.89–0.99). Questionnaire responses showed 92% of patients reported full-night tolerance of OAT, 58% noted reduced snoring, 24% reported tooth tenderness, 20% perceived bite changes, and 38% had discontinued MOG use. Digital model analysis from T1 to T2 showed minimal changes. Overjet (-0.2 ± 0.8 mm) and overbite (-0.1 ± 0.7 mm) decreased slightly, and arch widths remained stable ($p > .05$). Mandibular (-0.2 ± 0.4 mm, $p = .015$) and maxillary crowding (-0.3 ± 0.5 mm, $p = .007$) values became slightly more negative, reflecting a minor but statistically significant increase in crowding. Between-group comparisons showed no significant differences in any variable between consistent and inconsistent MOG users ($p > .30$).

Conclusions:

OAT was associated with minor dental changes after a mean follow-up of 21 months, including slight but significant increases in mandibular and maxillary crowding. Consistent MOG use did not reduce these effects. Longer follow-up studies are needed to clarify the role of MOGs in preventing OAT-related dental changes.

Sleep quality and daytime sleepiness is related to immune and comorbidity status in temporomandibular disorders

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Introduction: Sleep problems are well known to be interrelated with chronic pain. Temporomandibular disorders (TMD) is the second most common cause of orofacial pain but the exact mechanism underlying the disease itself and its related comorbidities is yet to be revealed. Alterations in immune status may be the shared link between TMD pain and various comorbidities including sleep problems that are commonly observed and is a main factor that lowers the quality of life of TMD patients. This study aimed to investigate levels and interrelationships among autoantibodies, cytokines, and comorbidities in TMD patients according to the level of sleep quality and daytime sleepiness to seek the possible role of sleep disturbance in the pathogenesis of inflammation and pain in TMD.

Materials and methods: Venous blood was harvested from 66 female TMD patients in their 20-30s. A battery of autoimmune indices (ss-DNA, ds-DNA, extracted nuclear antigens[SSA, SSB, Jo-1, RNP], IgG-anti-beta2-glycoprotein I antibody, anticardiolipin antibody, lupus anticoagulant, IgA, IgG, IgM and complements 3 and 4) and cytokines (interleukin [IL]-1 α , IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, IL-17, tumor necrosis factor- α , fibroblast growth factor [FGF], granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor [GM-CSF], vascular endothelial growth factor [VEGF]) were analyzed. Comorbidities were evaluated with structured questionnaires (Beck's depression index [BDI], Beck's anxiety index [BAI], Pennebaker Index of Limbic Languidness [PILL], Perceived Stress Scale, and Fibromyalgia impact questionnaire). Sleep related condition was evaluated with Epworth sleepiness scale (ESS) and Pittsburgh sleep quality index (PSQI). Collected data was statistically compared between groups with or without low quality sleep and excessive daytime sleepiness.

Results: Twenty-one patients(31.82%) had an ESS>10 and 31 patients(46.97%) had a PSQI $\geq$ 6 score. PILL($p=0.001$) and BAI($p<0.001$) scores were significantly higher in the ESS>10 group. PILL ($p<0.001$), BAI($p<0.001$), and BDI($p<0.001$) scores were significantly higher in the PSQI $\geq$ 6 group. RNP($p=0.031$) and Jo-1($p=0.037$) blood levels were significantly lower in the ESS>10 group. ESS showed significant correlation with PSQI($\gamma=0.563$, $p<0.01$), PILL($\gamma=0.601$, $p<0.01$), BDI($\gamma=0.272$, $p<0.05$, and BAI($\gamma=0.564$,

$p < 0.01$). PSQI showed significant correlation with PILL ($\gamma = 0.613$, $p < 0.01$), BDI ($\gamma = 0.516$, $p < 0.01$), BAI ($\gamma = 0.680$, $p < 0.01$), IgM ($\gamma = -0.281$, $p < 0.05$), and IL-4 ($\gamma = 0.282$, $p < 0.05$) levels.

Conclusions: Significantly higher levels of psychological problems along with altered levels of autoimmune indices and cytokines were observed in TMD patients with possible sleep disturbance. These results may point towards the existence of a nonspecific immune dysregulation and inflammation that is associated with more comorbidities in a subgroup of TMD patients with sleep issues.

Structuring Dental Sleep Medicine Education in Brazil: A Pathway Toward Specialty Consolidation and Improved Patient Care

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Introduction: Dental Sleep Medicine encompasses the diagnosis and management of conditions such as sleep-disordered breathing, sleep bruxism, and orofacial pain. Although the clinical demand for dental professionals trained in sleep-related disorders is increasing, educational frameworks in Brazil remain fragmented, limiting the development of consistent, evidence-based practices.

Materials and methods: A descriptive analysis of national educational data from the Brazilian Ministry of Education was conducted, along with a review of training programs at the which integrates Sleep Medicine, Temporomandibular Disorders (TMD), and Orofacial Pain into postgraduate dental curricula.

Results: Despite the existence of over 440,000 dentists in Brazil, Dental Sleep Medicine is not yet recognized as a formal specialty. Since 2011, only 91 dentists have been certified by the Brazilian Sleep Association. In contrast, TMD and Orofacial Pain have been recognized since 2002, with 1,660 certified professionals and 72 accredited programs. FICSAE currently offers:

- **A Lato Sensu postgraduate course in Sleep Medicine** (80 seats/year)
- **A postgraduate program in TMD, Orofacial Pain, and Sleep Dentistry** (48 seats/year)
- **Short continuing education courses** in the same domains

These programs are aligned with clinical protocols at Hospital Israelita Albert Einstein (HIAE), reinforcing a feedback loop between training and practice.

Conclusions: The consolidation of Dental Sleep Medicine as a recognized specialty depends on the implementation of structured, multidisciplinary educational programs. The FICSAE–HIAE model demonstrates how institutional investment in training can lay the groundwork for professional certification, improved interdisciplinary care, and ultimately, more effective and personalized treatment for patients with sleep-related orofacial conditions.

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Surgical Orthodontic Treatment of Patient with Moderate Obstructive Sleep Apnea

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Introduction: This case report presents a 38-year-old female who visited the hospital's orthodontic department with chief complaint of an unesthetic smile with excessive gingival display, and issues of anterior open contact and tilted mandibular molars. During routine orthodontic examination, a narrow nasopharyngeal was noted on the lateral cephalometric radiograph. The STOP-Bang questionnaire demonstrated to be a simple, practical, and reliable method identifying patients with risk of obstructive sleep apnea (OSA) in dental clinical settings. Subsequent PSG confirmed diagnosis of moderate OSA

(AHI=27.3/hr) and significantly influenced the decision making regarding non-surgical or surgical orthodontic treatment. Collaboration among healthcare providers from different specialties was essential in optimizing treatment outcomes.

Materials and methods: Complex skeletal malocclusions often necessitate an interdisciplinary approach. In addition to addressing skeletal discrepancies, the concomitant issue of compromised upper airway functions, most often in retrognathia cases, require thorough evaluation. During initial radiographic examination, a narrow nasopharyngeal airway was noted on the lateral cephalometric radiograph. To further confirm whether issues with upper airway patency were present, the STOP-Bang questionnaire was used for OSA risk screening. With a STOP-Bang score of 3/8, an otolaryngology consultation was arranged. The otolaryngologist scheduled an overnight PSG examination, and results revealed an AHI score of 27.3/hr, indicating moderate OSA. Nasopharyngolaryngoscopy was also used for examination, and tumors, cysts, lingual tonsils, or laryngeal pathology were ruled out, while tongue hypertrophy was noted. The diagnosis of moderate OSA significantly influenced the decision making regarding non-surgical or surgical orthodontic treatment.

Maxillomandibular advancement is considered one of the most effective surgical procedures in treating patients with moderate to severe OSA. Upon skeletal evaluation of the patient, maxilla retrusion was not present, and excessive advancement of the maxilla will have adverse effects on the patient's profile. Moreover, the most narrow dimension of the upper airway was identified at the retroglossal area, which is most influenced by mandibular retrusion. Hence, the surgical treatment plan prioritized advancement of the mandible and limited maxillary advancement.

Results: Based on superimposition of lateral cephalometric tracings before and after treatment, the maxilla was impacted by 2.5 mm, and point B of the mandible moved upward by 2.5 mm and forward by 7 mm. Combined with genioplasty, the pogonion moved upward by 10 mm and forward by 15 mm. The soft tissue facial contour angle improved from 24 degrees to 14 degrees.

Post-treatment PSG assessment revealed a reduction in AHI from 27.3/hr to 17.0/hr. Less daytime fatigue was reported by the patient.

Conclusions: Improvement in OSA severity following orthognathic surgery is demonstrated. AHI decreased by 37.7%, and the patient's subjective improvement (reduced daytime sleepiness) is notable, indicating a benefit in sleep quality. In surgical planning, amount of maxillomandibular advancement was limited due to esthetic considerations. Persistent symptoms suggest the need for ongoing evaluation and possibly adjunctive therapy.

The case highlights the critical role of dental professionals in screening, referral, and co-managing sleep disorders. Recognition and intervention in dental settings can lead to earlier diagnosis, improved outcomes, and a multidisciplinary approach to this prevalent but often overlooked condition.

Upper Airway Dimensional Changes Following Treatment in Patients with Temporomandibular Disorders: A Longitudinal CBCT-Based Study

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Introduction: This study aimed to evaluate changes in upper airway volume and length in patients with temporomandibular disorders (TMD) before and after treatment, and to investigate how alterations in mandibular position affect upper airway dimensions.

Materials and methods: A total of 102 patients diagnosed with TMD based on the Research Diagnostic Criteria for TMD (RDC/TMD) were enrolled. Each patient underwent clinical and radiographic evaluation, including cone-beam computed tomography (CBCT), before and after a one-year treatment. Condylar bony changes were assessed on sagittal and coronal CBCT views by dividing each mandibular condyle into nine sections and scoring the degenerative change according to presence of erosion, osteophytes, and subchondral cysts. Airway measurements were performed using AVIEW Modeler software and included volumetric and cross-sectional analyses of the velopharyngeal, oropharyngeal, and hypopharyngeal airways. Additional parameters including the anteroposterior and transverse diameters at the narrowest cross-section, total upper airway volume, upper airway length, and condylar volume were also evaluated.

Results: Of the 102 patients, 33 were classified into the improved group and 69 into the worsened group based on CBCT findings. The improved group demonstrated statistically significant increases in velopharyngeal airway volume and total upper airway volume ($p < 0.05$). In this group, the minimum anteroposterior diameters of all airway regions significantly increased following treatment, whereas the worsened group showed significant decreases in these dimensions ($p < 0.05$). Moreover, both upper airway length and condylar volume increased in the improved group but decreased in the worsened group ($p < 0.05$).

Conclusions: Improvements in condylar morphology following TMD treatment are associated with favorable changes in upper airway dimensions, particularly in the velopharyngeal region, total airway volume, and the minimum anteroposterior diameter across all regions. These findings suggest that appropriate TMD management may contribute to improved upper airway patency and potentially reduce the risk of OSA by optimizing mandibular and airway structures.

Variations of craniofacial structure and the pediatric upper airway

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Introduction: Constricted upper airway and cranio-facial structures are risk factors for sleep-disordered breathing in the paediatric population. Identification of adeno-tonsillar hypertrophy and associated cranio-facial factors require a large cross-sectional sample. Lateral cephalometric radiographs are routinely used in paediatric orthodontic screening, and have reproducible landmarks of the upper airway structure that can be assessed. The current study aims to 1) investigate for differences in airway measurements between groups of different age & gender, anteroposterior and vertical skeletal patterns, and ancestry, 2) report prevalence rates of adenoid and/or tonsillar hypertrophy, and 3) report upper airway, skeletal, dental and soft tissue cephalometric measurements in a large Singaporean paediatric orthodontic population.

Materials and methods: Consecutive lateral cephalograms of 203 boys and 201 girls ($n=404$) between 7.04 to 10.99 years of age were retrieved retrospectively, from a national dental centre. Upper airway, skeletal, dental and soft tissue variables were measured and

investigated for differences between groups based on age, gender, antero-posterior and vertical skeletal patterns, and ancestry. Prevalence of adeno-tonsillar hypertrophy was identified in this population.

Results: Mean values of various upper airway and cephalometric measurements were reported according to age and gender. Significant differences ($p < 0.05$) were noted for thirteen airway variables (Ad, Np (adenoids), Ad/Np, Op (tonsils), PM-U, SPT, NL/PM-U, PM-UPW, UMPW, PASmin, V-LPW, AH-FH, AH-CV) between groups differentiated by gender and age, six (Np (adenoids), Ad/Np, Tn, Op (tonsils), PM-U, NL/PM-U) and four (Ad, Ad/Np, NP/PM-U, AH-CV) variables between groups of different antero-posterior and vertical skeletal patterns respectively, and one variable (AH-CV) between Chinese and non-Chinese children. The overall prevalence of lymphoid tissue hypertrophy based on the lateral cephalograms was 92.3% (based on $Ad/Np \geq 0.5$ and/or $Tn/Op \geq 0.5$).

Conclusions: Mean values of various upper airway and cephalometric measurements were reported for a large paediatric orthodontic population in Singapore. Young, male, Chinese boys aged 7 to 8.99 years with Class I, Class II and high maxillomandibular plane angle had upper airway measurements that increased their risk for SDB. Greater mandibular retrusion and downward positioning were associated with adeno-tonsillar hypertrophy that restricted the paediatric upper airway.

Excessive Daytime Sleepiness (not Narcolepsy)

Assessment of wakefulness in Vietnamese patients with obstructive sleep apnea using a modified Maintenance of Wakefulness Test protocol

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Introduction: Obstructive sleep apnea (OSA) is marked by the recurrent collapse of the upper airway during sleep, causing fragmentation of normal sleep patterns and notable sleepiness during the daytime. The Maintenance of Wakefulness Test (MWT) assesses a patient's ability to stay awake in a dark environment without any external support. With this study, we aimed to evaluate the ability to maintain wakefulness among OSA patients in the Vietnamese population using a modified MWT protocol.

Materials and methods: A cross-sectional study, collecting patients from University Medical Center, Ho Chi Minh City, from November 2022 to August 2024. Adult patients with newly diagnosed, untreated OSA were recruited, excluding those on sleep-affecting medications or those with other conditions affecting alertness. Pilot testing revealed challenges with the standard MWT due to cultural napping habits, leading to protocol adaptation. The modified MWT allowed participants to nap between sessions at their usual times, required waking at least 30 minutes before each session, and subjects were not awakened if sleep occurred during the 40-minute sessions. Signals from the MWT electrodes were recorded continuously between sessions to measure the sleep latency (SL) of each session and the total sleep time (TST) during the test day.

Results: The study included 63 subjects, median age 48 (IQR 36-58), 79% male, median BMI 27.4 (IQR 25.1-29.8), 84% reported napping habits. Most of participants (71%) had severe OSA (median AHI 44, IQR 26-70). Objective MWT measurements showed average SL of 22 minutes (IQR: 11-30). A clear correlation was observed, with baseline AHI positively correlated with TST and negatively correlated with SL measured by MWT. In MWT, sleeping in session 1 increased the odds of sleeping in session 2 by 3.64 times (95% CI: 1.16, 11.9); greater TST in a preceding session was significantly associated with shorter SL in the subsequent session(s).

Conclusions: Higher TST in a preceding MWT session correlated with higher TST and shorter SL in subsequent session(s), indicating persistent difficulty staying awake, regardless of nap. The modified MWT protocol, tailored for cultural sleep practices, provides feasible and meaningful assessment of wakefulness in Vietnamese patients with OSA, thereby suggesting adaptation the MWT for countries with nap habits.

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Barcelona Sleepiness Index to Assess Subjective Sleepiness: An External Validation Study

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Introduction: Barcelona Sleepiness Index (BSI), which was validated to assess excessive daytime sleepiness (EDS) in patients with sleep disordered breathing, is a simple and brief instrument. BSI consists of two questions assessing sleepiness during rest and during activity in the previous weeks, and answers are graded from zero to three. Thus, it is easy to conduct without ambiguity compared to other widely used questionnaires. This study aimed at investigating the validity of BSI among patients with EDS and at analyzing its correlation with objective sleep measures.

Materials and methods: This retrospective study was conducted in the Centre for Sleep Medicine, Department of Neurology, Medical University Innsbruck, analyzing data acquired from 2017 to 2024. Patients who presented with subjective complaints of EDS and filled out both the Epworth Sleepiness Scale (ESS) and BSI questionnaire before undergoing two-night diagnostic video-polysomnography (vPSG) and multiple sleep latency test (MSLT) were included in the study. ESS ≥ 10 and BSI ≥ 2 points were considered abnormally increased EDS. Patients were classified into central disorders of hypersomnolence (CDH) and those without evidence of CDH (no-CDH). ESS and BSI performances were compared between the CDH and no-CDH groups.

Results: A total of 261 patients were included (mean age: 39.9 ± 15.6 , F/M: 129/132), of which 90 had CDH (27 with narcolepsy type 1, 10 with narcolepsy type 2, 11 with idiopathic hypersomnia, 42 with CDH not otherwise classified) and 171 had no-CDH. Among all patients, the median BSI score was 2, and the median ESS score was 13. Both were significantly higher in the CDH group compared to the no-CDH group (respectively, $p=0.005$ and <0.001). BSI and ESS scores correlated positively with each other ($r=0.52$, $p<0.001$). BSI showed a significant positive correlation with the presence of sleep onset REM episodes (SOREMs) in the vPSG ($r=0.24$, $p<0.001$) and the number of SOREMs in MSLT ($r=0.27$, $p<0.001$), and a negative correlation with sleep latency in MSLT ($r=-0.24$, $p<0.001$). ROC analysis revealed that ESS better discriminated CDH from no-CDH (AUC=0.74, sensitivity=0.65, specificity=0.71) compared to BSI (AUC=0.60, sensitivity=0.62, specificity=0.53). However, BSI showed a better performance than ESS to identify those with mean sleep latency <8 minutes (AUC=0.65) and to detect the presence of SOREMs (AUC=0.68) in MSLT.

Conclusions: BSI demonstrated a comparable performance for the detection of CDH and narcolepsy compared to ESS, and better performance for the determination of abnormal MSLT parameters in patients with CDH. BSI, as a brief and easily applicable questionnaire, strongly correlated with ESS scores and objective vPSG and MSLT measures related to CDH. Further studies are needed to evaluate its performance in larger cohorts and patients with different sleep disorders.

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Bordeaux Sleepiness Scale (BOSS): A new scale to predict sleep-related traffic accident in regular French highway drivers

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Introduction: Sleepiness at the wheel is a well-known risk factor for traffic accidents. The aim of this study is to explore the prevalence of sleepiness at the wheel and the risk factors associated with driving near misses and road accidents in regular French highway users. This study also compares performance of the new Bordeaux Sleepiness Scale (BOSS) (Philip et al., J Clin Sleep Med, 2023) to predict sleep-related accidents in a non-clinical population versus reference scale Epworth Sleepiness Scale (ESS).

Materials and methods: Regular French highway drivers were invited to participate in an internet survey between April-May and October-November, 2024. A total of 19,860 drivers (Mean age: 48.4 ± 12.7 years, 44.8% female) answered questions on socio-demographic characteristics, sleep behaviors, sleep disorders, lifestyle and health, substance use, driving habits, and near-accident and accident conditions. The Bordeaux Sleepiness Scale (BOSS) was used to determine the sleep-related driving risk.

Results: 29.6% reported at least one near-miss accident, and 8.8% reported at least one accident in the previous year. More than one out of three drivers (34.5%) experienced at least one episode of severe drowsiness at the wheel during the previous year (i.e., making driving difficult or forcing the driver to stop driving). Among these sleepy drivers, 41.8% reported at least one near-miss accident and 11.2% an accident in the past year. 62.4% of near-misses or accidents linked to sleepiness occurred on highways, and 54.4% on trips of over 2 hours. 71.1% of sleep-related near-misses and accidents occurred in a monotonous context (low traffic).

After adjustment for age, gender, mileage exposure and self-reported psychiatric disorders, the best predictive factors for sleep-related accidents were the occurrence of at least one episode of severe sleepiness at the wheel in the past year [adjusted odds ratio (OR) 5.9, 95% confidence interval (CI) 2.8-12.44, $P<0.001$], a BOSS score ≥ 3 [adjusted OR 3.2, 95% CI, 1.7-6.3, $P<0.01$], an Epworth score ≥ 11 [adjusted OR 2.4, 95% CI, 1.4-4.3, $P<0.01$], having total sleep time <7 h on rest days [adjusted OR 2.1, 95% CI, 1.1-3.9, $P<0.05$], being in shift work (2/8, 3/8, etc.) [adjusted OR 3.6, 95% CI, 1.4-9.3, $P<0.01$], being in social jetlag ≥ 2 hours [adjusted OR 2.1, 95% CI, 1.1-4.0, $P<0.05$], using cannabis [adjusted OR 4.3, 95% CI, 1.4-13.7, $P<0.05$] and having ever reported a near miss within the year [adjusted OR 65.0, 95% CI, 23.6-178.5, $P<0.001$].

Conclusions: Occurrence of sleepiness at the wheel still constitute a major risk factor for near misses and accidents. Poor sleep hygiene and sleep irregularity are fundamental predictors of sleep-related accidents. The occurrence of episodes of severe sleepiness at the wheel in the past year, and the

reporting of a near miss in the past year, are major risk factors for near misses and road accidents. The BOSS combining mileage exposure and self-perception of situational sleepiness is a more relevant scale than ESS to predict sleep-related driving risk in a non-clinical population.

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Connections between allergic rhinitis, floppy eyelid syndrome and the syndrome of obstructive sleep apnea and snoring

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Introduction: The syndrome of Obstructive sleep apnea and snoring (SOSAS) is a socially significant disease. It can be compared to infectious diseases with a pandemic potential. Diagnosis and treatment of the syndrome have to be carried out by interdisciplinary teams of medical specialists. Allergic conditions, including allergic rhinitis and subsequently developed nasal polyposis, are being diagnosed nowadays more often than in the past. According to recent results from scientific studies, more than 1.4 billion individuals are affected by allergic rhinitis. This floppy eyelid syndrome represents a condition in which the upper eyelids easily evert when tracted upward, leaving eyes susceptible to discomfort and vision loss. All disorders mentioned severely reduce the quality of life of patients affected.

Materials and methods: 180 patients (n) with proven symptoms of a disturbed sleep at night were thoroughly examined at Sector "Audio-vestibular and sleep medicine", University medical and dental center, Faculty of Dental medicine, Medical University – Varna. All examinations were done for the time period June 2023 - December 2024. Authors used polygraph analysis at home (HSAT) to study sleep quantity and quality, and rhinomanometry to examine the nasal breathing. All patients filled in specialized sleep questionnaires (Berlin questionnaire, ESS), assessing present symptoms of disturbed sleep, written informed consent forms, forms regarding health conditions, general diseases present, allergic status, surgical interventions in the maxillofacial region, recent hospitalizations. The study has received approval from Medical University - Varna Ethics committee (131/11.05.2023).

Results: All patients had varying degrees of severity of obstructive sleep apnea symptoms, moderate forms - 65%. 40 patients required surgical septoplasty, and 67 patients required conchotomy and radiofrequency-induced thermotherapy. It is interesting that 108 (56.67%) of all studied patients (n=180) had a proven allergy condition. The in-depth analysis of the data from patients' conditions showed that there is a significant worsening of sleep apnea symptomatology in allergic rhinitis and nasal polyposis patients. The patients who underwent surgery, got an improvement, but despite this, not a small part of them were offered CPAP-therapy and long-term treatment of the allergic condition. According to authors' results, most frequent causes of allergic rhinitis were: food, fungi, mold. Patients living in towns and in villages developed allergic rhinitis with the same frequency. More patients with allergies caused by food were diagnosed. Patients with nasal polyposis tend to snore more.

Conclusions: Associations between SOSAS and several eye diseases including floppy eyelid syndrome highlight the need for ophthalmologists to consider the syndrome in their patients and recommend future research studies. Latter is especially needed in cases when therapies for obstructive sleep apnea can be effective for ocular disorders as well. Coping with in advance with allergic conditions should be a protocol when treating all forms of SOSAS. The active prevention and treatment of SOSAS should not have a campaign character. Comorbidity in patients with proven metabolic syndrome, diabetes, hypertension and allergic conditions must be studied.

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Consensus recommendations for special challenges faced by technical personnel with elderly and very old patients in the sleep laboratory

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Introduction: Sleep disorders increase with increasing age. In the US American population 50% of all persons 65 yrs and older complain about sleep problems. Therefore, elderly patients make up a large portion of clients in the sleep laboratory with polysomnography for diagnosis and therapy. The technical staff confronted with elderly clients in the sleep laboratory faces several special challenges with this cohort, which are discussed and given recommendations to deal with them in this consensus statement.

Materials and methods: Based on the experience of challenges faced by elderly patients in the sleep laboratory, which have been revealed by consensus in an open in presence discussion of members of our assemblies (Geriatric Sleep Medicine of the German Sleep Society, Certified Sleep Technicians of the German Sleep Society and Geriatric Pulmonary Medicine of the German Society of Pneumology) at the 2024 annual conference of the German Sleep Society in Essen, Germany and written reports of members of the Certified Sleep Technicians of the German Sleep Society via email to assembly chairs, the assembly chairs voted on recommendations.

Results: The changes in electrophysiologic signals with lower amplitudes in the electroencephalogram of elderly people increase the difficulties to distinguish between sleep stages. Technicians must be aware of different normal values of sleep stage distribution, arousals, sleep efficiency and mean oxygen saturation. The automatic analysis of polysomnography devices can most often not be applied and electrophysiologic channels must be analyzed manually. The older, most often dryer skin of elderly persons leads to higher electric resistance weakening electrophysiologic signal quality.

Older sleep laboratory clients often need more care during the night and home polysomnographies are difficult to perform. Nycturia, the risk of falls and reduced cognitive function with disorientation during the night in elderly increase these difficulties.

Special challenges can come from dentures worn or taken out at night, a more often tendency to keep the mouth open during breathing, being frightened to wear a nasal or full-face mask, not understanding the procedure and the need for therapy overall and the forced influence and interventions of relatives before, during and after polysomnography. The collaboration with relatives on the other hand is often needed to perform the diagnostic and therapeutic procedures.

Conclusions: The developed recommendations by several assemblies of the German Sleep Society could be used as a hands on track for technical personnel in sleep laboratories world wide.

Decoding Excessive Daytime Sleepiness: Building a Better Questionnaire

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Introduction: Excessive daytime sleepiness (EDS) is commonly assessed using the Epworth Sleepiness Scale (ESS), although several of its items have limited clinical relevance. Other validated Patient-Reported Outcome Measure (PROMs) - Insomnia Severity Index (ISI), Beck Depression Inventory - II (BDI-II) and Pittsburgh Sleep Quality Index (PSQI) - are also frequently used to investigate aspects related to sleepiness and sleep quality.

Our goal was to identify items from the ISI, BDI-II, PSQI, and ESS most strongly associated with residual EDS (ESS > 10) in patients adherent to Positive Airway Pressure (PAP) therapy (≥ 4 h/night on 70% of nights over the past 3 months), with the aim of laying the groundwork for a new assessment tool.

Materials and methods: The questionnaires were completed by patients attending the Sleep Disorders Clinic of our institution. We first calculated the mean and standard deviation (SD) for each questionnaire item. To further assess their relevance, we then computed the Area Under the Curve (AUC), along with sensitivity and specificity for each item. Subsequently, we created a composite score based on ten selected items. The AUC of this composite scale was calculated against the ESS > 10

criterion. The optimal threshold was identified using the Youden Index, and corresponding sensitivity and specificity were computed.

Results: Data were obtained from questionnaires completed by 84 patients attending our clinic. ESS Items B and E demonstrated the strongest discriminative power (AUC = 0.919 and 0.851) and highest sensitivity (1.0 for both), while Items F and H showed the weakest performance (AUC = 0.579 and 0.615), though with high specificity (0.957 and 0.942). ISI Item 3 had the highest AUC (0.838), Item 4 was the most specific (0.746), and Item 2 the most sensitive (1.0). BDI-II items showed a more homogeneous AUC distribution, ranging from 0.758 (Item 19) to 0.539 (Item 2); Items 15 and 20 were the most sensitive (1.0 and 0.933), while Items 9 and 6 were the most specific (0.985 and 0.970). Within the PSQI, question 8 showed the highest AUC and strongest specificity, while questions 5b and 5c were the most sensitive (1.0 and 0.933). The composite scale yielded an AUC of 0.946. The optimal cut-off, identified via the Youden Index, was 15, with corresponding sensitivity of 0.867 and specificity of 0.910.

Conclusions: To ensure both sensitivity and specificity, preliminary selection may include ESS Items B, E, and H; BDI-II Items 15 and 20; PSQI Questions 8, 5b, and 5c; and ISI Items 2 and 4. This proposed selection maintains a 2:1 ratio of high-sensitivity to high-specificity items. The resulting composite scale showed excellent discriminative ability (AUC = 0.946), with an optimal cut-off of 15 (Youden Index). Since daytime sleepiness can stem from multiple factors—poor sleep quality, insomnia, mood—integrating items from different tools may improve early detection. This composite scale offers a quick, functional alternative to multiple questionnaires, especially in busy clinical settings. Further validation in independent samples is warranted.

Detection of Phoneme Sequences in Spontaneous Speech for the Characterization of Excessive Daytime Sleepiness : a new method to be compared to MSLT

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Introduction: Excessive Daytime Sleepiness (EDS) is a common symptom which is hard to evaluate objectively because of technicity of current polysomnographic recordings used (MSLT/MWT). Objective evaluation could be precious to improve accurate detection. We previously demonstrated the usefulness of voice analysis during reading tasks. To develop less intrusive measures that can be applied in everyday life, we suggest analyzing phoneme sequences during spontaneous speech—a method that, to our knowledge, has not yet been studied. Through this approach, we hope to assess errors in the articulation of phoneme sequence that may be related to EDS.

Materials and methods: First, we evaluated the performance of an automatic phoneme recognition system (HMM-TDNN) which provides both the detected phoneme and its temporal boundaries. It has been applied on the French Rhapsodie corpus, which contains prepared and (semi-)spontaneous speech. We used Token Error Rate for phoneme recognition performance and the “trackeval” tool to assess the quality of the temporal segmentation. This evaluation is extended by automatically identifying the most frequent phoneme sequences (e.g. d+a+t) using SRILM software. The HMM-TDNN system achieves acceptable results with an F-measure of 0.70 for the 10 most frequent three-phoneme sequences. These performances are further improved by regrouping phonetic units by articulatory modes (i.e., stops, fricatives, glides, nasals, and liquids for consonants; nasal, central, or front rounded/unrounded for vowels). For the 10 most frequent three-symbol sequences representing articulatory modes (e.g., stop+front_vowel+liquid), the F-measure reaches 0.80, a performance that allows further acoustic analysis.

We decided to apply this phoneme sequence detection method to the Medispeech corpus, an extension of the MSLT corpus. It includes both reading and (semi-)spontaneous speech of 34 French speakers suspected of EDS (170 recordings per speech type). It is annotated with both a subjective instantaneous measure of sleepiness (Karolinska Sleepiness Scale — KSS) and a physiological measure (Multiple Sleep Latency Test — MSLT).

Results: We calculate simple acoustic features from the articulatory mode sequences: mean and standard deviation of fundamental frequency and intensity, voicing percentage, and duration. These parameters are statistically analyzed using Linear Mixed-effects Models. The results reveal strong correlations between specific sequence parameters and clinical measures of sleepiness. For instance,

subjective instantaneous sleepiness variations (KSS) are linked to the mean intensity measured on the sequence front_vowel+liquid+front_vowel (**). Moreover, the sleep latency time measured during the MSLT correlates with variations in fundamental frequency, energy and duration measured on the front_vowel+fricative+front_vowel sequence (*). Finally, the averaged MSLT value also correlates to variations in fundamental frequency and energy measured on the same sequence (*), and the variations in duration of the stop+front_vowel+liquid sequence (*).

Conclusions: Studying articulatory mode sequences of phonemes showed promising relations with both subjective instantaneous and physiological sleepiness. These preliminary findings support the potential of this analysis method for automatic classification of EDS from spontaneous speech recordings. Moreover, other grouping (e.g. articulation place) can be studied to explore further relations with sleepiness measures.

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Dopaminergic Mechanisms Underpinning Excessive Daytime Sleepiness and Hypoglossal Nerve Stimulation Outcomes in OSA: Evidence from Transcriptomics and Animal Models

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Introduction: Since 2001, hypoglossal nerve stimulation (HNS) has been used worldwide to treat adult patients with obstructive sleep apnea (OSA). However, the long-term outcomes following HNS and the underlying mechanisms have not been comprehensively investigated, no studies have reported a persistent development course of a severe complication treatment-emergent central sleep apnea (TECSA) following HNS. Moreover, the prognostic indicators associated with successful HNS therapy to treat OSA and the occurrence of TECSA remain controversial. Therefore, this retrospective study aimed to evaluate the long-term outcomes of HNS and explore the prognostic indicators to improve clinical effectiveness and avoid complications following HNS. In addition, this study investigated underlying neurochemical mechanisms—focusing specifically on the regulation of hypoglossal motor neuron (HMN) function through integrated transcriptomic and animal model approaches.

Materials and methods: Twenty-seven patients who underwent HNS implantation since 2016 were included retrospectively. Demographic data, pre and postoperative sleep study characteristics, and device use recordings were collected. To assess daytime sleepiness, each patient completed the Epworth Sleepiness Scale (ESS); the PALM model accessed further analysis of the endotype of OSA. Possible factors influencing the success of HNS therapy and TECSA were evaluated and identified comprehensively. In parallel, a rat model of OSA with induced EDS was established. Transcriptomic and metabolomic profiling of the hypoglossal nucleus (HMN) was conducted to identify differentially expressed genes and pathways. Dopamine receptor-related signaling was highlighted and functionally validated through pharmacological modulation and electromyographic analysis of the genioglossus muscle.

Results: One year after activation of HNS, the mean baseline apnea-hypopnea index (AHI) was reduced from 34.5 ± 12.0 to 23.5 ± 16.4 , $p < 0.05$, the mean oxygen desaturation index (ODI) decreased from $31.3 \pm 14.8/h$ to 22.1 ± 12.1 , $P < 0.05$, and the success rate of treating OSA was 52.2%. The mean baseline ESS scores differed significantly between the success ($n=13$) and failure groups ($n=14$) ($p=0.03$), while no significant correlation was found between other baseline demographic characteristics, polysomnography data, and HNS device setting parameters. TECSA occurred in patients with elevated preoperative sleepiness and varied with HNS stimulation amplitude. Complementing clinical findings, further animal model experiments demonstrated that modulation of dopamine receptors within HMN significantly influenced genioglossus muscle function, suggesting a neurochemical mechanism underlying variability in HNS efficacy.

Conclusions: An elevated preoperative Epworth Sleepiness Scale score was associated with treatment outcome, demonstrating that excessive daytime sleepiness may help predict the effects of HNS. The integration of clinical, transcriptomic, and animal model data underscores the role of dopaminergic

signaling in the regulation of upper airway muscle responsiveness via HMNs, highlighting a novel neurochemical mechanism that may inform optimization of HNS therapy and the prevention of complications.

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Effects of Sleep Patterns and Daytime Sleepiness on School Attendance Among Students in Elementary and Junior High Schools

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Introduction: According to a Japanese national survey, the number of students who are chronically absent from elementary and junior high schools has reached approximately 350,000. Common reasons for absenteeism include “lack of motivation toward school life” and “irregular lifestyle habits.” Since an “irregular lifestyle” may be associated with irregular sleep behavior, understanding the amount and pattern of sleep and the degree of daytime sleepiness, and how it affects school attendance behavior, may provide valuable insights into the prevention and early intervention of school absenteeism. Thus, we aimed to clarify the relationship among (1) average sleep duration on weekdays and weekends, (2) the intensity of daytime sleepiness, and (3) frequency of attendance and absence in elementary and junior high school students.

Materials and methods: The survey was conducted among 929 elementary school (4th grade to 6th grade) and 332 junior high school students (1st grade to 3rd grade) between October 7 and November 1, 2024. Students were asked to digitally record their bedtimes and wake-up times for one week including weekends using an originally developed application. We analyzed the average sleep duration, as well as bedtime and wake-up time of their daily routines. Additionally, daytime sleepiness was assessed using the Japanese version of the Epworth Sleepiness Scale (JESS) and we analyzed the relation between sleepiness and absence and tardiness in junior high school students.

Results: The average sleep times in elementary school and junior high school students were 8.7±1.1 hours and 7.3±1.2. The average JESS score across the sample was 4.4 for elementary school students and 7.7 for junior high school students and 8.3% of the elementary school students and 25.9% of junior high school students scored ≥ 11, indicating excessive daytime sleepiness.

Junior high school students were divided into two groups based on their JESS scores. Group 1: JESS ≥ 11, and Group 2: JESS ≤ 10. A comparison was made between the average monthly number of absences and tardiness based on annual data, revealed that students in Group 1 had significantly more absences and instances of tardiness than in Group 2 (absence: 10.7 days vs 7.1 days: $p < 0.01$, tardiness: 7.4 days vs 4.2 days: $p < 0.01$).

The average sleep duration over one week and the JESS score showed a negative correlation ($p < 0.01$). In particular, students who averaged less than 6 hours of sleep had a significantly higher proportion of JESS scores of 11 or above.

Conclusions: In this study, it was found that sleep time was progressively shortened with age and approximately one in four junior high school students felt sleepy during the day. A higher rate of absenteeism and tardiness was observed, especially among the students who slept less than 6 hours or who felt sleepy. As the sleep habits of junior high school students were closely related to their school attendance status, screening for irregular or insufficient sleep using user-friendly application might be highly effective method to detect the abnormal sleep patterns and perform the preventive supports in order to minimize the absenteeism and tardiness.

Exploring SLEEPINESS through home monitoring with ultra long-term subcutaneous EEG and Ecological Momentary Assessment in sleepy treatment naïve obstructive sleep apnea patients starting CPAP treatment

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Introduction: Excessive Daytime Sleepiness (EDS) is a key symptom for patients with Obstructive Sleep Apnea (OSA). Despite important limitations in the longitudinal monitoring of EDS, the Epworth Sleepiness Scale (ESS), Maintenance of Wakefulness Test (MWT), and Multiple Sleep Latency Test (MSLT) are the best available objective tests to predict EDS. Limited information exists on the day-to-day fluctuations of sleepiness symptoms from the everyday life perspective of OSA patients. The most feared is sudden sleep episodes causing traffic accidents. The following study protocol investigates the novel possibilities of Ultra Long-Term EEG (ULT-EEG) home monitoring in sleepy OSA patients with a subcutaneous implant.

We hypothesize that the high-frequency testing from ULT-EEG, in combination with Ecological Momentary Assessment (EMA), can provide the information to develop new electrophysiological monitoring of sleep propensity as an alternative to the well-established yet subjective Epworth Sleepiness Scale.

Materials and methods: This clinical exploratory and experimental study includes 15 treatment-naïve patients with severe OSA with a baseline ESS above 10. The subjects will be implanted with a two-channel subcutaneous EEG monitoring device upon inclusion and a confirmative Polysomnography (PSG) and Multiple Sleep Latency Test (MSLT). 24/7 subcutaneous EEG is recorded 6 weeks before CPAP treatment and 6 weeks during CPAP treatment. Daily assessments with the Karolinska Sleepiness Scale (KSS), Psychomotor Vigilance Task test (PVT), and a sleep/nap diary will be collected using EMA methods.

Results: Data collection in process. We present preliminary results on ULT-EEG compliance from the 12-week data collection period.

Conclusions: This study combines data collection from sleepy OSA patients' natural environments by ULT-EEG and EMA methods to obtain sleepiness metrics suitable for developing and preliminary validating the possibilities of ULT-EEG sleepiness monitoring. We aim to prove a new concept of monitoring sleepiness symptoms in OSA patients and gain new insights into CPAP-related sleepiness rehabilitation.

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Investigation of Sleep Architecture and Individual Traits Associated with the Discrepancy Between Subjective and Objective Sleepiness: A Retrospective Observational Study

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Introduction: Excessive daytime sleepiness (EDS) is a common complaint in sleep clinics. However, some patients who report pronounced subjective sleepiness show no objective signs of sleepiness when evaluated using tools such as the Multiple Sleep Latency Test (MSLT). This discrepancy remains poorly understood and poses diagnostic challenges. While physiological assessments play an important role, they do not always reflect patients' real-world experiences. This study aimed to investigate how the discrepancy between subjective and objective sleepiness relates to sleep architecture, as measured by polysomnography (PSG), and individual characteristics. The study was approved by the Kurume University Ethics Committee (No. 22237).

Materials and methods: We retrospectively analyzed medical records of patients who visited Kurume University Hospital between 2020 and 2023 with complaints of EDS and underwent overnight PSG and daytime MSLT. From these, 153 patients (mean age: 24.8 ± 13.3 years) who had an Epworth Sleepiness Scale (ESS) score ≥11 and a mean sleep latency >8 minutes on MSLT were selected. Statistical comparisons were conducted for age, sex, PSG parameters (sleep latency, sleep efficiency, REM latency, WASO, total sleep time, and slow wave sleep [SWS] time and percentage), as well as

neurodevelopmental traits and other characteristics. Correlation, regression, and mediation analyses were performed, including stratified logistic regression by age group.

Results: The discrepancy group showed significantly higher SWS time and SWS percentage, and longer REM latency (all $p < 0.005$), with no significant differences in other PSG parameters, including WASO. No significant associations were found with questionnaire measures (BDI-II, ISI-J, ASRS, AQ-J-10, MEQ-SA). SWS% was positively correlated with MSLT latency ($r = 0.185$, $p = 0.0002$), whereas ESS showed only a minimal association ($r \approx -0.12$, $p = 0.02$, $<2\%$ variance). In multivariable models, SWS% and REM latency remained independent predictors of longer MSLT latency. However, when discrepancy was used as the dependent variable, age and AHI—but not SWS%—were significant predictors. Stratified regression revealed that discrepancy was mainly associated with SWS% in patients ≤ 18 years, whereas AHI emerged as the predictor in those ≥ 19 years. Discrepancy tended to widen with greater SWS and shrink with higher AHI. Mediation analysis further indicated that the effects of AHI and age on discrepancy were largely mediated through changes in SWS.

Conclusions: Patients who reported subjective but not objective sleepiness exhibited a favorable sleep profile with more deep sleep and longer REM latency. Although SWS was associated with longer MSLT latency, age and AHI—not SWS—were the main predictors of discrepancy. The contribution of ESS and other questionnaire-based measures was negligible. Discrepancy widened with abundant SWS and diminished with higher AHI, suggesting age-dependent mechanisms: preserved deep sleep in younger patients and respiratory disturbances in older patients. This single-center cross-sectional study relied on self-report questionnaires for patient traits and may have unmeasured confounders; multicenter studies are needed to validate these findings.

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Less Sleepy, More Success: Chronotype and Insomnia Patterns Distinguish High-Achieving Adolescents

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Introduction: Chronotype and sleep disorders have been linked to learning outcomes, yet data from South-Asian school settings remain sparse.

Furthermore, few studies have jointly assessed **chronotype, sleepiness, and academic achievement** using validated instruments within a real-world school context.

We examined how morningness–eveningness, subjective sleepiness, insomnia severity, and body mass index (BMI) relate to academic achievement in Indian adolescents preparing for high-stakes board examinations.

Materials and methods: This cross-sectional study included **470 students from Classes 10 to 12** enrolled in a co-educational school in North India. Participants self-reported their sleep characteristics using standardized tools: the **reduced Morningness–Eveningness Questionnaire**, the **Cleveland Adolescent Sleepiness Questionnaire**, and the **Insomnia Severity Index**. Anthropometric data (height and weight) were recorded to calculate **Body Mass Index (BMI)**. Academic performance data from final-term examinations were used to classify the top quintile of students ($n = 114$) as the **high-achiever group**.

Group comparisons were conducted between high achievers and the general cohort.

Results: High-achieving students demonstrated a significantly greater morning orientation compared to their peers ($p < 0.001$), alongside lower daytime sleepiness ($p = 0.003$) and virtually no cases of severe insomnia (1.8% vs 19.7%). Despite having a higher average BMI ($p < 0.001$), this group reported fewer sleep-related impairments. Spearman correlation analyses revealed that greater morningness was associated with both lower sleepiness ($\rho = -0.275$, $p < 0.001$) and reduced insomnia severity ($\rho = -0.239$, $p < 0.001$). Notably, sleepiness strongly correlated with insomnia symptoms ($\rho = 0.449$, $p < 0.001$), reinforcing the interdependence of circadian alignment, sleep quality, and daytime functioning in determining academic outcomes.

Conclusions: A pronounced morning chronotype, lower daytime sleepiness, and a virtual absence of severe insomnia characterised academically successful students, independent of sex distribution and despite their higher BMI. The inverse correlations between morningness and both sleepiness and insomnia underscore the protective role of circadian alignment for daytime alertness and sleep health.

These findings support implementing circadian-friendly school start times and targeted sleep-health programmes to foster academic performance in South-Asian adolescents.

Acknowledgments: We want to extend our heartfelt gratitude to all the participants who took part in this study.

Long-Term Clinical and Functional Evolution in Patients with Obstructive Sleep Apnea and Daytime Sleepiness Treated with CPAP: Results from the HYPNOSA Cohort Study

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Introduction: Obstructive Sleep Apnea (OSA) associated with Excessive Daytime Sleepiness (EDS) is a highly prevalent clinical phenotype with significant impact on physical and psychological wellbeing. The HYPNOSA study aims to characterize this phenotype and evaluate the evolution of symptoms, quality of life, and physiological parameters under CPAP therapy. This abstract presents descriptive interim findings at 6, 12, and 24 months of follow-up.

Materials and methods: HYPNOSA is a prospective, multicenter observational study including 616 patients diagnosed with OSA and EDS. Patients were evaluated at baseline and followed at 6, 12, and 24 months. Collected data included demographics, respiratory sleep parameters (AHI, CT90, mean SatO₂), ESS, EuroQol-5D, FOSQ, HADS, and CPAP adherence. Analyses were conducted using R v4.4.2.

Results: The population had a mean age of 55.6±11.5 years; 65.6% were male. Baseline sleep study showed severe OSA (mean AHI: 39.5/h), oxygen desaturation (SatO₂: 91.4%) and prolonged hypoxic burden (CT90: 21.7%).

Baseline clinical scales revealed a high burden of symptoms:

- **Epworth Sleepiness Scale (ESS):** mean 10.9 (P50: 11), with most reported sleepiness while watching TV (2.06±0.95) and lying down in the morning (2.22±0.98).
- **EuroQol-5D:** moderate limitation in mobility, pain, and daily activities (mean ~1.5), with anxiety/depression as the most impaired domain.

- **FOSQ:** mean score of 92.1 ± 24.4 , with marked functional impairment; 20 of 30 items scored >3.2 (quite a bit/much), especially in concentration, household chores, and keeping pace with peers. Lowest was general activity (2.69 ± 1.1).
- **HADS:** total score 12.07 ± 7.24 , indicating frequent symptoms of anxiety and low mood.

At 6 months, improvements were substantial:

- **ESS:** 7.95 ± 4.61 , with reduction in most somnolence items.
- **EuroQol-5D:** improved to 73.5 ± 16.5 , pain remained most reported limitation.
- **FOSQ:** increased to 100.07 ± 21.3 , 29/30 items >3.4 ; lowest again was general activity (2.8 ± 1.04).
- **HADS:** reduced to 4.17, indicating low-mild psychological symptoms.
- **IAH:** decreased to 3.2/h; **CT90 fell to 0.5%;** **SatO₂ improved to 95%;** average CPAP use: 6.2 h/night.

At 12 months, this trend continued: ESS 7.19; HADS 2.04; FOSQ 101.5; EQ-5D 72.5. At 24 months (in limited data), results remained stable: ESS 6.67, HADS 0.05, FOSQ 109.7, EQ-5D 76.7. CPAP adherence was consistently above 5.3 h/night.

Conclusions: Despite being relatively young and without major comorbidities, patients with OSA and EDS present with significant functional, emotional, and quality-of-life impairment. CPAP treatment leads to rapid and sustained improvement in sleep physiology, daily functioning, and psychological wellbeing. However, some limitations—especially general activity—persist. These findings support the value of long-term follow-up and structured management in this clinical phenotype.

Pitolisant for Excessive Daytime Sleepiness in Prader-Willi Syndrome: Phase 2 Study Results and Phase 3 Clinical Trial Design

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Introduction: Prader-Willi Syndrome (PWS) is a complex genetic disorder with symptoms that include hyperphagia, behavioral disturbances, and excessive daytime sleepiness (EDS). Pitolisant is approved in the United States for the treatment of EDS or cataplexy in adults with narcolepsy and the treatment of EDS in pediatric patients ≥ 6 years of age with narcolepsy.

Materials and methods: In a phase 2, proof-of-concept study (which was not powered to show statistical significance), patients with a confirmed diagnosis of PWS and a score ≥ 12 on the parent/caregiver version of the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) were randomized to receive higher-dose pitolisant, lower-dose pitolisant, or placebo (dose based on age group) for 11 weeks (3-week titration, 8-week stable-dose). The primary efficacy endpoint was change from baseline at Week 11 in ESS-CHAD score. Secondary/exploratory endpoints included the Caregiver Global Impression of Severity (CaGI-S) for EDS, Aberrant Behavior Checklist-2 (ABC-2), and Hyperphagia Questionnaire for Clinical Trials (HQ-CT; in conjunction with the Food Safe Zone Questionnaire).

Results: Among 65 enrolled patients in the phase 2 study (50.8% male), 34 (52.3%) were children (6 to <12 years), 19 (29.2%) were adolescents (12 to <18 years), and 12 (18.5%) were adults (≥ 18 years). Overall, mean (SE) change in ESS-CHAD score at Week 11 was greater in the higher-dose (-4.9 [1.23]) and lower-dose (-4.1 [1.06]) pitolisant groups compared with the placebo group (-3.7 [1.13]). There was an unusually large placebo response in the adolescent age group, due to data from a single outlier. Reductions in CaGI-S scores and HQ-CT scores were greater for pitolisant compared with placebo in the children and adult age groups. In children (6 to <12 years), mean reduction in all ABC-2 domain scores (irritability, social withdrawal, hyperactivity/noncompliance, inappropriate speech, stereotypic behavior) was greater for higher-dose pitolisant compared with placebo. The most common adverse events in pitolisant-treated patients (doses pooled) were irritability (17.4%) and anxiety (13.0%). The design of a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial (TEMPO;

NCT06366464) was informed by the results of the phase 2 study. The phase 3 trial is currently enrolling approximately 130 patients ≥ 6 years of age with PWS and EDS. Patients are randomly assigned (1:1) to receive pitolisant (weight-based dosing: 8.9-44.5 mg/d) or matching placebo tablets. The primary endpoint is change from baseline at Week 11 in EDS as measured by the PROMIS-SRI (Patient-Reported Outcomes Measurement Information System - Sleep Related Impairment [Parent Proxy]). Secondary endpoints include the ESS-CHAD, CaGI-S for EDS, Clinician Global Impression of Severity (CGI-S) for EDS, ABC-2, and HQ-CT.

Conclusions: In a phase 2 proof-of-concept study, pitolisant reduced EDS in patients with PWS. Pitolisant may also reduce behavioral disturbances and hyperphagia. The ongoing phase 3 clinical trial is further evaluating the efficacy and safety of pitolisant in a larger population of patients ≥ 6 years old with PWS and EDS.

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Posturographic findings in patients suffering from the Syndrome of Obstructive Sleep Apnea and Snoring

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Introduction: The Syndrome of obstructive sleep apnea and snoring (SOSAS) is a well-known socially significant disease, with severe repercussions on the quality of life of affected individuals. It is characterized by the presence of cessations in patients' breathing during sleep, leading to intermittent hypoxia and multiple awakenings. In addition to the negative impact on the cardiovascular, endocrine, respiratory, cognitive, the impact of impaired blood oxygenation on the audio-vestibular system is being intensively studied nowadays.

Materials and methods: For the period from January to December 2024, 100 patients (50 female and 50 male) with complaints of disturbed sleep, daytime sleepiness, fatigue, passed through the Sector "Audio-vestibular and Sleep Medicine" of the University Medical and Dental Center at Medical University - Varna. All patients included in the study completed both standard questionnaires for the assessment of symptoms related to sleep disorders (Berlin questionnaire, ESS), as well as those specifically developed for the purposes of the study. Information on the presence of allergies, common diseases, surgical interventions in the maxillofacial area, and medication intake was collected. A polygraphic sleep study at home was conducted. All patients were also tested on stabilometric equipment to assess their ability to maintain body balance. The information obtained was statistically analyzed using the SPSS software package.

Results: Different forms of obstructive sleep apnea, according to the values of the apnea-hypopnea index (the lowest established value was 3, the highest - 75) from the polygraph examination, the anamnesis taken and the completed sleep assessment questionnaires. SOSAS was identified in a total of 77 (76.5%) of the examined patients (45 males and 32 females). In 23 patients, only snoring was proven. Statistically significant deterioration of the dynamic postural status parameters (weight distribution between the two feet, length of the sway curve (stabilogram) and area of the maximum stability) was found in patients with a proven form of obstructive sleep apnea. A pronounced deterioration of the body balance and an increase in the values of the length of the stabilogram and the area of maximum stability were observed, with more pronounced changes being found in males.

Conclusions: Complete and thorough diagnostics of all the effects of SOSAS on patients allows for timely therapeutic measures to be taken in order to improve the quality of life of those affected.

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Primary Efficacy and Safety Results of a Phase 2, Double-Blind, Placebo-Controlled, Proof-of-Concept, Signal Detection Study of Pitolisant in Myotonic Dystrophy

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Introduction: Myotonic dystrophy type 1 (DM1) is the most common muscular dystrophy in adults. DM1 presents with multi-systemic symptoms including excessive daytime sleepiness (EDS) and fatigue, which occur in up to 80-90% of patients with DM1 and can impact daily functioning as much as muscular symptoms (myotonia and muscle weakness). DM1 may have direct effects on CNS sleep regulatory circuits, with patients exhibiting signs of central sleep-wake dysregulation. Pitolisant is a histamine 3 receptor antagonist/inverse agonist approved in the US for the treatment of EDS or cataplexy in adults with narcolepsy and the treatment of EDS in pediatric patients ≥ 6 years of age with narcolepsy. The aim of this phase 2 proof-of-concept study was to evaluate the efficacy and safety of pitolisant in adults with DM1.

Materials and methods: Eligible patients were enrolled into an 11-week double-blind phase. Patients were randomized (1:1:1) to lower-dose pitolisant, higher-dose pitolisant, or matching placebo. The primary efficacy endpoint was the change from baseline to Week 11 in Daytime Sleepiness Scale (DSS) score. Additional efficacy endpoints included changes in daytime sleepiness as measured by the Epworth Sleepiness Scale (ESS) and Clinical Global Impression of Severity (CGI-S) as well as changes in the Fatigue Severity Scale (FSS). Upon completion, eligible patients had the option to enroll in an open-label extension phase.

Results: A total of 30 patients aged 18-65 with DM1 were randomized in the study. The mean change from baseline in DSS score at end of the double-blind period was -3.8 and -1.8 for the higher- and lower-dose pitolisant groups, respectively, compared with 0.0 for placebo. Clinically meaningful improvements in ESS, CGI-S, and FSS scores were also demonstrated for pitolisant. A clear and consistent dose-response was observed, with the higher-dose pitolisant group showing a greater response than the lower-dose group. The most common adverse events were headache, insomnia, and nausea.

Conclusions: Pitolisant reduced EDS in adults with DM1 in a dose-dependent manner. The safety and tolerability profile of pitolisant in patients with DM1 was consistent with the known safety profile of pitolisant.

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Reduction in Sleep Inertia and Components of Daytime Sleepiness in Idiopathic Hypersomnia With Low-Sodium Oxybate Treatment in the Phase 4 DUET Study

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Introduction: Idiopathic hypersomnia is characterised by excessive daytime sleepiness and, in many patients, sleep inertia, including prolonged difficulty awakening, repeated returns to sleep, irritability, and/or confusion. Low-sodium oxybate (LXB, Xywav[®]) is approved in the United States to treat idiopathic hypersomnia in adults and excessive daytime sleepiness or cataplexy in patients ≥ 7 years of age with narcolepsy. Jazz DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) was a phase 4, prospective, multicentre, single-arm, multiple-cohort, open-label study (NCT05875974) evaluating LXB treatment effectiveness for daytime and nighttime symptoms of idiopathic hypersomnia or narcolepsy. The aim of the present analysis was to estimate the magnitude and temporal dynamics of sleep inertia and components of daytime sleepiness in participants with idiopathic hypersomnia treated with LXB.

Materials and methods: DUET included the following periods: screening (with 2-week washout for oxybate users), 8-day baseline (BL), 2- to 8-week LXB titration, 2-week stable dose, 8-day end of treatment (EOT), and 2-week safety follow-up. Exploratory endpoints included Psychomotor Vigilance Test (PVT; objective measure of behavioural alertness) and Karolinska Sleepiness Scale (KSS; subjective measure of sleepiness). The PVT and KSS were administered on day 8 of BL and EOT, after overnight polysomnography. The 10-minute PVT, a reaction-time task requiring participants to respond as quickly and accurately as possible to a visual stimulus, was completed 10, 40, and 90 minutes after polysomnographically assessed awakening. The KSS, a single-item, 9-point scale ranging from “extremely alert” to “extremely sleepy, can’t keep awake” was completed within 2 minutes after awakening and immediately before and after each PVT assessment. Nonlinear, mixed-effects regression models on PVT lapses (reaction times >500ms) and KSS ratings were used to estimate objective behavioural alertness and subjective sleepiness, respectively, at awakening and 2 hours after awakening, as well as the magnitude of sleep inertia (the portion of behavioural alertness or subjective sleepiness that dissipates after awakening). The model accounted for systematic inter-individual differences and heteroskedastic error variance. *P* values are nominal.

Results: Forty-six people with idiopathic hypersomnia enrolled and took LXB for ≥ 1 night. Most enrolled participants were female (80.4%) and White (84.8%); mean (SD) age was 38.1 (11.8) years. PVT results ($n=40$) indicated improvement from BL to EOT in behavioural alertness upon awakening (PVT lapses, 16.5 to 3.1; change [95% confidence interval, CI]: -13.4 [$-19.3, -7.6$]; $P<0.0001$) and after 2 hours (9.6 to 3.0; change [95% CI]: -6.6 [$-9.6, -3.6$]; $P<0.0001$) and improvement in sleep inertia magnitude (change [95% CI]: -13.7 [$-19.8, -7.6$]; $P<0.0001$). KSS results ($n=40$) indicated reduction from BL to EOT in subjective sleepiness upon awakening (KSS rating, 6.9 to 4.4; change [95% CI]: -2.5 [$-2.9, -2.1$]; $P<0.0001$) and after 2 hours (6.2 to 4.4; change [95% CI]: -1.8 [$-2.2, -1.4$]; $P<0.0001$), and improvement in sleep inertia magnitude (change [95% CI]: -5.0 [$-5.5, -4.5$]; $P<0.0001$). Treatment-emergent adverse events were consistent with the known LXB safety profile.

Conclusions: Compared with baseline, participants with idiopathic hypersomnia on optimised LXB treatment demonstrated reduced sleep inertia magnitude, less daytime sleepiness, and increased behavioural alertness.

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Residual Excessive Daytime Sleepiness in CPAP-Treated OSA Patients: A Retrospective Study from a Tertiary Australian Hospital

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Introduction: Obstructive sleep apnoea (OSA) is a frequent cause of excessive daytime sleepiness (EDS). EDS impairs quality-of-life and can lead to motor vehicle accidents and/or workplace injuries. CPAP (continuous positive airway pressure) is the gold standard treatment for OSA but up to 22% of CPAP-treated OSA patients report residual EDS on follow-up. The causes of residual EDS are multifactorial and can be broadly categorised into: 1) ineffective CPAP treatment, 2) another sleep disorder contributing to EDS, 3) medical disorders causing EDS, and 4) persistent EDS with no clear aetiology. Identifying the underlying cause(s) of residual EDS is essential for improving treatment adherence and patient quality of life. Despite increasing awareness, there is limited real-world data on the prevalence and causes of residual EDS in CPAP-treated OSA patients in Australian clinical settings, highlighting the need for this study.

Materials and methods: This retrospective study was conducted at Gold Coast Hospital University Hospital (GCUH), a tertiary referral centre with a catchment population of over 600,000 people across South-East Queensland and Northern New South Wales regions of Australia. Medical records were reviewed for patients aged ≥ 18 years who presented to the GCUH Sleep Medicine Outpatient Clinic with an OSA diagnosis between 2019-2024 (inclusive). Residual EDS was defined as Epworth Sleepiness Scale (ESS) of >10 or patients' subjective complaint of significant residual daytime somnolence during their post-CPAP commencement clinic review. Data collected included demographics, diagnostic modality, CPAP therapy details, co-morbidities and investigations/treatments for persistent EDS.

Results: Out of 354 patients treated for OSA at our sleep clinics, 35 (10%) reported residual EDS following CPAP commencement. The median age of these patients was 58 years (IQR 53-75 years), with 60% (n=21) being male. Nearly half (46%) had chronic pain or a mental health disorder as a co-morbidity. Median ESS and Apnoea-Hypopnoea Index (AHI) at OSA diagnosis were 14 (IQR 10.5-17) and 31.7 (IQR 20.5-51), respectively. Most patients (n=20) had a home-based diagnostic study while the majority (n=24) also had a lab-based CPAP titration. Six patients required in-lab CPAP titration, and three underwent vigilance testing to assess for central hypersomnolence disorders. Multiple contributing factors were identified in eight patients, with insomnia (n=7) being the most common. Other frequent causes included mask fit issues, inadequate pressure, and CPAP discomfort. Two patients were prescribed modafinil: one had a mean sleep latency (MSL) <8mins on vigilance testing (with no sleep-onset Rapid Eye Movement periods) but also had post-traumatic stress disorder and insomnia, while the other had a normal MSL.

Conclusions: Insomnia, a common co-occurrence with OSA, was the leading contributor to post-CPAP residual EDS in our cohort. Early screening and management with cognitive behavioural therapy and sleep hygiene strategies may improve patient quality-of-life. Chronic pain and mental health co-morbidities, which were prevalent in this group, can fragment sleep and should be identified at initial screening. CPAP intolerance and mask related issues remain global challenges, and limited access to lab-based titration and sleep scientist clinics may hinder timely resolution. Overall, post-CPAP residual EDS is often multifactorial and requires a systematic assessment and individualised approach.

Sexual dysfunction in men with Obstructive Sleep Apnea: The role of self-reported sleepiness in a population-based study

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Introduction: Sexual dysfunction is common in middle-aged and older men and may be underrecognized in those with obstructive sleep apnea (OSA), a prevalent but often undiagnosed condition in the general population. In recent years, excessive daytime sleepiness (EDS) in OSA has been linked to increased risk of adverse health outcomes, including cardiovascular and metabolic diseases, suggesting that EDS may reflect underlying mechanisms contributing to these outcomes. However, the relationship between OSA, sleepiness, and sexual dysfunction remains unclear. This study aimed to examine the association between sexual dysfunction and OSA, with a focus on self-reported sleepiness in a population-based male sample.

Materials and methods: This cross-sectional study used data from the Respiratory Health in Northern Europe (RHINE) cohort, a population-based, multicenter study conducted in Tartu (Estonia), Reykjavik (Iceland), Bergen (Norway), and Aarhus (Denmark). It included 1,700 men (mean age 61.0 years) who completed the Aging Males' Symptoms (AMS) questionnaire and provided data on OSA-related symptoms and relevant health covariates. For a description of the RHINE cohort, see PMID: 38256560. Diagnosed OSA was based on self-report, and suspected OSA was defined using the Multivariable Apnea Prediction (MAP) index (score >0.5 = high OSA risk). Subjective sleepiness was assessed using the Epworth Sleepiness Scale (ESS >10 = "risk of dozing") and self-report of "feeling sleepy" ≥3 days per week. These indicators defined four sleepiness phenotypes: non-sleepy, risk of dozing only, feeling sleepy only, and both symptoms. Associations between OSA, sleepiness phenotypes, and sexual dysfunction were analyzed using multivariable logistic regression adjusted for age, BMI, smoking, diabetes, hypertension, cardiovascular disease, and study center.

Results: Among the 1,700 participants, 13% reported a previous OSA diagnosis, and 77% of these were receiving current OSA treatment. Among those without diagnosed OSA, 45% met criteria for suspected OSA (MAP > 0.5). Sexual dysfunction was significantly more prevalent among men with suspected or diagnosed OSA compared to those without. In multivariable logistic regression, men with suspected

OSA reporting “both risk of dozing and feeling sleepy” had the highest odds of sexual dysfunction, with adjusted odds ratios (ORs) of 4.71 (95% confidence interval [CI], 3.32–6.68) for decreased morning erections and 3.82 (95% CI, 3.09–4.71) for decreased libido. In contrast, classic OSA symptoms such as snoring, gasping, and witnessed apneas showed no associations with sexual dysfunction.

Conclusions: Subjective sleepiness is strongly associated with sexual dysfunction in men with OSA, independent of traditional cardiometabolic risk factors. The combination of an elevated ESS score and frequent self-reported sleepiness may serve as a valuable clinical marker for identifying male OSA patients at heightened risk of sexual dysfunction. Incorporating sleepiness assessments into clinical evaluations for OSA may improve recognition of men at risk for broader health consequences.

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The Infamous Kleine-Levin Syndrome: An Unusual Response to Modafinil in a Teenage Female

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Introduction: Kleine - Levin Syndrome (KLS) is a rare sleep disorder, characterized by intermittent episodes of hypersomnia that correspond with changes in cognition, mood and behavior. Here we present the case of a young patient with episodic periods of hypersomnolence suspicious for KLS. Modafinil was utilized as an abortive measure with improvement of hypersomnolence and thus far has served as a preventative measure for new episodes as well.

Materials and methods: A 16 year old female, with a history of headaches and intermittent fatigue presented to the sleep clinic for periods of sleepiness. She reported that her symptoms started approximately one year prior without notable triggers. She noted that she has prolonged periods of normal function characterized by adequate nocturnal sleep hours where she feels refreshed, awake, alert and energetic. However, at irregular times throughout the year she has “bad weeks” that can last up to a month. These challenging weeks are characterized by anterograde amnesia, mood disruption, apathy, altered perception, cognitive dysfunction and exercise intolerance. This occurred despite longer than normal sleep hours. Rare hyperphagia reported. No hypersexuality reported. She was not taking any medications.

Results: Patient was evaluated by cardiology and neurology with unremarkable diagnostic testing/imaging and referred to sleep medicine. Nocturnal polysomnogram (PSG) with subsequent daytime multiple sleep latency test (MSLT) were both unremarkable. Labs for restless leg syndrome showed low ferritin and vitamin D, both of which were adequately supplemented without improvement of episodes/symptoms. Modafinil was started during her next episode of hypersomnolence and cognitive changes. This helped resolve the episode, notably the daytime sleepiness, with improvement of cognitive function and improvement of her other symptoms as well. While on modafinil, patient has not had an episode in nearly one year.

Conclusions: Kleine-Levin syndrome is a rare condition with a male predominance of 4:1. As it is a clinical diagnosis, other neurologic, metabolic and psychiatric causes must be evaluated and ruled out first. While polysomnogram does not typically show abnormalities, this must still be performed with a daytime multiple sleep latency test to rule out other etiologies. The timing of these studies may be critical in terms of whether the patient is acutely in an episode of KLS. Treatment modalities, including sleep hygiene and/or pharmacologic therapies to target specific symptoms are quite variable with limited literature. Modafinil may prove to be a useful treatment modality as an abortive measure and even potentially preventative of future symptomatology.

Towards Human-Centric Industry 5.0: Predicting Operator Sleepiness Using Wearable Sleep Data

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Introduction: Excessive daytime sleepiness (EDS) affects approximately 20% of the population and is a significant contributor to workplace and vehicular accidents, as well as overall poorer health outcomes. Common causes of EDS include sleep deprivation, obstructive sleep apnea, and the use of sedating medications. Monitoring and detecting mental or physical fatigue in the workplace is crucial to maintaining both productivity and worker health. While current systems analyze biometric signals, such as eye activity and complex measurements like ECG, EMG, and EEG, this paper proposes a non-invasive model that predicts operator sleepiness based on the previous night's sleep quality. Using a validated system to predict sleep events (e.g., microsleeps, N1, N2), our approach offers an efficient way to predict operator fatigue and optimize wellbeing in industrial settings.

Materials and methods: Dataset:

The dataset includes recordings from 4 subjects (mean age: 29 ± 2 , 1 female), who wore a Garmin smartwatch running a ConnectIQ application. The application collected data over 10 consecutive days and nights for each subject.

Sleepiness Evaluation:

Sleepiness was assessed using a proprietary, validated algorithm designed to predict sleep events. This algorithm generates an Alert prior to each sleep event, with an accuracy of nearly 90% when compared to medical doctor scoring based on Polysomnography (PSG). The number of Alerts during the daytime serves as the ground truth for determining sleepiness.

Sleep Quality Evaluation:

The sleep quality of each subject was evaluated using a proprietary algorithm capable of identifying the wake-sleep transition and classifying sleep stages. This algorithm has been validated against PSG medical doctor scoring, ensuring its accuracy in measuring parameters such as sleep onset latency, arousal index, and overall sleep quality.

Machine Learning Algorithm:

To predict sleepiness, we used the XGBoost algorithm. The model takes the following sleep quality parameters as input:

- Total Sleep Time (TST): The total duration of sleep.
- Sleep Onset Latency (SOL): The time taken to fall asleep.
- Sleep Efficiency (SE): The ratio of time spent asleep versus time spent in bed.
- Arousal Index (AI): The frequency of awakenings or disturbances during sleep.
- Duration of Longest Awake after Sleep Onset (DoLA): The longest duration of wakefulness after initially falling asleep.
- Sleep Quality (SQ): A composite measure of overall sleep quality.

The output of the model is binary, predicting whether the subject, that precise day, will be "Sleepy" or "Not Sleepy." Subjects that during the day presented more than 2000 seconds in Alerts are classified as "Sleepy," while those with fewer than 2000 seconds in Alerts are classified as "Not Sleepy."

Results: The dataset has been split into 70% for training and 30% for validation.

Sleepy label generated during the validation phase:

- Precision 100%
- Recall 75%
- F1-score 86%

Not Sleepy label generated during the validation phase:

- Precision 88%
- Recall 100%
- F1-score 93%

Conclusions: This study suggests that may be possible to predict an operator's sleepiness using a noninvasive ML approach that processes sleep quality data collected from wearable devices.

Hypersomnia

Altered sleep spindle morphology in idiopathic hypersomnia

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Introduction: Excessive daytime sleepiness (EDS) is the most disabling symptom of idiopathic hypersomnia (IH), profoundly impairing daily functioning and quality of life. Paradoxically, sleepiness emerges despite prolonged and apparently well-consolidated nocturnal sleep. This clinical presentation challenges conventional models linking EDS to sleep fragmentation and raises important questions regarding the integrity of sleep microarchitecture and its role in sustaining restorative processes. Within this framework, sleep spindles offer valuable insight into how thalamocortical coordination protects sleep by reducing cortical arousability. Their alteration may signal dysfunction within this network, leading to insufficient sleep restoration and contributing to EDS. Nevertheless, the morphological features of spindles remain unexplored in IH. Here, we investigated whether individuals with IH show alterations in sleep spindle density and morphology compared to healthy controls, and whether these features are associated with objective and subjective measures of EDS in IH.

Materials and methods: We retrospectively selected 62 adults with IH (mean age = 35.3 ± 10.5 years; 69.4% women) and 70 healthy controls (mean age = 35.9 ± 15.9 years; 40% women). Patients were diagnosed according to ICSD-3 criteria, based on clinical interview, questionnaires, overnight polysomnography, and the Multiple Sleep Latency Test (MSLT) with four naps. Exclusion criteria included apnea-hypopnea index ≥ 15 , psychiatric or neurological conditions, other sleep disorders, shift work, and use of medications prior to the polysomnography. Subjective EDS was measured using the Epworth Sleepiness Scale, while objective EDS was indexed by mean sleep latency on the MSLT. Automated spindle detection was performed on frontal (F3–F4) and central (C3–C4) EEG derivations during N2 and N3 sleep stages. In addition to spindle density (events/min), we extracted total count, duration (seconds), dominant and average frequency (Hz), peak-to-peak amplitude (μV), and root mean square (RMS) amplitude (μV). Group comparisons were conducted using ANCOVAs, and partial correlations assessed associations between spindle features and EDS. Sex and age were included as covariates in all analyses. Statistical significance was set at $p < 0.05$.

Results: Compared to controls, IH patients exhibited increased spindle count and density across both frontal and central derivations (all $p < 0.001$), but with significantly shorter durations ($p < 0.001$) and lower amplitudes, both in terms of peak-to-peak ($p = 0.005$ and $p = 0.006$, respectively) and RMS values ($p = 0.009$). In the frontal derivations, spindles also showed higher frequencies in IH (dominant: $p = 0.035$; average: $p = 0.032$). Furthermore, in central derivations, more severe objective EDS, as indicated by shorter MSLT latencies, correlated with smaller peak-to-peak amplitude ($r = 0.296$, $p = 0.021$) and smaller RMS amplitude ($r = 0.282$, $p = 0.029$). No associations were found between spindle features and subjective EDS.

Conclusions: These findings identify a novel electrophysiological signature in IH, characterized by paradoxically increased but morphologically impaired spindles. This pattern suggests a state of hyperstable yet functionally inefficient sleep, likely reflecting disrupted thalamocortical dynamics underlying EDS in IH.

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Analysis of Case Reports about Patients with Hypersomnia Using LLMs for Data Extraction

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Introduction: Hypersomnia affects 4-5% of general population (Dauvilliers et Buguet, 2005). Its etiological causes are diverse, and the treatment strategies are challenged by the limited evidence and variable therapeutic responses. While evidence from large observational studies and clinical trials is gradually emerging, case report data remains underutilized due to its perceived low evidentiary value. Nonetheless, case reports can offer valuable insights, especially in rare or poorly understood conditions. Extracting relevant clinical information from case reports is labor-intensive. Therefore, we aimed to develop a large-scale, data-driven analysis of published case reports in patients with hypersomnia using generative artificial intelligence (AI) in the form of Large Language Models (LLMs).

Materials and methods: A comprehensive search query using relevant MeSH terms identified all hypersomnia case reports on PubMed, from which titles and abstracts were obtained. The etiology and the clinical diagnosis of hypersomnia were the primary outcome measures. A structured data extraction with 43 questions was designed to identify relevant case reports and capture patient demographics, the clinical diagnoses, and the etiology of hypersomnia, if applicable. The LLM Qwen3-32B, accessed via the general-classifier Python library, was used to answer these questions for all the identified case reports. We evaluated LLM performance on a manually labeled ground truth dataset and conducted a quantitative analysis of the LLM-extracted data.

Results: The PubMed search yielded 2431 publications. On the ground truth dataset, the LLM-based data extraction achieved an overall accuracy of 93.9%, recall of 75.7%, precision of 76.4%, and an F1-score of 76.1% across all 43 questions; an F1-score >90% was achieved for 12 questions. LLM analysis identified 908 of the 2431 publications (37.4%) as case reports on individual patients with hypersomnia. Of these patients, 38.1% (n=346) were male and 30.3% (n=275) female (sex unreported in 31.6% cases). Age distribution indicated 56.5% (n=513) adults and 21.1% (n=192) pediatric with age unreported in 22.4% cases. Key reported sleep diagnoses included hypersomnia due to a medical condition (38.1% [n=346] with 29.1% [n=101] attributed to neurodegeneration), narcolepsy (37.4%, 340 instances), Kleine-Levin-Syndrome (18.1%, 164 instances), and sleep disordered breathing (17.7%, n=161), with obstructive sleep apnea being predominant (85.7% of patients with sleep disordered breathing, n=138). Most common other causes included substance abuse (13.9%, n=126), medication-related effects (11.7%, n=106), and toxic exposures (11.5%, n=104). 28.9% (n=262) patients had multiple etiological factors for hypersomnia.

Conclusions: This is the first study to systematically analyze all case reports on a sleep disorder using LLMs. First, our study shows that LLMs can accurately extract diverse data from case reports, enabling an efficient analysis of medical literature on a large scale. Second, hypersomnia has a large etiological landscape with comorbid medical condition, autoimmune conditions, and substance abuse being the most commonly described in case reports. We will further systematically evaluate the outcomes of case reports.

Acknowledgments: Not applicable.

A rare genetic variant in the cleavage site of *prepro-orexin* confers susceptibility to idiopathic hypersomnia

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Introduction: Idiopathic hypersomnia (IH) is a rare, heterogeneous sleep disorder characterized by excessive daytime sleepiness. The exact prevalence of IH remains unknown due to the absence of epidemiological studies. A high proportion of IH patients (26.9-39.1%) reported a family member with excessive daytime sleepiness. In contrast to narcolepsy type 1, which is a well-defined type of central disorders of hypersomnolence, the etiology of IH is poorly understood. No susceptibility loci associated with IH have been clearly identified, despite the tendency for familial aggregation of IH.

Materials and methods: We performed a variation screening of *prepro-orexin/hypocretin* and *orexin receptor* genes, and an association study for IH in a Japanese population, with replication (598 IH patients and 9826 controls). Two forms of orexin (orexin-A and -B) are generated by cleavage of one precursor peptide, prepro-orexin. A cleavage assay was conducted using proprotein convertase subtilisin/kexin (PCSK) type 1 and PCSK2 to examine differences in cleavage efficiency between the wild-type (Gly-Lys-Arg; GKR) and mutant (Gly-Arg-Arg; GRR) peptides.

Results: We identified a rare missense variant (g.42184347T>C; p.Lys68Arg; rs537376938) in the cleavage site of *prepro-orexin* that was associated with IH (minor allele frequency of 1.67% in cases versus 0.32% in controls, $P = 2.7 \times 10^{-8}$, odds ratio = 5.36). All patients with this mutation were heterozygous carriers. Subjective sleepiness as evaluated with the Epworth Sleepiness Scale scores in unmedicated conditions and arousal index (polysomnography) were nominally higher in the orexin mutation-positive patients compared with the orexin mutation-negative patients ($P = 0.049$ and $P = 0.046$, respectively), suggesting that mutation-positive IH patients suffered more sleepiness and sleep instability. No significant association between narcolepsy (type 1 and type 2) and rs537376938 was observed. In both PCSK1 and PCSK2 assays, the mutant peptide was less processed than the wild-type peptide. We also confirmed that the uncleaved forms of orexin-A and orexin-B peptides exhibited reduced signaling through orexin receptors than mature orexin-A and orexin-B peptides.

Conclusions: These results indicate that a subgroup of IH is associated with decreased orexin signaling, which is believed to be a hallmark of narcolepsy type 1.

Acknowledgments: The main findings have been previously reported in NPJ Genomic Medicine (DOI:10.1038/s41525-022-00298-w).

Challenges in the Treatment of Narcolepsy and the Positive Impact of Acetyl-L-Carnitine: A Case-Based Review with 20-Year Follow-Up

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Introduction: Narcolepsy is a chronic sleep disorder marked by excessive daytime sleepiness (EDS), disrupted nocturnal sleep, and, in some cases, cataplexy. Standard treatments—including wake-promoting agents, stimulants, and sodium oxybate—often provide incomplete symptom control and may cause significant side effects. Misdiagnosis is also common, particularly with mood disorders, contributing to delayed treatment and prolonged functional impairment. Current therapies primarily target monoaminergic and GABAergic systems, yet do not address potential deficits in neuronal energy metabolism. Emerging data suggest that mitochondrial dysfunction may play a role in central hypersomnias, supporting interest in metabolic modulators such as acetyl-L-carnitine (ALCAR). We present a case of treatment-resistant narcolepsy in which low-dose ALCAR supplementation resulted in a marked and sustained improvement in wakefulness, highlighting its potential as an adjuvant therapeutic strategy.

Materials and methods: A comprehensive case-based review was conducted using a detailed, longitudinal clinical history of a 50-year-old female patient diagnosed with narcolepsy following over 15 years of misdiagnosed mood disorder. Data include pharmacological regimens, objective sleep

testing, adverse effects, and patient-reported outcomes. The impact of low-dose ALCAR (250 mg/day) on wakefulness, symptom severity, and quality of life was documented over a 6-month period.

Results: The patient experienced persistent excessive daytime sleepiness and functional decline despite multiple treatment attempts over two decades. Initial pharmacologic management included antidepressants, Modafinil, Armodafinil, Adderall, Concerta, Jornay, Vyvanse, and sodium oxybate (Xyrem). Many of these treatments led to intolerable side effects—including severe gastrointestinal symptoms, Barrett's esophagus, and psychiatric distress—or failed to provide sustained benefit. Xyrem, though initially discontinued due to severe adverse reactions such as vomiting, shivering, and anxiety, was later successfully reintroduced beginning at a very low dose (0.25 g nightly) and gradually titrated up. The patient eventually stabilized on a regimen of 2.25 g of Xyrem taken twice nightly, combined with 125 mg of Modafinil daily.

This combination extended the patient's functional wake window to approximately four hours. In early 2025, the patient began taking 250 mg of acetyl-L-carnitine (ALCAR) each morning. This addition was associated with a further and sustained increase in her wakefulness window—from four to approximately six hours—with a marked reduction in the need for daytime napping and no reported side effects. The patient described significant improvements in alertness, daily functioning, and overall quality of life. Attempts to increase ALCAR beyond 250 mg/day resulted in undesirable overactivation, affirming the effectiveness of the lower dose. A follow-up self-observation revealed that accidental omission of ALCAR for one week led to a noticeable recurrence of brain fog and excessive sleepiness, which resolved upon resuming the correct supplement. This unintentional interruption served to reinforce the subjective benefit attributed to ALCAR.

Conclusions: This case highlights the multifaceted challenges in narcolepsy management and proposes acetyl-L-carnitine as a potential adjuvant therapy in refractory cases. Given its safety profile and observed benefit in this case, ALCAR warrants further investigation through controlled clinical trials.

Clinical Characterization of Patients with Abnormal Multiple Sleep Latency Test: A 10-Year Cohort Study

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Introduction: The Multiple Sleep Latency Test (MSLT) remains the gold standard diagnostic tool for central disorders of hypersomnolence, yet comprehensive characterization of patients with abnormal results is limited. We analyzed a decade of MSLT data from a diverse urban academic sleep center to identify distinctive clinical, polysomnographic, and functional profiles that differentiate Narcolepsy Type 1 (NT1), Narcolepsy Type 2 (NT2), and Idiopathic Hypersomnia (IH), aiming to enhance diagnostic precision in these challenging conditions.

Materials and methods: We retrospectively analyzed 893 consecutive patients who underwent polysomnography and MSLT at Weill Cornell Center for Sleep Medicine (2010-2020). Patients were classified according to ICSD-3 criteria as having normal MSLT (n=492), IH (n=294), Narcolepsy (n=107). Narcolepsy was further classified based on the presence of cataplexy. Comprehensive assessment included demographic data, Epworth Sleepiness Scale (ESS), Berlin questionnaire, detailed psychiatric and medical comorbidity profiles, medication usage patterns, polysomnographic metrics, and functional parameters. All subjects underwent an attended polysomnography (PSG) on the night preceding the MSLT protocol. Statistical analyses employed ANOVA and chi-square tests with significance at $p < 0.05$.

Results: Patients with abnormal MSLT demonstrated distinct clinical profiles beyond diagnostic criteria. NT1 patients had the most severe objective sleepiness (mean sleep latency: 4.51 ± 1.96 min) and highest ESS scores (14.7 ± 4.7 vs. 11.6 ± 5.1 in those with normal MSLT, $p < 0.0001$), yet showed significantly better functional outcomes with higher employment rates (78.6% vs. 47.6% in controls, $p = 0.0065$) and physical activity (52.2% engaged in regular exercise vs. $< 30\%$ in other groups, $p < 0.001$). In terms of self-reported psychiatric comorbidities, NT1 patients had significantly higher rates of anxiety (50.0%), depression (53.6%), and cognitive symptoms (memory loss: 21.4%) compared to other groups ($p < 0.001$). Sleep architecture analysis of MSLT revealed narcolepsy groups had significantly increased REM sleep percentage ($\sim 23\%$ vs. 11% in controls, $p < 0.0001$) and shortened sleep onset latency (NT1:

8.3 min; NT2: 6.0 min vs. controls: 35.2 min, $p < 0.0001$). IH patients demonstrated intermediate polysomnographic abnormalities but reported the highest rates of lack of energy (81.7%, $p < 0.0001$) and longest nap durations (18.8 minutes vs. 10.5 minutes in patients with normal MSLT findings). Caffeine sensitivity was significantly higher in NT1 (25.0%) and IH (21.4%) compared to NT2 (5.2%, $p = 0.0021$), suggesting distinctive pathophysiological mechanisms.

Conclusions: This comprehensive characterization reveals that clinical phenotypes of NT1, NT2, and IH extend significantly beyond standard diagnostic parameters. The paradoxical finding of better functional capacity in NT1 patients with severe objective sleepiness suggests complex compensatory mechanisms worthy of further investigation. The distinct patterns of psychiatric comorbidities, sleep architecture signatures, and functional outcomes provide valuable additional markers that can enhance diagnostic accuracy and inform targeted management strategies. These findings underscore the importance of holistic clinical assessment beyond isolated MSLT parameters when evaluating and treating patients with suspected central disorders of hypersomnolence.

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Clinical Significance of Fractional Exhaled Nitric Oxide (FeNO) in Narcolepsy Patients

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness, often accompanied by obesity and obstructive sleep apnea (OSA). Airway inflammation in OSA and obesity has been described and can be assessed by measuring the biomarker fractional exhaled nitric oxide (FeNO). In this preliminary study, we explored the significance of FeNO measurement in patients with narcolepsy.

Materials and methods: This study was a prospective and in-hospital population-based study. We enrolled patients with narcolepsy and compared them with patients with OSA and insomnia. Patients underwent pulmonary function tests, FeNO measurement, arterial blood gas analysis, polysomnography, and multiple sleep latency tests. All patients had eosinophil counts, and some underwent IgE testing. FeNO was measured daily during hospitalization, including before and after ventilator and pharmacological treatments.

Results: A total of 90 patients were included, divided into narcolepsy ($n = 30$), OSA ($n = 30$), and insomnia ($n = 30$) groups. The median apnea-hypopnea index (AHI) in the narcolepsy group was 16 ± 4.5 , with a mean age of 50.9 years and 29% females. Among narcolepsy patients, 45% were diagnosed with OSA, of which 53% had moderate to severe disease. FeNO levels were significantly higher in patients with moderate to severe OSA compared to those with no or mild OSA ($P = 0.024$). FeNO was positively correlated with the apnea-hypopnea index ($r = 0.65$, $p < 0.001$) and the lowest blood oxygen saturation ($r = 0.54$, $p < 0.001$). Among the 37 patients in the OSA group who underwent continuous positive airway pressure (CPAP) titration and treatment, successful titration was associated with lower nocturnal FeNO elevation (7.2 ± 3.3 vs. 11.0 ± 4.3 , $p = 0.02$). FeNO levels decreased after 1-4 days of CPAP treatment (11.7 ± 4.4 ppb, $p < 0.001$). In narcolepsy patients with OSA, FeNO did not decrease with AHI reduction after CPAP treatment compared to the OSA group. Pharmacological treatment significantly improved daytime sleepiness in narcolepsy patients but did not significantly change FeNO levels.

Conclusions: FeNO was not significantly correlated with daytime sleepiness in narcolepsy and did not change with CPAP treatment. FeNO levels were elevated in OSA patients and correlated with disease severity, decreasing after positive airway pressure treatment. This study supports the role of upper airway inflammation in the pathogenesis of OSA and suggests that FeNO may be useful for monitoring the effectiveness of CPAP treatment. The correlation between FeNO and daytime sleepiness requires further investigation.

Data-Driven Identification of OSA Subtypes through Endotypic Clustering in Multi-Cohort Population Studies

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Introduction: Obstructive sleep apnea (OSA) is a physiological and clinically heterogeneous disorder. Conventional severity metrics such as the Apnea-Hypopnea index (AHI) provide limited insight into underlying pathophysiological mechanisms. Four endotypic traits—loop gain (instability of ventilatory control), muscle compensation (upper airway dilator response), pharyngeal collapsibility (airway collapse tendency during sleep), and arousal threshold (Tendency to wake up easily in response to respiratory disturbances)—capture key physiological determinants of OSA. These traits support mechanistic subtyping beyond AHI. In this study, we performed unsupervised clustering of endotypic traits in large population-based cohorts to define physiologically distinct OSA subtypes and assess their clinical significance.

Materials and methods: We analyzed data from 14,643 participants across four population-based cohorts: Korea Image-based Sleep Study (KISS, n = 6,661), Sleep Heart Health Study (SHHS, n = 3,964), the Osteoporotic Fractures in Men Study (MrOS, n = 2,280), and the Multi-Ethnic Study of Atherosclerosis (MESA, n = 1,738). Four validated endotypic traits were estimated using the PUP framework with previously published techniques. After Z-score standardization, K-means clustering was applied, and the optimal number of clusters was determined using the Elbow method, Calinski-Harabasz index, and Davies-Bouldin index. AHI was excluded from clustering but analyzed along with polysomnographic, demographic, and endotypic variables after clustering. To assess the magnitude of between-cluster differences, effect sizes were calculated using Cohen's d (small: d=0.2, medium: d=0.5, large: d=0.8).

Results: Unsupervised clustering of four endotypic traits identified four physiologically distinct OSA subtypes (Cluster A: n = 7,843; B: n = 4,194; C: n = 1,738; D: n = 868). Demographic and polysomnographic measures showed clear gradients: gender, BMI, arousal index, AHI, obstructive and central apnea duration, and hypoxic burden increased from A to D, while sleep efficiency and mean oxygen saturation decreased. Effect size analysis indicated large between-cluster differences in arousal index, obstructive apnea duration, and oxygen saturation; medium effects in age, central apnea duration, and hypoxic burden; and only small effects in gender, BMI, WASO, sleep efficiency, central apnea index, and AHI.

Conclusions: Endotype-based clustering revealed four physiologically and clinically distinct OSA subtypes. These subtypes reflect underlying differences in ventilatory control, arousal threshold, and airway collapsibility, providing a mechanistic alternative to conventional AHI-based classification. This framework supports more precise phenotyping and may support the development of personalized treatment strategies for OSA.

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Discrepancy between subjective and objective sleepiness in adolescents is associated with neurodevelopmental disorders

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Introduction: Lack of correlation between subjective and objective measurements of daytime sleepiness is common. Possible predictors of the discrepancy between subjective and objective sleepiness were examined in adolescents.

Materials and methods: Two hundred and eleven pediatric patients (aged 10-18 years) with various sleep disorder symptoms were evaluated for subjective and objective sleepiness. Subjective sleepiness was defined as the scores of 11 or more on the Japanese version of Epworth Sleepiness Scale and objective sleepiness was defined as mean sleep latency of 8.0 min or less on the Multiple Sleep Latency

Test. Patients were then classified as concordantly sleepy (CS), objectively sleepy (OS), subjectively sleepy (SS), and non sleepy (NS). Discrepancy-related factors were identified with multivariable logistic regression analysis.

Results: Discrepancy between subjective and objective sleepiness was observed in 46.4% of the patients. When the CS group was set as the reference in the multivariable logistic regression analysis, younger age (odds ratio (OR)=0.75, 95% confidence interval (CI): 0.58 to 0.97), lower sleep efficiency (OR=0.93, 95% CI: 0.87 to 0.99), and neurodevelopmental disorders (OR=7.54, 95%, CI: 2.43 to 23.38) were significantly associated with subjective sleepiness. When the NS group was set as the reference, later bedtime (OR=2.56, 95% CI: 1.28 to 5.15) and neurodevelopmental disorders (OR=4.12, 95% CI: 1.30 to 12.99) were associated with subjective sleepiness. In subgroup analyses on autism spectrum disorders (ASD) and attention deficit hyperactivity disorders (ADHD), only ASD (SS vs. CS: OR=17.23, 95% CI: 3.46 to 85.9; SS vs. NS: OR=5.36, 95% CI: 1.43 to 20.03) exhibited statistical significance in the multivariable regression model. In contrast, ADHD was not related with discrepancy.

Conclusions: Nearly half of the patients exhibited discrepancy between subjective and objective sleepiness which need to be taken into consideration in the management of hypersomnia. Significant factors related to subjective discrepancy included: age, delayed bedtimes, and neurodevelopmental disorders in the adolescent population.

Does Kleine-Levin Syndrome Have Circadian Dysfunction?

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Introduction: Kleine-Levin Syndrome (KLS) involves periodic hypersomnia relapses and debilitating neurobehavioral disturbances, yet the existence of circadian rhythm dysfunction remains debated.

Materials and methods: We conducted a study integrating between-group comparisons with a within-subject design. Circadian rhythms were evaluated under a modified constant routine protocol in 22 KLS patients (mean age 23.5 ± 15.1 years) and 48 age-, sex-, and BMI-matched healthy controls (mean age 20.8 ± 6.2 years). Habitual sleep-wake patterns were assessed via wrist-worn actigraphy. Endogenous circadian markers—including phase [dim light melatonin onset (DLMO), core body temperature minimum (CBTmin)], amplitude, and MESOR—were derived from 24-hour melatonin and CBT profiles. Importantly, a subgroup of six KLS patients was evaluated in both remission and relapse states.

Results: Between-group comparisons revealed no significant differences in sleep-wake patterns, circadian phase markers (e.g., DLMO), amplitude, or MESOR between KLS patients and healthy controls. The one exception was a statistically lower baseline melatonin level in the KLS relapse group compared to controls (1.9 ± 1.1 vs. 3.2 ± 1.9 pg/mL, $p=0.007$), though this difference is unlikely to be clinically significant. In contrast, the within-subject paired analysis revealed a significant and dynamic phase advance during relapse. Specifically, DLMO advanced by a mean of 1.4 hours ($p=0.031$) and CBTmin advanced by a mean of 1.9 hours ($p=0.019$). In contrast to this phase shift, there were no significant changes in the amplitude or MESOR for either melatonin or CBT between the remission and relapse states. This marked phase shift in KLS patients contrasted with the high circadian stability observed in controls assessed twice.

Conclusions: KLS is not associated with persistent abnormalities in circadian phase, amplitude, or MESOR. Instead, the disorder is characterized by a distinct and dynamic phase advance during symptomatic relapses. These findings provide novel insight into the circadian pathophysiology of KLS, highlighting the circadian system's phase-shifting mechanism as a potential therapeutic target.

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Intellectual Quotient in Adults with Idiopathic Hypersomnia and Narcolepsy Type 1

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Introduction: Narcolepsy type 1 (NT1) and idiopathic hypersomnia (IH) are central disorders of hypersomnolence characterized by excessive daytime sleepiness and cognitive complaints. While NT1 has been associated with altered executive function and enhanced creativity, intelligence quotient (IQ) remains understudied in adults with NT1 and has never been systematically assessed in IH. This study aimed to evaluate IQ in adults with NT1 and IH compared to healthy controls, using a standardized measure of cognitive ability.

Materials and methods: We conducted a prospective, controlled study including 30 adults with NT1, 30 with IH, and 30 age-, sex-, and education-matched healthy controls, recruited at the French National Reference Center for Narcolepsy and Hypersomnia. Participants completed the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV), assessing Full Scale IQ (FSIQ) and four cognitive domains: Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed.

Results: On the Full Scale IQ, participants with IH (mean $\pm$ SD: 113.6 ± 14.3) and NT1 (104.1 ± 14.3) had scores similar to those of healthy controls (108.4 ± 17.0). One of the four indices, the Working Memory Index, was globally different between the three groups (IH: 109.0 ± 17.1 ; NT1: 99.0 ± 15.8 ; Control: 102.3 ± 13.4 , $P = 0.04$), with a trend for IH participants to have higher scores than NT1 participants (but $P = 0.04$). Of the subtests, Information, Visual Puzzle, and Digit Span tended to differ between the three groups, with no other differences between two groups. Higher IQ scores were moderately correlated with more years of education (but not with disease course or treatment). Pretest fatigue (but not Epworth Sleepiness Score) predicted poorer performance on the Working Memory Index.

Conclusions: Adults with NT1 and IH have normal intellectual functioning comparable to healthy controls. Despite subjective cognitive complaints, particularly in NT1, their IQ performance indicates preserved cognitive potential. These findings support the view that individuals with hypersomnolence disorders can achieve normal academic and professional outcomes, emphasizing the importance of recognizing their intact intellectual capabilities in clinical and educational contexts.

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Investigating GABA and Glx in Central Hypersomnolence Disorders: A Multicenter Harmonized Spectroscopy Study

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Introduction: Central disorders of hypersomnolence (CDH), including narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH), are characterized by excessive daytime sleepiness. NT1 is biologically defined by low or absent cerebrospinal fluid (CSF) hypocretin levels, but distinguishing NT2 from IH remains challenging due to the lack of reliable biomarkers. While dysfunction in default mode network (DMN) regions such as the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) has been implicated, neurochemical alterations in these regions remain poorly understood. Glutamate plus glutamine (Glx) and gamma-aminobutyric acid plus macromolecules (GABA+) may reflect altered excitatory-inhibitory signaling in CDH. However, it remains unclear whether the observed neurometabolic changes reflect stable disease traits or transient effects related to sleep-wake state, such as sleep deprivation. Moreover, the relationship between neurometabolite levels and clinical measures of sleepiness and sleep quality in CDH is still poorly understood.

Materials and methods: Using harmonized multi-center 3 Tesla MRI, we acquired MEGA-PRESS spectroscopy from both the mPFC and PCC, to quantify Glx and GABA+ in patients with NT1 (n=20), NT2 (n=19), or IH (n=28), and in healthy controls (n=21). Healthy controls were scanned in both well-rested and partially sleep-deprived conditions (maximum four hours of permitted sleep). Metabolites levels were quantified using Osprey, providing water-scaled and tissue-corrected absolute concentrations, as well as values normalized to total creatine (tCr). Group comparisons were performed using ANCOVA, comparing patient groups separately with rested and sleep-deprived controls. Within-subject effects of sleep deprivation were tested in controls using linear mixed-effects models. Partial correlations in the patient group were computed between metabolite levels and clinical measures: Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and multiple sleep latency test (MSLT). All statistical analyses were adjusted for site, age, and sex.

Results: No significant differences in Glx or GABA+ were observed when comparing CDH patient groups with rested controls. However, Glx/tCr ratios were significantly higher in sleep-deprived controls compared to all three patient groups in the PCC ($F(3,32)=10.96$, $p<0.001$). These findings were corroborated by linear mixed-effects models, which confirmed increased Glx/tCr in mPFC in healthy controls when partial sleep-deprived versus well-rested ($p = 0.03$). Across CDH patients, lower absolute Glx in PCC was associated with greater daytime sleepiness (ESS: $r=-0.52$, $p=0.0051$), while higher Glx/tCr ratios in PCC correlated with poorer sleep quality (PSQI: $r=0.44$, $p=0.0224$) and shorter sleep latency (MSLT: $r=-0.53$, $p=0.0102$). In mPFC, higher GABA+ levels were associated with shorter MSLT sleep latency ($r=-0.27$, $p=0.0424$).

Conclusions: We found no significant differences in Glx or GABA+ concentrations between the three CDH patient groups and well-rested healthy controls, suggesting that trait-like neurometabolic alterations in DMN regions may be subtle or absent. Notably, Glx/tCr ratios increased following partial sleep deprivation in healthy controls, potentially reflecting a state-dependent neurochemical response specific to acute rather than chronic sleepiness. Furthermore, associations between Glx and GABA+ levels and clinical measures of sleepiness and sleep quality suggest that individual variability in disease severity may be captured by these metabolites, supporting their potential as candidate biomarkers in CDH.

Limitations of the MSLT and Predictive Diagnostic Factors in Patients with Hypersomnolence

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Introduction: Narcolepsy is a neurological sleep disorder characterized by hypersomnolence, sleep fragmentation, and rapid eye movement(REM) sleep dissociation. However, the classifications of central disorders of hypersomnolence remain dynamic and debated. Some research has shown that sleep stage sequences during naps with sleep onset rapid eye movement(SOREM) periods differ significantly between patients with narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH). We hypothesize that SOREMP sequences, or the occurrence of SOREMPs in the early phase, may influence diagnostic changes.

Materials and methods: We selected patients who visited St. Vincent's Hospital between 2002 and 2023 for daytime sleepiness and underwent the multiple sleep latency test (MSLT) more than twice. Patients were divided into five groups: NT1, NT2, IH, REM dysregulation(REMD), and normal. We

analyzed diagnostic changes, SOREMPs in the first nap, and the duration of mean sleep latency using logistic regression analysis.

Results: A total of 126 patients were included (66 NT1, 30 NT2, 16 IH, 8 REM dysregulation, and 6 normal). Of these, 39 patients (30.7%) had changes in their diagnosis. The number of SOREMPs in the first MSLT was statistically significant ($p = 0.028$, $OR = 0.33$). The occurrence of SOREMPs during the first nap of the second MSLT also showed a significant association with diagnostic changes ($p < 0.001$, $OR = 0.05$).

Conclusions: This study confirms the utility of MSLT in diagnosing NT1 patients, though it has limitations in diagnosing other hypersomnolence disorders. The presence and number of SOREMPs in the first nap of the MSLT appear to influence subsequent diagnostic changes. Further studies with larger sample sizes and more structured designs are needed.

Long sleep duration and autonomic function: A systematic review

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Introduction: Long sleep has been linked to increased cardiovascular disease (CVD) risks, yet the underlying autonomic mechanisms remain underexplored compared to other physiological pathways. Most existing studies on sleep and autonomic function have focused primarily on sleep deprivation or insomnia. This systematic review aimed to investigate how long sleep duration is defined in current studies and how long sleep duration is associated with autonomic function outcomes across populations.

Materials and methods: Structured searches were conducted in PubMed, Embase, Web of Science, Scopus, and CINAHL for articles published in English with full text before April 2025. Search terms included “long sleep” or “long sleep duration” and “autonomic function” or “autonomic nervous system.” Studies were excluded if they treated sleep as a continuous variable without an explicit long sleep category or if conducted in non-human populations. The JBI critical appraisal checklist for systematic reviews and research syntheses was used for quality assessment.

Results: A total of 9 studies were included. Most were cross-sectional (78%), involving adolescents (22%), healthy adults (22%), and older adults (44%). Six studies (67%) used the PSQI to measure subjective sleep duration, while objective measurements predominantly utilized wrist-worn actigraphy devices (also 67%); one study used direct observation by medical staff. Definitions of long sleep varied: ≥ 7 hours (22%), ≥ 8 hours (22%), and ≥ 9 hours (56%). Autonomic function was mostly measured using heart rate variability (HRV) with short-term (1-5 minute) lead I ECG recording, as well as muscle sympathetic nerve activity, and orthostatic heart rate tests. Frequency-domain indices (total power, LF-HRV, HF-HRV, LF/HF ratio) and time-domain indices (SDNN, RMSSD) were frequently reported. Cross-study comparisons suggested that older long sleepers were more likely to have a higher risk of cardiac vagal control decline compared to healthy adults or adolescents, except for adolescents with mental illness. One study using both subjective and objective assessments found that self-reported long sleep duration was significantly associated with reduced parasympathetic withdrawal during orthostatic challenges, whereas objectively measured long sleep duration showed no such association.

Conclusions: This review highlights the inconsistency in definitions of long sleep duration, ranging from ≥ 7 hours to unclassified longer durations. In older adults and adolescents with mental illness, long sleep duration was associated with impaired autonomic function. Although objective measures are more accurate for assessing sleep duration, subjective and objective sleep measures capture different aspects of sleep. Therefore, the choice to use both should be carefully considered based on the study's aims. Future studies should establish optimal cutoffs to define long sleep duration and adopt consistent autonomic measurement protocols to inform interventions targeting sleep for cardiovascular risk reduction. It would also be meaningful to identify which combination of autonomic function indices best predicts overall autonomic health.

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Machine Learning Classification of Idiopathic Hypersomnia and Narcolepsy: Novel Clinical Predictors from a Decade-Long Urban Academic Sleep Center

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Introduction: Differentiating idiopathic hypersomnia (IH) from narcolepsy remains challenging despite established polysomnographic criteria. The Multiple Sleep Latency Test (MSLT) and polysomnography (PSG), while considered gold standards, present limitations in accessibility, cost, and interpretation variability. We investigated whether machine learning using multi-modal clinical data could improve diagnostic accuracy and identify novel predictors for these disorders.

Materials and methods: We retrospectively analyzed 19,398 records from Weill Cornell Center for Sleep Medicine (2010-2020) in New York City. From 893 patients with PSG and MSLT, we identified 294 with IH (32.9%), 107 with narcolepsy (12.0% Type 1 & 25.2% Type 2), and 492 with normal MSLT results (55.1%). Data preprocessing included normalization, imputation, and feature extraction from clinical questionnaires (Epworth Sleepiness Scale, Berlin Questionnaire), PSG metrics (sleep architecture, respiratory events), and MSLT parameters (sleep/REM latencies, SOREMPs). Seven machine learning algorithms were evaluated with various dimensionality reduction techniques (PCA, t-SNE, UMAP), with model performance assessed through 5-fold cross-validation. Random Forest with t-SNE demonstrated superior performance (accuracy: 81.7%, AUC: 0.912, F1: 0.813) and was used to identify novel predictive features through correlation analysis.

Results: Our t-SNE approach significantly outperformed other techniques (t-SNE: ~82% accuracy vs. PCA: 53%, UMAP: 56%). The model identified key predictors across multiple domains: (1) validated sleepiness measures (ESS Total: 0.013, specific ESS questions: 0.006-0.008); (2) sleep timing variables (weekday bedtime: 0.180, sleep onset latency: 0.161-0.180); and (3) lifestyle factors (coffee consumption: 0.007, alcohol consumption: 0.366-0.517, occupation active [movement/non-sedentary] : 0.317-0.462, need alarm clock [to wake up from sleep] : 0.283-0.431). Clinical phenotyping showed NT1 patients had the highest ESS scores (14.7±4.7) and unexpected characteristics including highest rates of occupational engagement (78.6% vs. 39.2% NT2, 51.7% IH) and distinctive comorbidity patterns (anxiety: 50.0%, depression: 53.6%, anemia: 21.4%).

Conclusions: Our machine learning approach identifies previously unreported behavioral and clinical markers that enhance differential diagnosis of hypersomnolence disorders. This large cohort from a diverse urban population demonstrates that diagnostic algorithms incorporating both traditional and novel predictors can achieve >80% accuracy, potentially reducing reliance on resource-intensive sleep studies. The identification of previously overlooked clinical predictors opens possibilities for more accessible screening tools and personalized management approaches, particularly valuable for reducing the substantial diagnostic delays (often 8-15 years) currently observed in these disorders.

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Metabolomic Profiling of Kleine-Levin Syndrome In and Out of Episode using Liquid Chromatography-Mass Spectrometry

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Introduction: Kleine-Levin syndrome (KLS) is a rare episodic hypersomnia disorder lacking diagnostic biomarkers and mechanistic insights. This study utilized liquid chromatography-mass spectrometry (LC-MS) to profile serum and cerebrospinal fluid (CSF) metabolomes in KLS patients, aiming to identify diagnostic biomarker panels and elucidate metabolic changes across symptomatic (in-episode) and asymptomatic (out-of-episode) phases.

Materials and methods: We enrolled 74 KLS patients (mean age: 19.2 ± 11.4 years; 68.9% male) diagnosed at the Sleep Division, Peking University People's Hospital (2004–2021). Samples included 50 in-episode and 56 out-of-episode serum samples, plus 27 in- and 27 out-of-episode CSF samples. Serum from 64 healthy controls served as reference. Untargeted LC-MS metabolomics/lipidomics

profiling was performed, followed by KEGG-based pathway analysis. A novel SVM-RFE (Support Vector Machine-Recursive Feature Elimination) algorithm identified KLS-associated metabolic features, with binary logistic regression screening diagnostic markers. Cross-fluid metabolic dynamics were analyzed in 19 patients with paired serum-CSF samples.

Results: LC-MS identified 559 serum metabolites and 334 lipids with robust data quality. A six-marker serum panel (carnitine C10:3, 3-hydroxybutyrate, decanoic acid [FFA 10:0], glycochenodeoxycholic acid [GCDCA], phenylalanylphenylalanine [Phe-Phe], SM [d18:1_24:1]) achieved an AUC of 0.950 (sensitivity: 0.854; specificity: 0.923). In serum, metabolic dysregulation in KLS during in-episodes and out-of-episodes primarily involves phenylalanine metabolism, glycerophospholipid metabolism, and steroid hormone biosynthesis pathways. CSF metabolic profiles show systemic suppression of amino acid metabolism, with significant reductions in branched-chain amino acids (valine, leucine) and aromatic amino acids (tryptophan), alongside decreased levels of pyruvate (a key tricarboxylic acid cycle intermediate) and pipercolic acid (a lysine metabolite). Serum/CSF relative abundance ratios for the same metabolites in individual subjects revealed elevated ratios for tryptophan and phenylalanine, suggesting potential dysfunction in the active transport system.

Conclusions: This study identified a serum biomarker panel for KLS diagnosis and, for the first time, characterized CSF metabolic shifts between in- and out-of-episode. The mechanism of KLS may be associated with the impairment of the active transport system, the disruption of the blood-brain barrier, and the central neuroinflammatory response.

Multimodal digital assessments of hypersomnia with an instant messaging program

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Introduction: Hypersomnia, characterized by prolonged sleep duration and/or daytime sleepiness, is a common symptom in depression. While hypersomnia assessments rely on self-report, clinical appraisal, and polysomnography (PSG), patients with hypersomnia may present with a wide range of behavioral expressions that may not be captured well by traditional assessments, e.g., trouble concentrating and anxiety, which, however, were correlated with specific linguistic and acoustic features. Advances in digital health have enabled ecologically valid and continuous monitoring through multimodal assessment. As prior studies have validated speech features as reliable markers, this study investigates hypersomnia symptoms in a Hong Kong youth sample using a Telegram-based speech-based ecological momentary assessment (EMA) that collects audio data, aiming to identify behavioral markers and evaluate the effectiveness of automated feature extraction via machine learning and deep learning models.

Materials and methods: This is part of an ongoing study on depression detection using EMA, which initially recruited 328 youth participants. Among those who completed the study (n=300, 19% with depression), 26 individuals had hypersomnia symptoms (mean age: 20.64; 75.18% female), identified via the post-EMA outcomes of the Structured Clinical Interview for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS 2003), and the remaining 274 did not exhibit hypersomnia symptoms (mean age: 21.12; 84.62% female). Within the hypersomnia group, 17 reported ≥ 1 -hour sleep extension, and 9 reported ≥ 2 -hour increases. Exclusion criteria included a history of neuropsychiatric disorders (other than depression and anxiety), any voice, speech, or language disorder, or being deemed unable to provide informed consent. Over seven days, participants completed twice-daily mood assessments, with a minimum compliance rate of 70% required for inclusion. From the resulting voice recordings, a domain-specific pipeline extracted 84 interpretable acoustic and linguistic features, incorporating both static and temporal dynamics. To model complex feature interactions and latent structures, classification of hypersomnia symptoms was performed using the state-of-the-art machine learning algorithms with five-fold cross-validation and SMOTE applied for class balancing.

Results: With age, gender, and depression symptom controlled, patients with hypersomnia symptoms demonstrated significant differences in acoustic features, including higher short-term pitch variability

($P=.04$), reduced short-term loudness variability ($P=.003$), and a lower rate of change in the power spectrum ($P=.01$), indicating reduced speech energy and psychomotor slowing. Linguistic analysis revealed an increased short-term fluctuation in the use of negation words ($P=.04$), and an increased risk-related words usage variability ($P=.02$), reflecting disrupted affective or cognitive regulation. Combining acoustic, linguistic modalities, and demographic information, the Multilayer Perceptron and Long Short-Term Memory (LSTM) model achieved an F1-score of 0.74 for binary classification (sensitivity=0.35; specificity=0.71) between hypersomnia and other participants, and an F1-score of 0.76 for the multi-class classification.

Conclusions: Digital assessment using speech and language features offers a scalable, ecological approach to identify hypersomnia symptoms. Our findings reveal distinct acoustic and linguistic markers associated with hypersomnia and demonstrate the feasibility of automated classification, supporting early detection.

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Nap-Related Variability of MSLT in Central Disorders of Hypersomnolence, Insufficient Sleep, and Delayed Sleep-Wake Phase Disorder

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Introduction: Multiple Sleep Latency Testing preceded by polysomnography (PSG-MSLT) is the standard evaluation for patients with suspected central disorders of hypersomnolence (CDH). The validity of MSLT depends on adequate sleep prior to testing and proper alignment of test time with the patient's circadian rhythm. Insufficient sleep syndrome (ISS) and delayed sleep-wake phase disorder (DSWPD) can be associated with abnormal MSLT potentially leading to misdiagnosis. We analyzed nap-to-nap variability in MSLT parameters in patients with CDH, ISS and DSWPD to elucidate variations in nap patterns by clinical diagnosis.

Materials and methods: This retrospective cohort included 1,474 patients who underwent PSG-MSLT for hypersomnolence (January 2003-August 2024) at Cleveland Clinic. Patients were classified as narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), idiopathic hypersomnia (IH), ISS and DSWPD based on physician clinical diagnosis. Those with hypersomnolence due to other conditions (e.g., OSA, psychiatric disease; $n=618$) or undifferentiated hypersomnia ($n=227$) were excluded. Nap-to-nap variability in sleep latency (SL), sleep onset REM periods (SOREMPs) and REM latency (REML) was assessed across diagnostic groups. Kruskal-Wallis, ANOVA, and Chi-square tests with Bonferroni corrections were used for patient and overall measures, while linear and logistic mixed effect models were used to evaluate trends and overall differences across naps.

Results: Of 676 patients (33.1 ± 13.5 years, 75.4% female), 90(13.3%) had NT1, 155(22.9%) NT2, 313(46.3%) IH, 55(8.1%) ISS, and 63(9.3%) DSWPD. While groups did not differ in age, proportion of females was higher in IH than NT2 and ISS (81.8% vs. 70.3%; 63.6%; $p=0.007$). More Caucasians had IH than NT1 or NT2 (79.4% vs. 63.3%; 65.8%; $p=0.003$). Mean sleep latency (MSL) was shortest in NT1 and longest in DSWPD (NT1 median [IQR]: 3.8[2.1,6.7]; NT2:5.0[3.2,7.1]; IH:7.4[5.1,9.9]; ISS:10.0[5.8,14.6]; DSWPD:12.8[9.3,15.8] min; $p<0.001$). Prevalence of ≥ 2 SOREMPs (%) was higher and REML (mean $\pm$ sd) shorter in NT1 and NT2 than other groups [NT1(84.4%, 9.4 ± 5.5); NT2(74.3%, 12.5 ± 4.4); IH(1.6%, 17.2 ± 2.7); ISS(20%, 15.2 ± 4.2); DSWPD(12.7%, 16.2 ± 3.4); all $p < 0.001$]. SL trajectories varied by group ($trend p < 0.001$). ISS and DSWPD showed increasing SL across trials, with the change being smaller for IH (ISS:slope = 0.92[95% CI:0.57,1.28]; DSWPD:0.97[0.64,1.30]; IH:0.61[0.46,0.76]; all $p < 0.001$). NT1 and NT2 showed stable SL across trials. (NT1:slope = 0.04[95% CI: -0.23,0.32], $p=0.76$; NT2:0.18(-0.03,0.39), $p=0.09$). Nap-level trends of SOREMP trajectories varied by group ($trend p=0.04$). ISS and DSWPD showed declining odds of SOREMPs across trials (ISS:OR = 0.65[95% CI:0.51,0.84], $p < 0.001$; DSWPD:0.69[0.53,0.90], $p=0.007$). NT1 and NT2 showed consistently high and IH consistently low SOREMP frequency (NT1:OR = 0.94[95% CI:0.82,1.08], $p=0.39$; NT2:0.91[0.82,1.01], $p=0.073$; IH:0.87[0.74,1.02], $p=0.091$). REML trajectories also varied across groups ($trend p=0.006$). NT2 and ISS showed increasing REML across trials (NT2:slope = 0.23[95% CI:0.04,0.43], $p=0.019$; ISS:0.67 [0.34,0.99], $p < 0.001$). NT1 showed stable short REML; IH and DSWPD stable long REML

(NT1:slope = 0.23[95% CI: -0.02,0.49], $p=0.075$; IH:0.02[-0.12,0.16], $p=0.78$; DSWPD:0.24[-0.07,0.54], $p=0.13$).

Conclusions: ISS and DSWPD demonstrated progressively increasing SL and declining SOREMP occurrence across successive naps, suggesting influence of fluctuating sleep pressure or circadian misalignment. In contrast, NT1, NT2, and IH exhibited stable SL and consistent SOREMP patterns, indicating persistent hypersomnolence. These findings underscore the utility of nap-by-nap MSLT analysis in differentiating CDH from ISS and DSWPD.

Neurobehavioral features in central hypersomnia disorders: preliminary results of subjective and objective measures

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Introduction: Central disorders of hypersomnolence (CDH), such as narcolepsy and idiopathic hypersomnia, are characterized not only by excessive daytime sleepiness but also by cognitive impairments, mood disturbances, and autonomic dysregulation. Despite their clinical relevance, the interplay between these dimensions remains poorly understood, particularly in terms of how subjective experiences relate to objective physiological and behavioral measures. This study explores the relationship between depressive symptoms, autonomic arousal, and neurobehavioural performance in patients with CDH, integrating subjective and objective measures.

Materials and methods: Nineteen patients with CDH (M/F 7/12; mean age 29.15±8.49 years) and sixteen healthy controls (M/F 7/9; mean age 27.65±7.53 years) were recruited. Patients were diagnosed according to ICSD- 3-TR criteria, based on clinical interview, overnight polysomnography, and the Multiple Sleep Latency Test with four naps. Subjective measures included the Epworth Sleepiness Scale (ESS) for daytime sleepiness and the Patient Health Questionnaire-9 (PHQ-9) for depressive symptoms. Objective measures included pupillometry, assessing baseline pupil diameter and the pupil light reflex (PLR), and the Psychomotor Vigilance Test (PVT) which evaluates sustained attention and response speed. Group comparisons were conducted using Mann-Whitney U tests for non-parametric variables. Spearman correlations were used to explore associations between subjective and objective measures. Statistical significance was set at $p < 0.05$.

Results: ESS scores were significantly higher in CDH patients compared to controls ($W = 20.500$, $p < .001$), as were PHQ-9 scores ($W = 31.500$, $p < .001$). No significant differences emerged between groups in pupillometry parameters or PVT performance. Interestingly, depressive symptoms (PHQ-9) were negatively correlated with PLR latency (i.e., time between light stimulus and pupil constriction onset) ($r = -0.723$, $p = 0.018$). Additionally, a significant negative correlation was found between PVT anticipations and baseline pupil diameter ($r = -0.648$, $p = 0.023$).

Conclusions: The results reveal a dissociation between subjective and objective neurobehavioral markers in individuals with CDH. While subjective sleepiness clearly distinguished patients from healthy controls, objective indices of vigilance and autonomic reactivity did not show significant group differences. Importantly, depressive symptoms were more pronounced in the CDH group, highlighting the potential impact of psychiatric comorbidities that warrants further investigation. The significant negative correlation between PHQ-9 scores and PLR latency suggests that higher depressive symptoms are associated with a faster pupillary constriction response, potentially reflecting altered autonomic regulation. Additionally, the observed association between larger baseline pupil diameter and increased PVT anticipations indicates that higher resting arousal levels may be linked to more impulsive behavior during vigilance tasks. This finding could reflect a compensatory mechanism or a dysregulation in arousal systems affecting inhibitory control. Overall, the study confirms the prominent subjective burden of sleepiness and depression in patients with CDH, despite the absence of consistent objective impairments. These results underscore the need to integrate multimodal assessment tools to

better capture the complexity of CDH and inform more personalized and effective therapeutic strategies.

Prevalence, clinical, and sleep laboratory characteristics among patients presenting with excessive daytime sleepiness in Thailand, a tertiary care setting

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Introduction: Excessive daytime sleepiness (EDS) is a significant clinical issue associated with high morbidity, including increased risk of accidents, impaired cognitive performance, and mood disturbances. In Thailand, research on hypersomnolence disorders remains limited. This study aimed to determine the prevalence, clinical features, and sleep laboratory characteristics of patients presenting with EDS at Siriraj Hospital.

Materials and methods: This retrospective study analyzed data from patients who presented with EDS and underwent a Multiple Sleep Latency Test (MSLT) at the Siriraj Sleep Center between January 2018 and December 2023. The primary outcome was the prevalence of hypersomnia disorders. Secondary outcomes included clinical features and sleep laboratory findings.

Results: A total of 99 patients were included in the analysis. Of these, 45.5% were male. The average age was 32 years, the total sleep time was 7.53 ± 1.17 hours, and the mean Epworth Sleepiness Scale (ESS) score was 12.17 ± 5.87 , with significant differences observed among narcolepsy (NC), idiopathic hypersomnia (IH), and sleep insufficiency and others groups ($p = 0.033$) which significant 2-group comparison of idiopathic hypersomnia and others group. The most common diagnosis was sleep insufficiency ($n=18$), followed by obstructive sleep apnea (OSA; $n=15$), idiopathic hypersomnia ($n=14$), and narcolepsy ($n=12$).

Conclusions: Clinical presentations of disorders of hypersomnolence were usually overlapped and most were nonspecific. Objective testing with PSG and MSLT were essential for making a precise diagnosis.

Acknowledgments: Siriraj Sleep Center, Thailand

Risk of Sodium-Associated Negative Clinical Outcomes in Individuals With Idiopathic Hypersomnia in the United States: A Real-World Analysis

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Introduction: Individuals with idiopathic hypersomnia (IH) experience an elevated prevalence of cardiovascular, cardiometabolic, and renal comorbidities which may be exacerbated by excess sodium. This study aimed to assess the risk of sodium-associated negative clinical outcomes (NCOs) among individuals with IH compared with those without IH, and to evaluate whether risk is further elevated among individuals with pre-existing sodium-associated risk factors.

Materials and methods: Komodo Research Data (01/01/2016–31/01/2024) were used to retrospectively identify US individuals diagnosed with IH (*index*: first-observed IH diagnosis), and a cohort of individuals without IH (*index*: randomly selected date within ≥ 48 months of continuous plan eligibility), using a 1:5 ratio of individuals with and without IH. All individuals were required to have ≥ 12 months' continuous enrolment in both the pre- and post-index periods. Entropy balancing was used to balance demographic characteristics (age, sex, race/ethnicity, US region of residence, health plan type, index year) at index between cohorts. The IH cohort was stratified into higher-risk (≥ 1 sodium-associated risk factor during the 12-month pre-index period) and lower-risk (no risk factors in the pre-index period) subgroups. Sodium-associated NCOs were defined through pragmatic literature review and clinical expert discussion and were categorised as cardiovascular (hypertension, heart failure,

stroke, transient ischaemic attack, major adverse cardiovascular event [MACE; ie, heart failure, stroke, myocardial infarction, unstable angina, or coronary revascularisation procedures]), cardiometabolic (oedema), and renal (proteinuria, chronic kidney disease, kidney failure) conditions. Development of incident NCOs or progression of NCOs were identified during the post-index period. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for each NCO using weighted and unweighted Cox proportional hazards model to compare 1) the IH and non-IH cohorts and 2) the higher- and lower-risk IH subgroups.

Results: After balancing, demographics were similar between the IH (n=11,951) and non-IH (n=59,755) cohorts (mean [standard deviation] age: 41.7 [15.7] vs 41.8 [16.0] years, respectively; 66.4% female in both cohorts). Individuals with IH had a higher risk (HR [95% CI]) of any NCO versus individuals without IH (1.71 [1.64–1.77]). Specifically, risk (HR [95% CI]) of hypertension (1.68 [1.61–1.76]), MACE (1.49 [1.30–1.71]), oedema (1.75 [1.58–1.93]), and renal NCOs (1.42 [1.29–1.57]) was higher in individuals with versus without IH. Among individuals with IH, 63.1% were defined as higher-risk (n=7542). Higher-risk individuals had an increased risk (HR [95% CI]) of any NCO relative to lower-risk individuals (1.68 [1.56–1.81]). Further, higher-risk individuals had increased risk (HR [95% CI]) of hypertension (1.36 [1.26–1.47]), MACE (15.63 [8.31–29.39]), oedema (7.17 [5.29–9.72]), and renal NCOs (6.59 [4.89–8.89]) versus lower-risk individuals.

Conclusions: Individuals with IH have an elevated risk of developing incident or experiencing progression of cardiovascular, cardiometabolic, and renal NCOs versus individuals without IH. Many individuals with IH had pre-existing sodium-associated risk factors, for whom the risk of NCOs was particularly heightened. These results emphasise the need to reduce sodium intake and mitigate the risk of NCOs among individuals with IH, especially for those with pre-existing comorbidities.

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Sleep Actigraphy in Participants With Narcolepsy or Idiopathic Hypersomnia Taking Low-Sodium Oxybate: Results From the DUET Study

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Introduction: Actigraphy provides an empirical, noninvasive, continuous method for monitoring sleep patterns in real-world settings. Jazz DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) was a phase 4, prospective, multicentre, single-arm, multiple-cohort, open-label study (NCT05875974) evaluating effectiveness of low-sodium oxybate (LXB; Xywav®) on daytime and nighttime-related signs and symptoms in participants with narcolepsy or idiopathic hypersomnia.

Materials and methods: DUET included a screening period (with 2-week washout for oxybate users), 8-day baseline (BL) period, 2- to 8-week LXB titration period, 2-week stable-dose period (SDP), 8-day end-of-treatment (EOT) period, and 2-week safety follow-up period. Participants wore a wrist actigraphy device (GENEActiv; 3-axis accelerometer, measurement frequency set to 20 Hz for continuous recording up to 30 days) during BL, SDP, and EOT. Exploratory outcomes (from BL to EOT; uncontrolled for multiplicity) included total nocturnal sleep duration, number of awakenings, sleep onset latency (SOL), and wake after sleep onset (WASO). Least-squares means (LSM) were adjusted for BL values using ANCOVA.

Results: Fifty-five participants with narcolepsy and 46 with idiopathic hypersomnia enrolled and took LXB for ≥1 night; 13 narcolepsy participants transferred to a different cohort (analysed separately); 34 and 40 completed the study, respectively. In narcolepsy and idiopathic hypersomnia cohorts, respectively, participants were mostly female (72.7%; 80.4%) and White (80.0%; 84.8%), with a mean (SD) age of 33.4 (12.9) and 38.1 (11.8) years. Participants with evaluable actigraphy data at BL and EOT (≥5 of 8 days in each) were n=22 (narcolepsy) and n=32 (idiopathic hypersomnia); missing data were due to device failures, insufficient wear time, and electronic capture/transfer errors. Mean (SE) total

nocturnal sleep duration (minutes) was similar from BL to EOT for narcolepsy (418.7 [16.5] to 397.4 [18.8], LSM [SE] change, -21.3 [15.8], $P=0.1949$), and reduced for idiopathic hypersomnia (410.6 [11.8] to 386.0 [11.0], LSM change [SE] -24.6 [7.7], $P=0.0035$). Mean (SE) number of awakenings reduced from BL in both cohorts: narcolepsy, 22.4 (1.0) to 18.6 (0.9), LSM change (SE), -3.8 (0.9), $P=0.0003$; idiopathic hypersomnia, 21.4 (0.9) to 18.0 (1.0), LSM change (SE), -3.4 (0.6), $P<0.0001$. Mean (SE) SOL (minutes) showed no change in narcolepsy (8.6 [1.4] to 12.7 [2.5], LSM change [SE], 4.1 [2.5], $P=0.1204$) and increased from BL in idiopathic hypersomnia (5.7 [0.9] to 10.3 [1.6], LSM change [SE], 4.6 [1.6], $P=0.0073$). Mean (SE) WASO duration (minutes) reduced from BL in narcolepsy (179.0 [11.9] to 160.5 [7.3], LSM change [SE], -18.5 [7.4], $P=0.0211$) and showed no change in idiopathic hypersomnia (161.8 [5.4] to 137.7 [9.1], LSM change [SE], -10.8 [8.7], $P=0.2244$). Treatment-emergent adverse events were consistent with the known safety profile of LXB.

Conclusions: Based on actigraphy, participants with narcolepsy taking LXB showed decreased awakenings and WASO duration, suggesting less disrupted sleep with treatment, compared with BL (off-treatment). Participants with idiopathic hypersomnia taking LXB showed decreased total nocturnal sleep time, and fewer awakenings, which may reflect more restorative sleep. These results augment previously reported polysomnography findings in these participants, adding to the established effectiveness of LXB treatment for narcolepsy and idiopathic hypersomnia.

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Sleep architecture with low-sodium oxybate treatment in idiopathic hypersomnia: results from the DUET study

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Introduction: Jazz DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) was a phase 4, prospective, multicentre, single-arm, multiple-cohort, open-label study (NCT05875974) evaluating the effectiveness of low-sodium oxybate (LXB; Xywav[®]) treatment on daytime and nighttime-related signs and symptoms, including polysomnography (PSG)-based sleep architecture, in participants with idiopathic hypersomnia or narcolepsy. This abstract includes results from the idiopathic hypersomnia cohort.

Materials and methods: DUET included a screening period (2-week washout for current oxybate users), 8-day baseline period (BL; with overnight PSG and assessments on day 8), 2- to 8-week LXB titration period (participants initiated LXB treatment with individualised dosing adjustments to achieve their optimal dosage), 2-week stable-dose period (SDP), 8-day end-of-treatment period (EOT; with overnight PSG and assessments on day 8), and 2-week safety follow-up. Nocturnal PSGs were scheduled using an *ad libitum* protocol, allowing a minimum of 10 hours in bed, unless the participant naturally awakened earlier; bedtime was determined by habitual bedtime. PSG recordings were centrally scored. Exploratory PSG endpoints were analysed in the idiopathic hypersomnia cohort completer set; least squares mean (LSM) changes were adjusted for baseline values. Total shifts from deeper to lighter sleep/wake stages were defined as N1/N2/N3/REM to wake and N2/N3/REM to N1. P values were uncontrolled for multiplicity and therefore considered nominal.

Results: Forty-six participants with idiopathic hypersomnia enrolled and took ≥ 1 LXB dosage (safety set); 40 completed the study (completer set). In the safety set, most participants were female (80%) and White (85%) with a mean (SD) age of 38.1 (11.8) years. In the completer set, mean (SE) total sleep time (TST) at BL and EOT was 467.5 (17.7) and 413.4 (15.5) minutes, respectively (LSM change [95% CI], -54.1 [-81.3, -26.9]; $P=0.0003$). Mean (SE) total number of shifts from deeper to lighter sleep/wake stages at BL and EOT was 60.9 (4.8) and 43.7 (4.3), respectively (LSM [95% CI]: -17.1 [-23.7, -10.5]; $P<0.0001$). Mean (SE) time spent in N1 sleep at BL and EOT was 47.8 (4.1) and 33.0 (3.5) minutes (LSM [95% CI]: -14.8 [-20.3, -9.3]; $P<0.0001$), percentage of sleep stage per TST was 10.3% and 8.0% ($P=0.0017$); in N2 sleep, 270.0 (10.2) and 225.8 (11.5) minutes (LSM [95% CI]: -44.3 [-66.7, -21.9]; $P=0.0003$), 58.5% and 54.2% ($P=0.0286$); in N3 sleep, 51.9 (5.6) and 92.5 (8.5) minutes (LSM [95% CI]:

40.6 [25.8, 55.4]; $P < 0.0001$), 11.2% and 22.8% ($P < 0.0001$); and in REM, 97.7 (7.4) and 62.1 (5.6) minutes (LSM [95% CI]: -35.7 [-46.0, -25.3]; $P < 0.0001$), 20.0% and 15.0% ($P < 0.0001$).

Conclusions: Participants with idiopathic hypersomnia treated with open-label LXB demonstrated reduced TST on *ad libitum* PSG versus BL, with corresponding increases in N3 sleep, decreases in N1, N2, and REM, and reduced stage shifts. These results suggest a potential correction of the underlying differences in sleep architecture between people with idiopathic hypersomnia and controls that have been described previously in a meta-analysis. These findings also represent the first evaluation of the impact of LXB treatment on PSG sleep architecture in individuals living with idiopathic hypersomnia.

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Tonic immobility evaluation in patients with primary hypersomnias with motor paralysis triggered by emotions

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Introduction: Tonic immobility (TI) is characterized by a reversible, intense state of motor inactivity and reduced responsiveness exhibited by many vertebrates when facing situations of extreme fear or inescapable threat. This behavior is considered the last defense mechanism in the context of potential overwhelming danger. TI has also been studied as a common response in humans with post-traumatic stress disorder (PTSD), particularly in victims of sexual assault. Patients with narcolepsy experience a motor phenomenon called cataplexy that is triggered by emotions. While typical cataplexy is associated with hypocretin deficiency and the presence of HLA-DQB1*06:02, which are features of narcolepsy type 1, atypical cataplexy can occur in both narcolepsy type 1 (NT1) and type 2 (NT2). Its underlying mechanisms remain unclear, but psychiatric factors are considered one of the primary suspected causes.

Materials and methods: Patients with primary hypersomnia were previously diagnosed with NT1, NT2 and Idiopathic Hypersomnia (IH) according to ICSD-3 criteria. They were classified into NT1 and NT2 based on cerebrospinal fluid (CSF) hypocretin levels—low in NT1 and normal in NT2. All patients underwent genetic testing for high-definition HLA types. Those presenting with cataplexy, atypical cataplexy, or other motor phenomena triggered by emotions with paralysis were evaluated for trauma history, presence of PTSD and depression, and signs of TI. To assess trauma history, the Life Events Checklist-5 (LEC-5) was used. This assessment was followed by the Tonic Immobility Scale (TIS) to evaluate the TI response during or immediately after the worst traumatic (TIS trauma) experience and during episodes of motor phenomena triggered by emotions (TIS Motor Paralysis). To gain further insight into their mental health, two additional psychometric scales were administered: the PTSD Checklist for DSM-5 (PCL-5) and the Patient Health Questionnaire-9 (PHQ-9).

Results: Of the 68 patients with primary hypersomnia, 25 patients who reported emotion-triggered motor events with paralysis were included. Of these, 14 had NT1 (low hypocretin); all were positive for HLA-DQB1*06:02. Eight had normal hypocretin (6 NT2 and 2 IH) and three had no hypocretin data. Typical cataplexy, considered present if the patient presented symptoms with laughter lasting less than 2 minutes, was present in 12 patients with NT1, while atypical episodes, involving only negative emotions, asymmetrical or lasting more than 5 minutes, were reported by all NT2 and IH patients. Comparing TIS trauma and TIS motor paralysis we found a greater positive correlation (Pearson coefficient) in the group with atypical cataplexy ($r^* = 0.8$, CI = 0.44-0.94, $p = 0.0006$) than in the group with typical cataplexy ($r^* = 0.64$, CI 0.11-0.89, $p = 0.012$). Using the t test, we also found significantly higher scores in TIS trauma ($p = 0.04$) and TIS motor paralysis (0.03) in the group with atypical cataplexy compared to typical cataplexy.

Conclusions: This is the first study to assess tonic immobility (TI) symptoms in primary hypersomnia patients categorized by biomarkers such as hypocretin levels and HLA status. These results open a discussion about the pathophysiology of atypical motor phenomena triggered by emotions with paralysis that are not related to hypocretin deficiency.

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Insomnia

Aberrant Effective Connectivity Within and Between the Default Mode Network, Executive Control Network and Salience Network in Chronic Insomnia Disorder – towards identifying the hyperarousal state

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Introduction: The hyperarousal hypothesis is a key conceptual model for the pathogenesis of chronic insomnia disorder (CID). The model is based on the observed persistent state of physiological, cognitive, and emotional hyperactivation in CID patients, but its neurofunctional mechanisms are not fully understood.

Resting state functional MRI studies in CID patients have demonstrated altered functional connectivity (FC) in the default mode network (DMN), executive control network (ECN) and salience network (SN), which are involved in self-referential processing, internal mentation, emotional plasticity, and goal-directed attention.

While FC offers insights into co-activation patterns among brain regions, it does not provide directionality or causality of these interactions. In contrast, effective connectivity (EC) describes the influence of one brain region over another, incorporating temporal and causal effects of the regions in a neural circuit.

We hypothesized that effective connectivity between key nodes of the DMN, ECN and SN is disrupted in individuals with CID, impairing the SN's ability to modulate and “switch” between DMN and ECN, as the neurofunctional substrate of the hyperarousal state in CID.

Materials and methods: We recruited 31 CID patients, compliant with the ICSD-II/TR criteria, and 24 age-, sex-, and education-matched healthy controls (HC). All participants filled out Insomnia severity index (ISI), Beck depression inventory (BDI) and Epworth sleepiness scale (ESS) and were scanned on a 3T MRI system, obtaining structural and functional data. SPM 12 (Statistical Parametric Mapping) was used to analyse the results. Spectral dynamic causal modelling (spDCM) was applied to the chosen regions of interest (ROIs) within and between the DMN, SN and ECN. One-sample test was used to define the connections significantly different from zero within each group, and two-sample test was performed to determine the connections significantly different between both groups. Two-stage false discovery rate correction was applied.

Results: There were three significant connections, present only in the CID group – suppressive from the dorsolateral prefrontal cortex (DLPFC) to the right hippocampus (HippR) (-0.110 ± 0.258 , $p=0.035$), excitatory from the dorsomedial prefrontal cortex (DMPFC) to the ventromedial prefrontal cortex (VMPFC) (0.206 ± 0.342 , $p=0.018$), and excitatory from the common medial prefrontal cortex (MPFC) to the right anterior insula (AIR) (0.067 ± 0.172 , $p=0.019$). The analysis in the control group revealed two significant excitatory connections – from the posterior cingulate cortex (PCC) to AIR (0.148 ± 0.242 , $p=0.001$), and from precuneus to PCC (0.441 ± 0.388 , $p=0.033$), which are absent in the patients' group. In addition, CID patients scored higher on the ISI (18 ± 4.00 vs 4 ± 2.85 , $p < 0.001$) and BDI (13 ± 7.57 vs 5 ± 4.72 , $p < 0.001$) questionnaires compared to HC. Significant negative correlations between DLPFC to HippR connectivity and both ISI ($\rho = -0.507$, $p < 0.001$) and BDI ($\rho = -0.272$, $p < 0.05$) scores were identified.

Conclusions: Our results indicate that effective connectivity among the DMN, ECN and SN is altered in individuals with CID. Disruptions within the DMN and between the DMN, SN and ECN reflect an impaired ability to appropriately shift between internally and externally directed cognitive states—an imbalance potentially underlying the hypervigilant state of CID.

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Actigraphy-Derived Circadian Rhythm Patterns as the Predictors of Anxiety and Depression in Individual with Insomnia Symptoms: Results of Principal Component Analysis

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Introduction: Emerging evidence links insomnia, circadian rhythm disruption, and mood disorders like anxiety and depression. However, the specific associations between disrupted circadian patterns and mood disorders in insomnia are not well understood. This study examined these relationships in adults with insomnia symptoms.

Materials and methods: Participants were community-dwelling residents from Hong Kong with insomnia (Insomnia Severity Index, ISI ≥ 10), excluding those with comorbid Major Depressive Disorder (MDD) and anxiety disorders. They completed 7-day wrist actigraphy using the ActiGraph GT3X, and mood disorders were assessed via the Structured Clinical Interview for DSM-5 Disorders (SCID-5). Six circadian rhythm parameters were extracted to assess rhythm stability, fragmentation, and day-night activity distribution, including Interdaily Stability (IS), Intradaily Variability (IV), average activity intensity and onset time of the lowest 5-hour nocturnal period (L5, L5hr), and the highest 10-hour diurnal period (M10, M10hr). Principal Component Analysis (PCA) was applied for dimensionality reduction, with components explaining more than 15% of the variance retained, supported by the elbow point in the scree plot. Multivariate logistic regression (adjusting for sex, age, education, marital status, employment, income, BMI, ISI score, and sleep duration) examined associations between circadian dimensions and MDD and Generalized Anxiety Disorder (GAD). To validate the findings, XGBoost models were used, with SHAP values determining feature importance and contribution.

Results: A total of 267 participants (Mean age: 43.4 years, 20.6% male) were included. Among them, 17 (6.4%) had GAD and 18 (6.7%) had MDD. Based on PCA, three principal components were extracted: Dimension 1 (Dim.1, 31.6% of variance), Dim.2 (22.4%), and Dim.3 (19.5%), together accounting for 73.5% of the total variance. Dim.1 was characterized by a delayed circadian phase (M10hr, L5hr), high IV, low IS, and lower daytime activity (M10), reflecting a delayed, unstable, and disorganized rhythm pattern. Dim.2 showed a delayed circadian phase with high IS and low IV, indicating a delayed yet well-consolidated rhythm structure. Both higher Dim.1 and Dim.2 were associated with younger age. Dim.3 was associated with elevated daytime and nighttime activity levels and low IS, suggesting reduced day-night differentiation. Results showed that Dim.1 was significantly associated with a higher probability of MDD (OR = 1.61, 95% CI: 1.12–2.31), and Dim.2 with GAD (OR = 1.69, 95% CI: 1.09–2.64). The XGBoost models showed good predictive performance, with AUCs of 0.88 for MDD and 0.78 for GAD. SHAP values indicated higher Dim.1 values were correlated with higher risk of MDD, and higher Dim.2 with higher risk of GAD.

Conclusions: The concurrence of insomnia and a delayed, irregular and disorganized circadian rhythm pattern were associated with higher risk of MDD, while that of insomnia with a delayed but regular circadian pattern are associated with higher risk of GAD. Future research is needed to determine whether treating different subtypes of circadian rhythm patterns in insomnia could alleviate mood symptoms and even prevent the onset of mood disorders.

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A Multidimensional Risk Model for Sleep Disturbances in Psychosomatic Rehabilitation Patients

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Introduction: Sleep disturbances and insomnia are highly prevalent among patients in psychosomatic rehabilitation. With high comorbidity and complex health profiles, these patients are especially vulnerable to chronic insomnia. This study aimed to develop a theoretical model integrating diverse risk and protective factors influencing sleep outcomes in this vulnerable group.

Materials and methods: A randomized sample of 356 patients (mean age = 49.04, SD = 9.96; 51.2% female) was drawn from a pool of 2,179 admissions. At admission, participants completed standardized assessments on sleep quality, insomnia, mental and physical health, and lifestyle factors.

Results: Poor sleep quality affected 81.1% of patients, and 64.1% met criteria for insomnia. Regression and path analyses identified mental and physical health, stress, lifestyle behaviours, and environmental factors as significant predictors of sleep outcomes (sleep quality: $F[13,150] = 4.401, p < .001$; insomnia: $\chi^2[13] = 25.842, p = .018$). Somatic complaints emerged as the most robust single predictor.

Conclusions: Findings support a comprehensive, multidimensional model of sleep disturbances that accounts for psychological, physiological, and behavioural factors. These insights highlight the need for integrated treatment strategies in psychosomatic rehabilitation settings.

Analysis of the clinical effect of pulsed electromagnetic field on primary insomnia

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Introduction: To investigate the therapeutic effect of pulsed electromagnetic fields (PEMFs) on primary insomnia.

Materials and methods: A total of 120 patients with primary insomnia admitted to the The First Hospital of Hebei Medical University from January to December 2021 were randomly divided into conventional treatment and sham stimulation group (control group) and conventional treatment and PEMFs stimulation group (PEMFs group), with 60 patients in each group. Before and after 2 weeks of treatment, Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the sleep quality, and Insomnia Severity Index (ISI) was used to evaluate the severity of insomnia.

Results: The total effective rate of PEMFs group was higher than that of control group [81.67% (49/60) vs. 41.67% (25/60); $\chi^2 = 20.306, P = 0.000$]. After treatment, the total PSQI score ($F = 228.729, P = 0.000$), sleep quality ($F = 87.291, P = 0.000$), time to fall asleep ($F = 181.842, P = 0.000$), sleep time ($F = 143.355, P = 0.000$) and ISI score ($F = 361.348, P = 0.000$) of the 2 groups were significantly lower than those before treatment. PSQI total score ($F = 13.297, P = 0.000$), sleep quality ($F = 7.573, P = 0.007$), time to fall asleep ($F = 9.776, P = 0.002$), sleep time ($F = 8.566, P = 0.004$), and ISI score ($F = 5.350, P = 0.000$) in PEMFs group after treatment were significantly lower than those of the control group.

Conclusions: PEMFs are safe and effective in the treatment of patient with primary insomnia, which can significantly improve the sleep quality, and can be used as a non - drug treatment for patients with primary insomnia.

A new model of care for men with depression and co-occurring insomnia in primary care: A feasibility and acceptability trial

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Introduction: Mental health disorders are very common in men and 75% of suicides are in men. Despite this, men frequently do not seek help for mental health, and depression in men is often unmanaged.

Ninety percent of men with depression experience insomnia, but insomnia is completely neglected in depression management. As men may be more comfortable talking about their sleep than mental health, insomnia is a way to “open the door” on mental health for men. Research shows that psychological treatment of insomnia has a large therapeutic benefit on depression and reduces suicidal ideation. This aim of this research program was to implement a feasibility and acceptability trial for a scalable, cost-effective new model of care for men suffering depression and co-occurring insomnia.

Materials and methods: Male patients (aged 18-80 years) with probable insomnia disorder (Sleep Condition Indicator (SCI) total score ≤ 16 and symptoms present for at least 3 months), and depressive symptoms (Patient Health Questionnaire (PHQ-9) score ≥ 5) were invited to take part in a treatment study conducted within primary care. Participants were offered nurse delivered Brief Cognitive

Behavioural Therapy for insomnia (CBTi) which included 4 weekly sessions of 30-45 minutes, which has strong supporting evidence for the treatment of insomnia when tailored for primary care. Participants completed the SCI and PHQ-9 at pre-treatment and 3-month follow up. To date, 19 participants have completed 3-month follow-up. Semi structured qualitative interviews were conducted with practice staff and patients to explore their experiences of the treatment and suggestions for future development, to identify potential barriers and facilitators to delivery of the treatment program in primary care.

Results: A total of 28 men participated in this study (Age mean=56.1 years, SD=17.0). Baseline scores prior to treatment indicate probable insomnia disorder (SCI mean=8.5, SD=4.9) and moderate depression (PHQ-9 mean=13.5, SD=5.1). Data from the 19 men who have completed 3-month follow-up to date indicate significant improvements in insomnia symptoms from pre (SCI mean=9.8, SD=4.4) to post treatment (SCI mean=21.5, SD=4.6, $p<.001$). Depressive symptoms also improved from pre (PHQ-9 mean=13.0, SD=5.3) to post treatment (PHQ-9 mean=5.1, SD=3.7, $p<.001$). These improvements were also clinically meaningful for both insomnia symptoms (mean change 11.6; Reliable Change Index [RCI]=7) and depression (mean change 7.9; Minimal Clinically Important Difference [MCID]=5). The semi-structured interviews highlighted that nurse time and GP support were critical to the positive patient experience and engagement in the treatment.

Conclusions: Treating insomnia has a positive impact on both sleep and depressive symptoms in men with comorbid depression and insomnia. Preliminary results show the delivery of nurse based CBTi is both acceptable and feasible within primary care. Further research needs to consider funding models to allow for early detection and treatment of co-occurring depression and insomnia.

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An investigation of lighting interventions to modify sleep quality in University students

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Introduction: Sleep quality in young adult university students is poor, with fragmented sleep, long sleep onset latencies, and reduced total sleep time. The common influential factors of social and work schedules and stress have been identified as triggers and outcomes of poor sleep. The known role of lighting's influence on the circadian rhythm is also a significant factor in young adult university students' sleep with their dependence on electronic devices, thus constantly stimulating visual neuromuscular pathways when checking their social media. The aim of the investigation was twofold: to measure adherence to abstaining from electronics one hour before bedtime and the utility of exposure to lighting that facilitates relaxation and focus.

Materials and methods: This IRB-approved study invited participants from a midwestern university to participate in the survey in exchange for course credit. Seven undergraduates with a mean age of 20.9 years participated in the study. There were four females and three males. All participants were interviewed using a standard sleep history intake interview and were requested to keep a sleep log for two weeks. A random assignment of lighting conditions was given, and each participant returned to their residence hall room at two assigned times for twenty minutes of light exposure in the room. The rooms were measured by a light meter, and an app-controlled bright bulb and lamp were provided with the lighting assignment. A calm, focused, and ordinary lighting exposure was assigned mid-morning for twenty minutes and again in midafternoon.

Results: The participants were generally mildly sleep deprived, with an average at the onset of the study of 68% sleep efficiency. At the end of week one, the average sleep efficiency was 72%, and after week two, the average sleep efficiency was 77%. A statistically significant chi-square index was obtained in comparing the calm lighting condition and sleep efficiency but not with the focus or ordinary lighting conditions. On study evaluation forms, participants rated the morning lighting time and morning lighting condition of calm lighting settings as highly favorable at 94%. The degree of sleepiness, a positive history of transient insomnia centered on the anticipation of stressful events such as an exam variable, and a favorable rating of the focus lighting condition was associated as measured nonparametric correlation. All participants reported compliance with no electronics one hour before bedtime.

Conclusions: Young adult university students have poor sleep health. The commonly reported factors of extreme social schedules, devaluing sleep, and stress influence and result from poor sleep health. It

is plausible that a lighting variable proposed to sleepers may be helpful, much like the sleep hygiene lists. Modifying one's lighting exposure to alter the activation experienced throughout the day may be a valuable and easy intervention for the young adult university student. The reliance on electronics becomes an asset here, where the lighting levels could be checked before sitting in that zone for twenty minutes. The study is planned to continue, and with more participants, the effects of lighting on sleep quality in young adult university students will be further examined.

A pilot survey of Australian health professionals on melatonin use in typically developing children with chronic insomnia

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Introduction: Although melatonin is commonly used in children with insomnia, data regarding its prescription practices in Australia are scarce. This pilot survey aims to describe melatonin use by a cohort of Australian health professionals in typically developing children with chronic insomnia.

Materials and methods: A cross-sectional open survey was administered to a cohort of Australian health professionals electronically across three states (NSW, Victoria and Queensland), collecting information about melatonin prescribing practices in typically developing children. Participants were recruited at a paediatric conference event. Data collection included the following variables: patient age range, dosages used, time of administration, treatment duration, association with other treatments, perceived efficacy, and side effects. Data are expressed as a percentage of total responses

Results: A total of 101 health professionals responded to the survey. This included 48 Paediatricians, 45 General Practitioners and 8 Psychiatrists. Majority (95.4%) used melatonin in clinical practice. Melatonin was prescribed in all ages (including under 2 years of age), but most frequently used in those aged 10 years and over (54.2%). The most common indication was difficulty falling asleep (84.9%). Other prominent indications included parental request (26.4%), anxiety (21.7%), daytime irritability (9.4%) and movements in sleep (7.5%). Most combined use of melatonin with good sleep habits (92.4%). Other prominent medications used consisted of clonidine (31.4%), antihistamine (16.2%) and tricyclic antidepressants (10.5%). Many practitioners continued melatonin use for over 3 months duration (34.3%), with some electing to continue until sleep improved (21.9%). A total of 28.6% participants reported any side effects related to melatonin. These were mild and included headaches, nightmares, vivid dreams, bed wetting, tiredness, daytime somnolence, parasomnias and worsening daytime behaviour. A significant percentage (41%) of participants have ever recommended that patients purchase melatonin from overseas.

Conclusions: This pilot survey demonstrates that no clear consensus exists about the use of melatonin in typically developing children among the surveyed participants. There is a need for clear guidance and further education with the development of an Australia-wide guideline to rationalise and optimise the use of melatonin in children.

App-delivered sleep therapy for older individuals with insomnia (The ASTEROID Study): A randomised controlled trial

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Introduction: Behavioural therapy for insomnia using sleep restriction is a decompartmentalised form of CBTi but has not been tested in older adults with insomnia. This study investigated the efficacy of digital behavioural therapy for insomnia (dBTi) compared to digital sleep health education (active

control) at reducing insomnia symptoms (Insomnia Severity Index: ISI) in older adults with insomnia at 8 weeks.

Materials and methods: The ASTEROID study was a 2-arm single-blind, randomised controlled trial. Participants were randomised to either dBTi or sleep health education. Recruitment was online and participants were ≥ 60 years, had an ISI ≥ 10 and access to a smartphone. Exclusion criteria: shift workers, recent travel (>2 h time zone), serious medical or psychiatric conditions, high risk of sleep disorders, and recent psychotherapy for insomnia (~ 12 months). The intervention (dBTi) was delivered using SleepFix, a mobile application providing sleep restriction over 6 weeks and the control consisted of three bi-weekly digital modules about sleep, insomnia and strategies to improve sleep. The primary endpoint was ISI at 8 weeks, with follow-up at 16 and 26 weeks. Secondary outcomes were sleep quality, fatigue, sleepiness, anxiety and depressive symptoms. All analyses were conducted using intention-to-treat. Registration NCT05067569.

Results: Between September 2022 and November 2023 we randomised 273 participants to dBTi ($n=136$) or sleep education ($n=137$). The mean age was 67.9 ($SD \pm 5.6$) years, with 223 (81.7%) females, most were retired ($n=166$, 61%) and had a baseline ISI of 17.2 ± 4.4 . The mean ISI was significantly lower in the dBTi group compared to control at 8 weeks ($p < 0.001$; 10.5 [95% CI $9.2-11.9$] vs 14.1 [$13.1-14.9$]). There were further reductions in ISI at weeks 16 and 26 in the dBTi group compared to control (all $p < 0.001$; week 26: 8.6 [$7.1-10.2$] vs 13.7 [$12.9-15.4$]). The dBTi group also showed improved secondary outcomes at all time points compared to control, except for anxiety symptoms at 26 weeks ($p=0.184$). There was a higher attrition rate in the dBTi group ($n=56$ completers) compared to the control ($n=72$) at 26 weeks.

Conclusions: We have shown sleep restriction therapy administered using a digital therapeutic reduces insomnia symptoms in older people with insomnia and has positive effects on sleep, daytime symptoms and depressive symptoms. Digital-based sleep restriction therapy could be implemented as a first-line treatment in a stepped care model or with psychologist supervision to increase patient accessibility.

Acknowledgments: We would like to acknowledge all the participants in this study.

Applying Tinnitus Retraining Principles to COMISA Desensitisation/Habituation Programs

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Introduction: COMISA, the co-occurrence of insomnia and obstructive sleep apnea (OSA), poses unique challenges, as CPAP therapy often exacerbates insomnia due to aversive sensations like claustrophobia (mask discomfort) and suffocation (continuous air pressure). Jastreboff and Hazell (2008) note that over 75% of tinnitus sufferers naturally habituate to intrusive sounds, becoming unaware over time unless consciously focusing. This selective perception principle underpins tinnitus retraining therapy (TRT), using white noise to desensitize patients. Similarly, a graded desensitization program for COMISA can habituate patients to CPAP sensations and insomnia hypervigilance-provoking sounds (eg distracting sounds nearby), reducing hypervigilance, insomnia severity (correlated with ISI) and improving CPAP adherence.

Materials and methods: Jastreboff and Hazell's TRT program posits that tinnitus becomes problematic due to selective perception, where emotional significance amplifies awareness. TRT uses CBT to reframe tinnitus as neutral and sound therapy (white noise at decibels slightly above perceived loudness of tinnitus) to facilitate habituation. Over time, patients perceive tinnitus only when intentionally focused, as the brain filters it out. For COMISA, CPAP sensations (Q3: claustrophobia, Q4: suffocation) and sounds (Q7: hissing) are analogous to tinnitus, amplified by hypervigilance common in insomnia. The 8-item COMISA questionnaire identifies specific aversions (e.g., Q5: mask intolerance, Q6: nasal blockages), with higher scores (0–10, strongly disagree to agree) indicating greater distress, correlating with ISI. A TRT-inspired program can desensitize patients by gradually exposing them to CPAP sensations and sounds, reframing them as non-threatening, and fostering habituation to improve sleep quality and CPAP adherence.

A 12-week graded desensitization program for COMISA adapts TRT's sound therapy and CBT principles to address CPAP aversions, using the COMISA questionnaire to tailor interventions. The goal is to reduce selective perception of claustrophobia, suffocation, and mask-related sounds, enabling habituation akin to tinnitus management.

Administer COMISA questionnaire (Q1–Q8, 0–10) and ISI to identify aversions (e.g., Q3: claustrophobia, Q7: hissing) and insomnia severity. Fit CPAP mask with optimal seal; note nasal/sinus issues (Q6). CBTi and Reframing (Weeks 1–2): Educate on core sleep hygiene, stimulus control method & Bed Restriction principles, and education on selective perception: CPAP sensations are amplified by insomnia-related hypervigilance, like tinnitus. Reframe mask sensations as neutral (e.g., “Air pressure supports breathing, not threat of suffocation”), referencing Q4 responses. Graded Sensory Exposure (Weeks 3–6): Air Pressure Introduction, with respiratory specialist's help, setting CPAP machine at low pressure increasing durations, monitoring 'suffocation' scores. Sound Exposure: Introduce white noise/raindrops/fan via phone/electronic device to reduce focus on external sounds of traffic or bed environment & “bat away” ruminative or obsessive thoughts, fading over time as alternative association develops & habituation occurs.

Results: pending preliminary patients' data (July 2025)

Conclusions: By adapting TRT's principles, COMISA sufferers can condition positive CPAP associations & reducing insomnia severity and improving adherence. The desensitization program leverages graded exposure to aversive auditory/proprioceptive stimuli, mirroring tinnitus habituation, where sufferers can learn to ignore perceived threatening signals. Questionnaire-guided interventions target specific aversions (Q1–Q8) & build agency. Future studies should validate outcomes, correlating reduced COMISA scores with ISI, supporting CBTi approaches for COMISA management.

A prospective study of the impact of the natural course of insomnia symptoms on work productivity

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Introduction: The economic losses due to insomnia symptoms account for 91% of presenteeism and absenteeism. Numerous epidemiological studies have consistently reported that the presence of insomnia symptoms is associated with presenteeism and absenteeism. However, since the previous studies were cross-sectional studies, the causal relationship remains unclear. This study aims to clarify the impact of the natural course of insomnia symptoms on presenteeism and absenteeism.

Materials and methods: This study included 4242 daytime workers who attended the annual medical check-up in both 2018 and 2019 (11–12-month follow-up rate is 73.5%). In this study, the presence or absence of insomnia symptoms was asked with a single question, “Do you have insomnia symptoms?”, and the response was either “Yes” or “No”. They were categorized into four groups: normal (No-No; n = 3032, 71.5%), new onset (No-Yes; n = 329, 7.8%), recovery (Yes-No; n = 300, 7.1%), and persistent (Yes-Yes; n = 581, 13.7%). Presenteeism was assessed by asking about work performance in the past month, rated on a scale of 0% (“total lack of performance”) to 100% (“no lack of performance”) in 10% increments, while absenteeism was asked about the number of days absent due to injury or illness in the past month. Statistical analysis method used a linear mixed model (LMM), with group (normal, new onset, recovery, and persistent), time (baseline and follow-up), group*time (interaction) as independent variables, and demographic, workplace, comorbidity factors as covariates.

Results: The result of LMM showed that a significant interaction effect on presenteeism ($\chi^2(3) = 4.73$, $p = 0.003$). Post hoc comparison showed that presenteeism score in the new onset group was significantly lower at follow-up than at baseline. At the follow-up, the persistent group had significantly lower presenteeism score than all other groups, and the new onset group had significantly lower presenteeism score than the recovery and normal groups. The result of LMM showed no significant interaction effect on absenteeism ($\chi^2(3) = 0.61$, $p = 0.61$), but main effect of the group was significant. In the post hoc, the persistent group had significantly higher absenteeism than the normal group.

Conclusions: The presence of insomnia symptoms leads to an immediate worsening of presenteeism, which subsequently becomes chronic, whereas recovery from insomnia symptoms leads to an immediate improvement in presenteeism. Our study revealed a causal relationship between insomnia symptoms and presenteeism. In contrast, the persistence of insomnia symptoms is associated with chronic absenteeism, suggesting that there may be a potential time lag between the onset of insomnia symptoms and the development of absenteeism.

A Small-World Network Study on Acupuncture Treatment for Chronic Insomnia

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Introduction: Insomnia is the dissatisfaction with sleep duration and quality despite adequate opportunities and environment, affecting daytime functionality. Global insomnia rates are rising, with prevalence up to 12%-20%. Chronic insomnia increases risks for cardiovascular disease, cognitive and emotional disorders, metabolic issues, and even cancer. Addressing insomnia has become vital. Functional Magnetic Resonance Imaging (fMRI) is a key non-invasive method to study the brain's response to acupuncture, a current research focus. This project combines Acupuncture and fMRI to investigate acupuncture's effects on brain networks in chronic insomnia, using the Small-World Network method to explore specific acupuncture points' impact.

Materials and methods: Totally 30 insomnia subjects were randomly divided into the treatment group and the control group. (1:1). 15 healthy subjects were recruited to match insomnia patients with age, gender and education level. After enrollment, T1 images and Bold were taken from all subjects using 3.0T magnetic resonance (SIEMENS MAGNETOM Verio Syngo MR B17, Germany) and a 32-channel cranial coil. Based on MATLAB2013b (Mathworks, Natick, MA, USA), through SPM12 software for data pre-processing, the large-scale brain functional network was constructed by GREYNET software, and the images were presented by Brain Net Viewer software. The differences of global attributes and node attributes of the brain network between the two groups were compared, the three sets of square difference analysis, the statistical differences of network measures between the groups were compared, and the paired T-test was used to analyze the changes of network measures.

Results: Compared with healthy controls, the small-world attribute of insomnia patients is weakened. Acupuncture treatment in both the treatment group and the control group could enhance the small-world attribute, clustering coefficient, shortest path and network efficiency of insomnia patients. Compared with before treatment, the difference was statistically significant ($P < 0.05$). Acupuncture treatment in treatment group and control group can significantly improve PSQI, ISI and brain network efficiency has a negative correlation. Compared with the control group, the difference was statistically significant ($P < 0.05$). In the two groups, the efficiency of acupuncture intervention in insomnia network was enhanced: dorsolateral superior frontal gyrus L, orbital middle frontal gyrus R, anterior cingulate and paracentric gyrus L, cuneus lobe L, paracentral lobule L; Hippocampus L and amygdala L were significantly enhanced in treatment group. Treatment group may play a role in treating insomnia and improving the state of liver fire and heart disturbance through brain regions such as hippocampus, amygdala and anterior cingulate gyrus, which are the important brain regions for the treatment of insomnia.

Conclusions: Acupuncture treatment can enhance the small-world attribute of insomnia patients. Acupuncture treatment in treatment group can significantly change the negative correlation between PSQI, ISI and brain network efficiency in insomnia patients. Brain regions such as the hippocampus, amygdala, and anterior cingulate gyrus may be important target regions for acupuncture treatment of insomnia. This research contributes to a deeper understanding of the pathophysiological mechanisms of insomnia, reveals the association between insomnia symptoms and the structure and function of brain networks, and provides clues for formulating personalized acupuncture treatment plans for insomnia patients.

Association between insomnia disorder and healthcare resource utilization in the United States military health system

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Introduction: Insomnia disorder is common among U.S. military Service Members and negatively impacts health and military readiness. Among civilians, insomnia is associated with substantial economic burden; yet, little is known about the economic burden of insomnia within the US Military Health

System (MHS). The MHS is a large, integrated healthcare delivery system with worldwide operations and thus ideal for health services research. The purpose of this study was to determine the association between insomnia disorder and healthcare resource utilization in the MHS.

Materials and methods: Our data source was the Military Data Repository (MDR) between years 2016-2021. This large data repository includes encounter, procedure, medication, and durable medical equipment information for Active-duty military personnel, military dependents, National Guard, and Reserves. Demographic and military information was obtained from the MDR. Inclusion criteria were age <65 years, active-duty military personnel, 12 months of continuous enrollment before and after first insomnia diagnosis (i.e., the index date), and no evidence of insomnia during the 12 months prior to first diagnosis. Insomnia and comorbid medical and psychiatric conditions were defined based on International Classification of Disease-10th Edition codes. Beneficiaries with insomnia were matched 1:1 with non-insomnia controls on >20 demographic, military, and medical and psychiatric comorbidity variables. Mixed effects models were used to compare non-insomnia related healthcare resource utilization (HCRU) between groups across multiple points of service: outpatient, inpatient, and emergency department (ED).

Results: The final sample included 40,978 MHS beneficiaries with insomnia and 40,978 matched non-insomnia controls. Most (35.9%) beneficiaries with insomnia were between ages 25-34 years, and 20.7% were women. 4.2% of beneficiaries with insomnia had one comorbid medical or psychiatric condition, and 1% had >2 comorbid conditions. Relative to matched non-insomnia controls, beneficiaries with insomnia demonstrated greater 12-month HCRU at every point of service (all P values <0.001). The incident rate ratio for non-insomnia inpatient visits was RR (95% CI) = 1.96 (1.85,2.08); for non-insomnia outpatient visits was 2.24 (2.23,2.24); and for non-insomnia related ED visits was 1.60 (1.57,1.63).

Conclusions: Insomnia is associated with substantially increased healthcare resource utilization in the US military health system. Future research should seek to advance personalized medicine approaches to improve outcomes of evidence-based insomnia care.

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Association between symptoms of depression and insomnia

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Introduction: Patients with insomnia who have trouble to fall asleep or / and to maintain sleep quite often also report symptoms beyond like those of depression or daytime sleepiness. The consideration of these variables can be helpful in phenotyping, treatment planning and evaluation of insomnia. The aim of the present study was to explore factors or factor combinations that are related to the severity of insomnia.

Materials and methods: From n= 175 (f= 108) patients diagnosed with insomnia (mean age: 46.4± 14.5 yrs, range 18 - 83 yrs) demographic and anamnestic variables, sleep questionnaires (ISI, ESS, RLS-DI, Stop-Bang), and revised Beck Depression Inventory (BDI-II) are recorded. Responses of the 21 items of BDI-II were evaluated statistically using an exploratory factor analysis. This analysis identified possible predictors of the depression symptoms that contribute to the insomnia severity and complaints. To verify these, they were examined using regression analysis to predict insomnia symptoms. The study was approved by the local Ethics Committee of the Charité-Universitätsmedizin Berlin. Participants have given written informed consent.

Results: The mean ISI-Score was 18.8 ± 0.3 and the mean total BDI-II-Score was 12.3 ± 0.6. There was a positive correlation between ISI-Score and BDI-II-Score (r= .418, p <.001). Factor analysis of BDI-II revealed two latent factors: "pessimism" and "tiredness or fatigue" (p < .001). Linear regression revealed a significant correlation between the identified BDI-II factor "tiredness or fatigue" and the severity of insomnia (r = .55, p < .001). Pessimism and ISI-Score did not show significant correlation (r = .16, p < .05).

Conclusions: The mean ISI-Score was 18.8 ± 0.3 and the mean total BDI-II-Score was 12.3 ± 0.6. There was a positive correlation between ISI-Score and BDI-II-Score (r= .418, p <.001). Factor analysis of BDI-II revealed two latent factors: "pessimism" and "tiredness or fatigue" (p < .001). Linear regression revealed a significant correlation between the identified BDI-II factor "tiredness or fatigue" and the

severity of insomnia ($r = .55, p < .001$). Pessimism and ISI-Score did not show significant correlation ($r = .16, p < .05$).

Association of medications commonly used for insomnia (MCUFI) with abnormal physical activity patterns: A Deep Learning Study Based on NHANES 2003-2006 Database

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Introduction: Medications commonly used for insomnia (MCUFI) are widely regarded as an initial approach by clinicians, with high risk of physical activity(PA) impairment. No large-scale studies have explored the effect of MCUFI on PA patterns assessed by longitudinal objective PA data.

Materials and methods: This study aims to evaluate the PA patterns in MCUFI group, and establish a series of classification models for MCUFI usage with reshaped three-dimensional spatiotemporal PA data, using a multi-layer network based on the Convolutional Long Short-Term Memory (Conv-LSTM) architecture. The deep learning classifiers were developed and validated by internal cross-validation and independent test set. SHapley Additive exPlanations (SHAP) method was used to quantify the relative importance of each time point in the models.

Results: A total of 14,631 participants were included in this study, using the National Health and Nutrition Examination Survey (NHANES) dataset. The MCUFI group demonstrated significantly reduced intensity across all time periods (all $p < 0.001$). Specifically, the group showed a slower growth rate in PA from nighttime to daytime ($p < 0.001$) and a slower decrement rate from daytime to nighttime ($p < 0.001$). Within the MCUFI group, males showed higher activity intensity only during daytime compared to females ($p = 0.028$). Participants using benzodiazepines had significantly reduced intensity than those using other types of MCUFI ($p < 0.001$). The Conv-LSTM model demonstrated robust classification performance across multiple tasks. Particularly, the model achieved moderate performance in detecting MCUFI use (area under the curve, 0.745 [95% CI, 0.728–0.763] for the validation set and 0.700 [95% CI, 0.691–0.710] for the test set).

Conclusions: This study has confirmed the association between MCUFI usage and abnormal PA patterns, with variations observed in gender and type of MCUFI. Further, a series of interpretable deep learning classification models have been established, demonstrating moderate performance.

Association of Personality Profiles with Sleep Disturbance, Depression and Anxiety in Individuals with Insomnia Disorder: A Latent Class Analysis

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Introduction: Insomnia disorder is highly comorbid with psychiatric disorders, such as anxiety and depression. Certain personality trait profiles have been identified as transdiagnostic risk factors for co-occurrence and increased severity of psychiatric disorders. However, empirical research exploring personality profiles in individuals with insomnia and their relationship with insomnia severity and mood symptoms remains limited. The present study aims to understand the relationship between personality profiles and depression, anxiety, insomnia severity, and well-being in individuals with insomnia disorder.

Materials and methods: 218 Chinese participants who underwent Diagnostic Interview for Sleep Patterns and Disorders(DIS) and the Structured Clinical Interview for DSM Disorders(SCID) to screen for sleep and psychiatric disorders, respectively were recruited from the community study in Hong Kong and. All Participants (Mean age=46 yrs $\pm$ 14.93; female: 76.6%; Presence of comorbid psychiatric disorder: 35.3%) has completed questionnaires including the Big Five Inventory(BFI) for personality

traits, symptoms of anxiety, depression, and insomnia, well-being measurement including quality of life, and other insomnia-related measures such as excessive daytime sleepiness, sleep reactivity, sleep hygiene, and rumination. The subjects also completed 7-day sleep diary recording of their sleep-wake patterns, including total sleep duration(TST), sleeptime(ST), wake after sleep onset(WASO), sleep onset latency(SOL), and waketime(WT). Latent class analysis(LCA) was used to identify personality subgroups controlling for age, sex, and psychiatric history. ANOVA was further conducted to investigate the between-subject differences of sleep and mood-related outcomes in personality subgroups.

Results: LCA identified three subgroups characterized as vulnerable, typical, and resilient profiles. The vulnerable group (9.2%) exhibited significantly higher neuroticism($N: 4.07 \pm 0.338$) and lower conscientiousness($C: 2.55 \pm 0.491$), agreeableness($A: 3.01 \pm 0.532$), openness to experience($O: 2.48 \pm 0.639$), and extraversion($E: 1.95 \pm 0.516$), while the resilient group (23.4%) showed the opposite pattern ($N: 2.49 \pm 0.488$; $C: 3.97 \pm 0.348$; $A: 3.94 \pm 0.399$; $O: 3.50 \pm 0.661$; $E: 3.05 \pm 0.561$). The typical group (67.4%) scored nearly average on all traits ($N: 3.30 \pm 0.469$; $C: 3.30 \pm 0.525$; $A: 3.35 \pm 0.399$; $O: 3.11 \pm 0.524$; $E: 2.63 \pm 0.498$). The vulnerable group demonstrated significantly higher insomnia severity ($F[2,215]=9.08$, $p<0.001$), more depressive ($F[2,215]=16.9$, $p<0.001$) and anxiety symptoms ($F[2,215]=24.9$, $p<0.001$), lower quality of life ($F[2,215]=19.3$, $p<0.001$), compared to typical group, then followed by resilient group. Vulnerable group also reported significantly higher mental fatigue ($F[2,215]=3.15$, $p=0.045$), greater daytime sleepiness ($F[2,215]=3.35$, $p=0.037$), and sleep reactivity to stress ($F[2,215]=5.16$, $p=0.006$) compared to Resilient group only. Resilient group has significantly less rumination ($F[2,215]=12.2$, $p<0.001$) and better sleep hygiene ($F[2,215]=3.61$, $p=0.029$) compared to the other groups while typical and vulnerable group had no significant difference. No significant difference were found in all variables related to sleep-wake patterns among three groups.

Conclusions: High Neuroticism along with low extraversion, agreeableness, conscientiousness, and openness to experience are associated with increased risk of sleep and mood disturbance among individuals with insomnia disorders, suggesting the existence of subgroups within the insomnia population. These findings indicate the need for further phenotyping subgroups of insomnia in order to develop personalized treatment for insomnia.

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Associations of Subjective and Objective Sleep with Impulsivity and Probabilistic Reasoning

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Introduction: Growing evidence suggests that insomnia symptoms are associated with heightened impulsive behaviors and altered decision-making patterns. However, there remains limited research regarding the link between objectively measured sleep and decisional impulsivity, a form of decision-making characterized by the acceptance of undue uncertainty, or failure to adapt to environmental changes. According to the dual systems model, since the developing brain is characterized by the imbalance of increased reward-seeking and immature impulse control, inadequate sleep may exacerbate one's propensity to hasty decision making during late adolescents and early young

adulthood. This study aimed to explore the associations of objective and subjective sleep with trait impulsivity and decision-making, specifically performance on a probabilistic reasoning task, in youth.

Materials and methods: Youth participants aged 18-25 were recruited and were invited to complete a battery of self-report questionnaires including Insomnia Severity Index (ISI) for insomnia severity, Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and the Barratt Impulsiveness Scale (BIS) for trait impulsivity. Objective sleep was prospectively assessed over seven nights using wrist actigraphy. Probabilistic reasoning was measured by a behavioral task (beads task) with two scenarios (easy, less uncertainty vs. intermediate, more uncertainty). Multiple regression analyses were used to examine the association of subjective and objective sleep parameters with self-reported impulsivity and probabilistic reasoning task performance.

Results: Thirty-seven participants (mean age: 18.5 ± 1.71 years, female: 62.3%) were included in the study. Multiple regression analyses showed that actigraphy-estimated wake after sleep onset (WASO) was significantly and negatively associated with beads task performance in the easy scenario ($\beta = -0.79$, $p = .036$), even after controlling for subjective sleep (ISI and PSQI scores), suggesting that increased nocturnal wake time after sleep onset was associated with fewer beads drawn before decision-making, reflecting a more impulsive, jumping-to-conclusions reasoning style. No significant association was found between WASO and performance in the intermediate scenario with more uncertainty. Additionally, there were no significant associations observed between other objective sleep parameters (Sleep Onset Latency, Total Sleep Time, Sleep Efficiency) or subjective sleep measures (ISI, PSQI) and task performance in either scenario. Furthermore, objective or subjective sleep parameters were not significantly associated with trait impulsivity, as measured by BIS.

Conclusions: Disrupted sleep, characterized by objectively measured increased nocturnal awakenings, was significantly associated with more impulsive decision-making. On the other hand, subjective reports of insomnia symptoms and sleep quality were not linked to decision-making performance. Further research should consider exploring underlying mechanisms and examining sleep macro- and micro-structure in relation to decision-making and impulsivity in youth.

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Audio neuromodulation to treat insomnia in adults: an observational study

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Introduction: Insomnia affects 31% of adults,¹ incidence rates varying by population^{2,3}, profession⁴, age, co-morbidities and other factors⁵. Characteristics vary⁶, with major impacts on daily functioning, mental and physical health⁷. Standard therapies include sleep hygiene⁸, CBT⁹, and medication¹⁰ but provide inconsistent benefits. Neuromodulation, including TMS, tDCS and cranial nerve stimulation have yielded variable results.¹¹ We designed a pilot study of an audio neuromodulation device to ascertain if sleep quality could be improved.

Materials and methods:

A non-prescription audio neuromodulator (SleepEngine™, Cambridge Sleep Sciences Ltd., 115B Innovation Drive, Oxfordshire, OX14 4RZ, UK) previously showed positive results in adults self-reporting insomnia¹². The device emits rhythmic pulsed sounds hypothesized to promote better sleep, sequenced for 6 – 8 hours and masked by white noise. To assess its effect under monitored conditions, a prospective observational study was conducted after ethical review. One British NHS General Practitioner recruited 20 participants (16 females, 4 males; mean age 51.19, range 22–67) reporting over six months of insomnia, unresponsive to other measures. Exclusion criteria included BMI >35, sleep apnoea, systemic neurologic disease, chronic pain, depression, anti-psychotic medication use, recreational drug use, or any disease likely to impair sleep. No new sleep-related interventions could be introduced during the study.

After a one-week baseline, participants used the device nightly with the sound profile in the same format for 12 weeks, followed by 8 weeks washout after device withdrawal. The primary endpoint was the Pittsburgh Sleep Quality Index (PSQI) at weeks 0, 12, and 20. PSQI scores range from 0–21, with

higher scores indicating worse sleep¹³. Secondary outcomes included sleep diaries, a patient reported sleep score (1 = poor, 5 = excellent) and qualitative feedback.

Results: No significant differences were seen between sex, age or other characteristics. Baseline mean PSQI was 11.15 (range 4–16) and declined significantly over time. Between baseline and end of treatment, there was a statistically significant reduction (mean difference paired t-test; $p = 0.0000204$). A further significant improvement was observed between end of treatment and end of washout ($p = 0.0371$), and the overall reduction from week 0 to 20 was highly significant ($p = 0.000000124$). From baseline to week 16, Wilcoxon signed-rank test revealed a statistically significant reduction in time to fall asleep ($p = 0.00053$) from 0.96 (0.23 – 3.5) to 0.58 (0.1 – 1.39) hours.

Nighttime awakenings showed a non-significant trend toward reduction during the same period from median 2.07 (range 0.57 – 6.43) vs. 1.72 (0 – 6.57) respectively; $p = 0.056$.

Participants experienced a significant reduction in time spent awake during the 12-week study period decreasing from 1.18 hours (range 0.11 – 4.14) to 0.33 hours (0.01 – 2.14), respectively; $p = 0.00039$ (paired t-test)

Patient reported sleep scores improved significantly from baseline to end of week 12 from median 2.64 (1.0 – 3.85) to 3.86 (2.86 – 5.0) respectively; $p = 0.00016$, (paired t-test).

Conclusions: No adverse effects from device use were reported, and participants expressed interest in continuing device use after the trial. These findings suggest a progressive improvement in sleep quality across the study period and these encouraging results merit further investigation.

Brain Network Study of Transcranial Plasma Therapy for Chronic Insomnia

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Introduction: This study intends to explore the characteristic brain network changes in patients with chronic insomnia (CI) by studying transcranial magnetic stimulation combined with electroencephalogram monitoring (TMS-EEG) and resting-state functional magnetic resonance imaging (rs-fMRI) in patients with chronic insomnia (CI) and normal people; our team's previous experiments confirmed that low-temperature plasma (LTP) stimulation may be a new non-invasive neuromodulation technique. Therefore, we intend to observe the therapeutic effect of LTP stimulation on CI patients, and explore the mechanism of LTP stimulation in the treatment of CI based on TMS-EEG and rs-fMRI techniques.

Materials and methods: Thirty-five CI patients (CI group) and 20 healthy volunteers (HC group) were selected for TMS-EEG and rs-fMRI data acquisition. Subsequently, 35 CI patients were randomly assigned to LTP stimulation group (LTP group, 20 cases) and sham stimulation group (Sham group, 15 cases). Each group was intervened for 14 days and 40 minutes a day. The two groups of patients were evaluated by sleep-related scales at baseline, after intervention and 1 month follow-up, and TMS-EEG and rs-fMRI data were collected after intervention.

Results: 1.1) In the early stage of stimulation, the information outflow in the bilateral prefrontal cortex (Fp1, Fp2) decreased in the CI group; in the late stage, the information flow in the left prefrontal region (FP1) increased. 2) The functional connectivity between right ventromedial prefrontal cortex (vmPFC) and bilateral frontal area, bilateral posterior cingulate gyrus and bilateral cerebellum was significantly decreased in CI group. The functional connectivity between right vmPFC and bilateral cingulate gyrus and bilateral insula was significantly enhanced ($P < 0.05$). 2.1) Compared with the baseline, the scores of the LTP group were significantly lower after intervention and at one-month follow-up ($P < 0.001$). 2) In the early stage of stimulation, the information outflow in the left frontal lobe (F3) was reduced in the LTP group; in the late stage of stimulation, the information flow in the left prefrontal region (FP1) increased. 3) In the LTP group, the functional connectivity between the right vmPFC and the left medial superior frontal gyrus and the left anterior cingulate gyrus was significantly enhanced ($P < 0.05$).

Conclusions: 1. CI patients have abnormal network connections between the prefrontal lobe and the temporal lobe and occipital lobe over time. The right vmPFC of CI patients had weakened connection with the executive control network and enhanced connection with the salience network. The connection with bilateral cerebellum was weakened. 2. LTP stimulation can improve insomnia in patients, and the effect can last for at least 1 month. 3. LTP treatment can reverse the abnormal changes of EEG network and make the network connection return to normal. Further, LTP treatment

may improve insomnia symptoms by enhancing the connection strength between the right vmPFC and the salience network and the default mode network.

Can a Hug Improve Sleep? A Randomized Controlled Trial of Partner Embrace in Individuals with Insomnia Symptoms

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Introduction: Insomnia is a highly prevalent sleep disorder, associated with increased risks of physical and mental health problems. Recent evidence from our team suggests that couple relationship quality plays an important role in shaping sleep outcomes. Enhancing relational quality may therefore represent a novel, non-pharmacological strategy to alleviate insomnia symptoms. Hugging, as a common form of affective touch, has been theoretically linked to improved relational well-being. Based on this, we hypothesized that partner hugging could improve insomnia symptoms by enhancing relationship quality and reducing stress.

Materials and methods: This randomized controlled trial compared the effects of sleep hygiene education alone (n = 59) versus sleep hygiene education plus daily partner hugging (n = 59) on insomnia symptoms (primary outcome), as well as sleep quality, couple relationship quality, depression, anxiety, and stress (secondary outcomes). Participants were adults (ISI score ≥ 10) cohabiting with a stable partner ≥ 5 days per week, recruited via social media from December 27, 2024, to April 7, 2025. Assessments were conducted at baseline, post-intervention, and 1-month follow-up. Sleep hygiene education consisted of a 20-minute online session. The hugging intervention involved three 20-second hugs daily (morning, after work, and bedtime) for one month. The primary analysis followed the intention-to-treat principle; per-protocol analysis was conducted for sensitivity testing. Missing data were not imputed. Generalized Estimating Equations (GEE) were used to analyze between-group differences over time.

Results: A total of 118 participants (mean age = 38.27 years, SD = 10.66; 73.9% female) were included. Compared to sleep hygiene education alone, the hugging group showed significantly greater improvement in subjective sleep quality at post-intervention (Cohen's d = 0.63; 95% CI: 0.24 to 1.03), though this effect was not sustained at 1-month follow-up. While no significant between-group differences were found for other secondary outcomes, participants in the hugging group reported significant reductions in perceived stress both at post-intervention and 1-month follow-up compared to baseline (Cohen's d = -0.69 and -0.89, respectively). These findings were robust in sensitivity analyses. Notably, intimacy scores were higher in the hugging group at the 1-month follow-up.

Conclusions: This study suggests that partner hugging may serve as a simple, low-cost, and scalable intervention to improve sleep quality among individuals with insomnia, potentially by reducing stress and enhancing relational intimacy. These findings highlight the therapeutic potential of affective physical contact in sleep health interventions.

Changes in insomnia severity and psychological distress in a community cohort completing THIS WAY UP digital sleep intervention

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Introduction: Insomnia is the most common sleep disorder, affecting 10-15% of the population and contributes to poor mental and physical health outcomes. Cognitive behavioural therapy is considered the gold standard treatment for insomnia, however access to this therapy is challenging. Digital interventions for insomnia are becoming increasingly popular to overcome accessibility barriers. The effectiveness of, and adherence to, these programs across different age groups is currently unknown. This study aimed to examine the effectiveness of a digital CBT-I program on insomnia severity and psychological distress across the lifespan, and explore age-related differences in program completion rates.

Materials and methods: The sample comprised of 9,567 participants who enrolled in the Managing Insomnia program on the ThisWayUp website (www.thiswayup.org.au) between January 2022 and December 2023. The Managing Insomnia program includes four online self-directed lessons. Participants completed the Insomnia Severity Index (ISI) and the Kessler 10-item Psychological Distress scale (K-10) before each lesson of the intervention.

Effect on ISI and K-10 outcomes were observed by running linear mixed models with age group (18-25, 26-39, 40-65, 66-79, and 80+), timepoint (Lesson 1, Lesson 4) and age group and timepoint interaction as fixed effects and participant ID as random effect. Chi-squared analyses were conducted to examine differences in completion rates between groups at each timepoint.

Results: Moderate to large effect size reductions in ISI were observed across the lifespan ($p < 0.001$; $g = 0.56 - 1.01$) with change of at least 4 points (MCID) on ISI. Effects of treatment on insomnia symptom severity significantly differed by age group; the 26-39 year olds had a faster improvement in ISI compared to all other age group, except participants 80+ years ($F(df) = 24.12 (4)$; $p < 0.001$).

Significant but small effect size reductions in K-10 were observed across the lifespan ($p < 0.001$; $g = -0.11 - 0.16$), but did not differ significantly across age groups ($F(df) = 12.24 (4)$; $p = 0.02$). There were significant differences ($p < 0.001$) in program completion rates between age groups at all timepoints. Older adults (aged 66 and above) were 2-3 times more likely to complete all 4 modules compared to 18-39 year olds.

Conclusions: This self-directed internet-based CBT for Insomnia program resulted in significant improvements in insomnia symptom severity and psychological distress across all age groups. In particular the trajectory of improvement in younger adults was faster than other age groups. Importantly, older adults were more likely to complete the program compared to younger age groups. This study lends support to the recommendations implementation of digital interventions for sleep in older adults.

Characteristics and Relationship of Cognitive and Physiological Hyperarousal in Patients with Insomnia: A Primary Study

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Introduction: To investigate the factors influencing arousal characteristics and hyperarousal in patients with insomnia, and to explore the relationship between physiological and cognitive hyperarousal. By supplementing the existing hyperarousal model, the research seeks to provide theoretical foundations for developing targeted clinical interventions

Materials and methods: This study enrolled 56 patients diagnosed with insomnia disorder at Beijing Anding Hospital outpatient clinic between May 2024 and March 2025. Of these, 40 patients were randomly assigned to either the experimental or control group using a randomized controlled allocation table, while 20 community-recruited healthy controls were included. Demographic data were collected through a self-designed general information questionnaire. All participants underwent baseline and 4-week assessments of heart rate variability (HRV), Pittsburgh Sleep Quality Index (PSQI), Dysfunctional Beliefs and Attitudes about Sleep Scale-Chinese Version (DBAS-CV), Pre-Sleep Arousal Scale (PSAS), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Morningness-Eveningness Questionnaire-5 (MEQ-5), and Anxiety Sensitivity Index-3 (ASI-3). The experimental group received weekly sleep hygiene education and mindfulness-based exercises over four weeks, with assessments conducted at baseline and weekly intervals (1st, 2nd, 3rd, and 4th week). HRV measurements were obtained pre- and post-mindfulness intervention. Statistical analyses were performed using SPSS 26.0. Continuous variables were reported as mean $\pm$ standard deviation, and categorical variables as frequency and percentage composition. Linear mixed-effects models were applied to analyze the temporal relationship between mindfulness intervention and immediate HRV changes in patients, with statistical significance defined as $p < 0.05$.

Results: The baseline analysis revealed that patients with insomnia exhibited significant hyperarousal compared to the healthy control. Statistically significant differences ($p < 0.05$) were observed in the PSAS physiological dimension (16.30 ± 4.94 vs 11.25 ± 0.49), PSAS cognitive dimension (26.98 ± 6.80 vs 13.25 ± 4.51), and daytime HRV metrics (RMSSD: 33.41 ± 1.70 vs 52.75 ± 3.22 ; SDNN: 34.02 ± 1.78 vs

51.05±3.80). Path analysis demonstrated that BAI directly drove physiological hyperarousal ($\beta=0.398$, $p=0.002$), while difficulty falling asleep (PSQI2), short sleep duration (PSQI3), and daytime dysfunction (PSQI7) indirectly exacerbated cognitive hyperarousal through maladaptive cognition. Dysfunctional beliefs about sleep (DBAS) emerged as a key moderating variable, significantly reducing cognitive arousal levels ($\beta=-0.242$, $p=0.021$).

The intervention study demonstrated that after a 4-week mindfulness-based intervention, the experimental group showed a significant reduction in total PSQI scores (14.40±2.80 vs 9.05±3.55, $p<0.001$) and improvement in the cognitive arousal dimension (28.15±7.03 to 20.20±6.92, $p=0.001$), while the improvement in physiological arousal dimension did not reach statistical significance (17.45±4.68 to 15.05±7.04, $p=0.22$). Dynamic HRV monitoring revealed that even a single mindfulness session induced significant autonomic regulatory effects: a heart rate reduction of 3.86 bpm ($p<0.0001$), SDNN elevation of 5.83 points ($p=0.004$), and stress index (PSI) decrease of 9.58 points ($p=0.032$). However, cumulative effects over the 4-week intervention period failed to attain statistical significance ($p>0.05$).

Conclusions: (1) Insomnia patients exhibited 24-hour hyperarousal states across physiological, cognitive, and emotional domains;(2) Anxiety and dysfunctional beliefs about sleep emerged as primary determinants influencing somatic and cognitive hyperarousal;(3) A bidirectional interaction existed between somatic and cognitive hyperarousal, modulated by anxiety and dysfunctional sleep-related beliefs, while simultaneously demonstrating relative inter-dimensional dissociation between somatic and cognitive hyperarousal manifestations.

Circadian rhythm timing and associations with sleep symptoms in insomnia disorder

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Introduction: Circadian rhythmicity is intricately intertwined with sleep timing and continuity but it may be altered in people with insomnia disorder. This study tested whether the timing of melatonin onset is associated with sleep symptoms in insomnia disorder.

Materials and methods: In total, 128 people diagnosed with insomnia disorder were recruited. Participants completed daily sleep diaries and wore an actigraph for up to 14 days prior to an in-laboratory sleep study. Participants underwent salivary melatonin collection to estimate dim-light melatonin onset (DLMO) on the following night. Regressions and analyses of variances on DLMO tertile groups tested associations between melatonin timing (DLMO, phase angle differences calculated as DLMO minus each sleep timing variable) with sleep timing and continuity variables derived from sleep diaries and actigraphy.

Results: There were significant associations between DLMO timing and sleep timing (sleep onset time and wake time from diaries, bedtime from diaries and actigraphy), $r_{(s)}=0.27 - 0.37$, but not with sleep continuity (e.g., sleep latency, wake after sleep onset, sleep duration). The phase angle between sleep onset time and DLMO was associated with sleep latency, sleep duration, and sleep efficiency, $r_{(s)}=-0.32 - 0.41$. Participants with a longer sleep onset time phase angle ($>3h$) had longer sleep latencies (*Mean diff*=43.2 mins, *SE*=13.0, $p=0.004$) and shorter sleep durations (*Mean diff*=-65.7 mins, *SE*=20.8, $p=0.006$) than participants with a shorter phase angle ($<2h$). Other phase angles (DLMO and mid-sleep, wake time) were not consistently associated with sleep.

Conclusions: Melatonin onset timing influences sleep timing in insomnia disorder. Larger phase angle differences between sleep onset and DLMO are linked to poorer sleep continuity. These findings highlight the importance of considering circadian alignment and its impact on sleep in understanding the pathophysiology of insomnia and in developing targeted treatment interventions.

Clinical Features and Cortical and Cognitive Arousal in Adolescents with Insomnia and Objective Short Sleep Duration

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Introduction: Adolescence is a critical developmental stage characterized by biological and psychosocial changes that may increase one's risk for sleep and mental health problems. Insomnia, a common issue among adolescents, is often associated with impaired daytime functioning and poor mental health. Previous studies suggested that objective short sleep duration (ISSD) is a marker of biological severity in insomnia, associated with heightened cortical arousal, increased medical problems, and poorer treatment prognosis. However, the clinical profile and underlying mechanism of ISSD remained unclear, especially in adolescents. This study aimed to examine the differences in clinical features, cortical and cognitive arousal in adolescents with ISSD.

Materials and methods: Seventy-eight adolescents aged 12-20 were recruited, including 59 adolescents with DSM-5 insomnia disorder and 19 healthy sleepers (HS) with self-reported 7-10 hours of sleep per night. Participants underwent a clinical interview, completed self-report questionnaires and 2-night laboratory-based polysomnographic (PSG) assessments, with the first night serving as the adaptation night. Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI) measured insomnia severity and sleep quality. Pre-sleep Arousal Scale (PSAS) measured somatic and cognitive arousal. Children's Depression Rating Scale-Revised (CDRS-R) measured clinician-rated depression symptoms. Insomnia participants with total sleep time less than 7 hours as measured by PSG were categorized as ISSD, and the rest were categorized as insomnia with normal sleep duration (INSD).

Results: One participant was excluded due to PSG technical issues, leaving 77 participants (mean age 17.68 and 58% female) for analysis (ISSD, $n = 18$; INSD, $n = 40$). The results showed ISSD had poorer PSG-based sleep efficacy compared to INSD ($p < .05$). Both INSD and ISSD groups showed more severe clinician-rated depressive symptoms and insomnia symptoms, poorer subjective sleep quality, and higher cognitive and somatic arousal compared to HS (*all* $ps < .001$), but there were no significant differences in these measures between the two groups. INSD showed heightened high-frequency power band (Beta-1, 15-25 Hz) compared to HS during the N1 stage and exhibited more low-frequency power band (Alpha, 8-12.5 Hz) during the N3 stage compared to ISSD (*all* $ps < .001$). ISSD had heightened high-frequency band power (Beta-2, 25-35 Hz) during Rapid Eye Movement (REM) sleep compared to INSD ($p = .03$) and HS ($p = .05$). A significant positive association between cognitive and cortical arousal was found in the ISSD ($B=0.655, p=.001$), but not in INSD ($B=-0.165, p=.176$) and HS ($B=-0.103, p=0.718$). No significant differences were found in the association between somatic and cortical arousal across groups (*all* $p>.05$).

Conclusions: ISSD is characterized by heightened high-frequency beta activity during REM sleep and a positive correlation between cortical and cognitive arousal, highlighting a distinct insomnia phenotype with biological differences. It provides physiological evidence to differentiate the mechanisms between phenotypes. Future research should explore tailored interventions and examine the implications of different insomnia phenotypes in treatment response.

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Clinical subtypes of co-morbid insomnia and obstructive sleep apnea (COMISA): Results of a cluster analysis

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Introduction: Variations in the bidirectional relationship between obstructive sleep apnea (OSA) and insomnia in co-morbid insomnia and OSA (COMISA) may form distinct subtypes of COMISA, which have not been previously characterized. This study aims to identify and characterize subtypes of COMISA and assess their association with risks of physical (metabolic syndrome and high CVD risk) and mental (depression and anxiety) disorders.

Materials and methods: Participants were a community-recruited COMISA cohort with an initial sample size of 445 potential subjects that yielded 256 individuals who met diagnosis for COMISA and who were used to identify subtypes using a two-step clustering methodology. Demographics and multidimension clinical characteristics were collected and compared among obtained subtypes. Logistics models were used to evaluate whether these subtypes were associated with cardiometabolic and mental disorders. A clinical cohort of 1816 COMISA patients was used to validate the determined clusters applying the same two-step clustering methodology.

Results: Cluster analysis yielded three clusters (COMISA subtypes): “moderate OSA and moderate insomnia” (cluster 1), “moderate OSA and severe insomnia” (Cluster 2) and “severe OSA and moderate insomnia” (Cluster 3), consisting of 58.2%, 21.9% and 19.9% of the entire cohort, which was validated using the clinical COMISA cohort. The clusters differed significantly on a variety of clinical measurements, including blood indicators related to cardiometabolic risk, inflammation and liver function, depression symptoms, and encephalogram (EEG) spectral power. Cluster 2 was associated with elevated risk of moderate-to-severe depression symptoms, while Cluster 3 was associated with increased risk of CVD and metabolic syndrome.

Conclusions: COMISA patients were found to form three clusters or subtypes. These subtypes were differentially associated with increased risk of cardiometabolic illnesses and depression. These findings provide important preliminary evidence of the existence of phenotypes of COMISA which are likely to have clinical relevance and provide a foundation in precision medicine for treatment of COMISA.

Acknowledgments: We would like to acknowledge the volunteers and patients who agreed to participate in this study.

Co-Designing a Sleep Hygiene eBook for Young People with and without Learning Disabilities: A Qualitative Focus Group Study

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Introduction: Individuals with learning disabilities (LD) often face significant health inequalities, including poorer sleep quality, compared to the general population. While improved sleep hygiene could help address these sleep problems, there are limited evidence-based and accessible resources available to support younger people and those with LD adopt the basic principles of sleep hygiene practice. Current resources are often unregulated, outdated, or target only caregivers to interpret. In collaboration with intended users and stakeholders this project co-designed an evidence-based e-book resource appropriate for younger people with and without LD, and caregivers.

Materials and methods: Using a purposive sampling approach 18 participants (13 male; mean age = 25 years) were recruited for this qualitative study (8 individuals with diagnosed learning disabilities/difficulties and 10 caregivers). Focus groups were conducted online, were audio-recorded with consent, and lasted an average of 75 minutes (range 68-81 minutes). Based on relevant literature a semi-structured interview guide was developed addressing issues of sleep initiation and maintenance, barriers to sleep, and the impact of sleep on daytime functioning. Data were analysed using reflexive thematic analysis (Braun & Clarke, 2006; Byrne, 2022). The interviews were transcribed verbatim, and NVivo software (Version 1.3.535) was used for data storage, coding, and analysis.

Results: Thematic analysis identified four key themes: (1) Bedtime Patterns and Sleep Cues, (2) Creating a Relaxing Sleep Environment, (3) Sleep Disruptors and Adaptation, and (4) Sleep Management through Routines and Guidance. Participants discussed their bedtime routines and the specific sleep cues they relied on, such as particular activities or environmental signals that indicated the start of sleep preparation. Dim lighting, soft bedding, quiet surroundings, pre-sleep emotional regulation, and anxiety and stress reduction were independently identified as important for sleep promotion. Individuals with

LD presented a need for clearer, more accessible sleep hygiene advice. This feedback emphasised the difficulty of applying generic sleep hygiene recommendations without modification. Following the analyses, key themes were matched against current evidence-based sleep hygiene advice, and a set of simplified principles were agreed. These principles were then used to inform a pictorial, accessible e-book focussing on actionable 'rules' for better sleep. Drafts of the "Sleep Smart" e-book were then considered by a sample of professional and non-professional users whose feedback resulted in the final version.

Conclusions: Through direct engagement with end users, insights were gained which informed the creation of a tailored sleep hygiene e-booklet. Focus group discussions underscored the necessity for a resource that is accessible to younger people with below-average reading age, but nevertheless of value to caregivers, younger people generally, and clinicians. The "Sleep Smart" e-booklet provides practical, relevant guidance aimed at improving sleep quality and overall well-being for individuals with learning disabilities and learning difficulties.

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Cognitive-Emotional Traits and Sleep Mental Content Features in Insomnia: Associations With Mental Content Recall and Subjective Sleep Quality

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Introduction: The relationship between Insomnia Disorder (ID), sleep perception, and nocturnal mentation -including both recall and qualitative content- remains insufficiently understood. While ID is consistently associated with altered sleep perception and more negatively toned mental activity, findings regarding recall frequency and the qualitative features of nocturnal mentation are still mixed and underexplored. This study aimed to examine whether, and how, insomnia symptoms and cognitive-emotional traits influence the recall and content of nocturnal mentation, and whether these variables predict individual differences in subjective sleep perception.

Materials and methods: Twenty-six participants (age= 29.58 ± 6.5; 14F/12M) were assigned to two groups based on their Insomnia Severity Index (ISI) scores: 13 with ID symptoms (ISI ≥ 12) and 13 controls (ISI ≤ 7). Over 14 consecutive days, participants completed a Sleep Diary and a Mental Content Diary within 15 minutes of awakening. The Sleep Diary assessed subjective sleep parameters, including perceived depth and restorativeness. The Mental Content Diary captured the presence, recall, and qualitative features of nocturnal mental activity, rated for emotional, perceptual, and thought-like characteristics. Participants also completed the Difficulties in Emotion Regulation Scale (DERS), Ruminative Response Scale (RRS), and the Penn State Worry Questionnaire (PSWQ).

Results: No significant group differences in recall frequency emerged. However, participants with insomnia symptoms reported significantly lower perceived sleep depth ($p=.015$) and restorativeness ($p=.038$) than controls. Spearman correlations showed that recall frequency was negatively associated with rumination ($r=-.526$; $p=.006$) and with difficulties maintaining goal-directed behavior under negative emotion (DERS-Goals; $r=-.42$; $p=.030$). Higher levels of worry were associated with more perceptual ($r=.525$; $p=.006$), emotional ($r=.425$; $p=.030$), and realistic ($r=.425$; $p=.030$) features of mentation, while greater impulse control difficulties (DERS-Impulse Control) were linked to more perceptual content ($r=.396$; $p=.045$). A multiple linear regression showed that perceived sleep depth was significantly predicted by group status (ID symptoms; $\beta=-.889$; $p=.002$) and the presence of thought-like mentation ($\beta=-.310$; $p=.024$), explaining 39.4% of the variance ($R^2=.394$). Sleep restorativeness was also predicted by group (ID symptoms; $\beta=-.615$; $p=.032$), but not by any mental content features.

Conclusions: This study provides new insights into the interplay between cognitive-emotional traits, nocturnal mental content, and subjective sleep perception in individuals with and without ID symptoms. Although mental content recall and features did not differ between groups, individuals with ID symptoms perceived their sleep as significantly less deep and restorative. Importantly, this negative perception was not associated with the emotional intensity of mental content, but rather with its

thought-like quality, supporting theoretical models that link heightened nocturnal cognition to altered sleep perception. Unlike clinical status, cognitive-emotional traits emerged as significant correlates of nocturnal mentation, with worry and impulse control difficulties associated with more perceptual, emotional, and realistic content. While rumination and reduced ability to stay focused on goals during negative emotional states were linked to diminished recall. Overall, these findings highlight the clinical relevance of integrating nocturnal mentation characteristics and individual cognitive-emotional profiles in the clinical assessment of insomnia, suggesting that mental content during sleep may represent a meaningful marker of disrupted sleep experience.

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Cognitive Function and Frontotemporal Functional Connectivity in Patients with Major Depressive Disorder and Comorbid Insomnia Symptoms: A Cerebral Hemodynamics Perspective

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Introduction: The underlying mechanism of major depressive disorder (MDD) with insomnia symptoms (IS) is still unclear. Our research is aimed to investigate the changes in the frontotemporal functional connectivity and cognitive function in patients with MDD and comorbid IS.

Materials and methods: We recruited 82 patients with MDD, including 50 comorbid with IS (MDD-IS), 32 without insomnia (MDD-nIS), and 35 healthy controls (HCs). The MATRICS Consensus Cognitive Battery (MCCB) was used to assess their cognitive function, and a resting-state functional near-infrared spectroscopy (fNIRS) was applied to measure the intensity of their frontotemporal functional connectivity (FC).

Results: A comparative cognitive function analysis showed both MDD-IS and MDD-nIS groups had significantly more impairments than the HC group in multiple domains: information processing speed, attention/vigilance, working memory, verbal learning, visual learning, and reasoning/problem-solving (all with $p < 0.001$, except reasoning/problem-solving with $p = 0.008$). In social cognition, the MDD-IS group had more pronounced impairments than the MDD-nIS group, which also performed worse than the HC group ($p < 0.001$). Using fNIRS, distinct frontotemporal and interregional functional connectivity (FC) changes were found among MDD subgroups differentiated by sleep disturbance. Compared to MDD-nIS and HC groups, the MDD-IS group exhibited significant frontotemporal hypoconnectivity ($p = 0.02$), with specific deficits in four pathways: left triangular part-left premotor cortex ($p = 0.010$), right triangular part-left oculomotor cortex ($p = 0.018$), right triangular part-right premotor cortex ($p = 0.026$), and left oculomotor cortex-right premotor cortex ($p = 0.003$). Further analysis revealed additional dysconnectivity between prefrontal and premotor regions in MDD-IS patients compared to HC, involving connections between left and right dorsolateral prefrontal cortex (DLPFC) and right premotor cortex ($p = 0.002$ and $p = 0.017$, respectively). Subgroup-specific reductions were observed in MDD-IS patients compared to MDD-nIS, particularly in connectivity between the left triangular part and left oculomotor cortex ($p = 0.049$), and between left oculomotor and left premotor pathways ($p = 0.034$). Notably, both MDD subgroups showed impaired connectivity between the right oculomotor and right premotor regions compared to HC ($p = 0.004$), indicating this pathway may be a transdiagnostic neural signature of MDD. Correlation analyses showed significant associations between cognitive performance and interregional FC in the MDD-IS subgroup. Verbal learning capacity was positively correlated with connectivity between the left oculomotor and right premotor cortices. Visual learning performance demonstrated coordinated neural coupling through four pathways: left DLPFC-right premotor cortex, left triangular part-left oculomotor cortex, right DLPFC-right premotor cortex, and left oculomotor-right premotor cortex. Reasoning and problem-solving abilities were positively associated with connectivity patterns between the left triangular-left oculomotor and left triangular-left premotor regions.

Conclusions: These findings indicate that MDD patients with sleep disturbances exhibit characteristic cognitive impairments potentially linked to dysfunctions in frontotemporal and oculomotor-premotor networks. This research advances our understanding of the neural circuits through which sleep disturbances affect cognitive phenotypes in depression, and the related FC patterns could serve as potential biological markers and therapeutic targets.

Cognitive Impairment in Obesity Individuals With and Without Insomnia: The Role of Cortisol Dysregulation

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Introduction: This study aimed to investigate the impact of insomnia on cognitive impairment in individuals with obesity, compare cognitive performance between obese patients with and without insomnia, and explore the potential role of cortisol levels in this association.

Materials and methods: A total of 50 obese participants (BMI ≥ 30 kg/m², aged 18–65 years) were recruited and divided into an insomnia group (n=24) and a non-insomnia group (n=26), with 30 healthy-weight controls (BMI 18.5–24.9 kg/m², no insomnia) included for comparison. Cognitive function was assessed using the MATRICS Consensus Cognitive Battery (MCCB), information processing speed, attention/alert working memory, verbal learning, visual learning, reasoning/problem-solving, social cognition, and total cognition. Plasma cortisol levels were measured at 8:00 AM. Group differences were analyzed using analysis of covariance (ANCOVA) adjusted for education level, and correlation analyses were performed to evaluate associations between cortisol levels, cognitive performance, and clinical variables.

Results: The obesity-with-insomnia group exhibited significantly lower performance in processing speed (p=0.021), verbal learning (p=0.009), and composite cognitive scores (p=0.004) compared to the non-insomnia group, with both obese groups performing worse than healthy controls (all p<0.01). Plasma cortisol levels were significantly elevated in the insomnia group (p<0.001), while no difference was observed between the non-insomnia and control groups. Correlation analyses revealed positive associations between insomnia severity and cortisol levels (r=0.308, p=0.006), as well as between cortisol levels and BMI (r=0.400, p<0.001).

Conclusions: Insomnia may exacerbate cognitive impairment in individuals with obesity, potentially linked to dysregulated cortisol activity. These findings highlight the importance of addressing sleep disorders in obesity management to mitigate cognitive decline.

COMISA in Heart Failure: Greater Impact and Worse clinical Outcomes Compared with Isolated Sleep Disorders

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Introduction: We aimed to evaluate the clinical impact of COMISA on patients with HF, compared to insomnia or sleep apnea alone, and to test the hypothesis that COMISA confers greater risk to HF outcomes than isolated sleep disorders.

Materials and methods: A retrospective cohort analysis was performed using open-access national health data and published studies. HF patients were identified from Portuguese health records (e.g. hospital discharge registries and mortality data), and classified into three groups based on co-diagnoses: Insomnia-only, Sleep Apnea (SA)-only, and COMISA (both insomnia and SA). Prevalence of insomnia and OSA in HF across age strata was estimated using Portuguese epidemiological sources (including INSA/SNS reports and the EPICA heart failure study). Key outcomes (e.g. HF hospitalizations, major adverse cardiac events [MACE], and all-cause mortality) were compared between groups over a follow-up period. Cox proportional hazards models adjusted for age, sex, and comorbidities were used to assess the association of COMISA with outcomes, and interaction analyses were performed to examine differences by age group.

Results: Among Portuguese HF patients (spanning young adult to ≥ 80 years), insomnia and OSA were each highly prevalent, and a notable proportion (approximately 20%) had co-morbid COMISA. Patients with COMISA had more severe HF symptoms and worse New York Heart Association functional class at baseline than those with insomnia-only or SA-only (P < 0.01). Over a median follow-up of 3 years, the COMISA group showed a higher rate of HF-related acute decompensations and MACE compared to the other groups. In multivariate analysis, COMISA was associated with a significantly elevated risk of composite cardiac events (hazard ratio ~ 2.3 vs. no-sleep-disorder, P < 0.005), exceeding the risk observed with insomnia-only or SA-only. COMISA patients had roughly double the yearly HF

hospitalization rate of those with a single sleep disorder. All-cause and cardiovascular mortality tended to be higher in COMISA as well, although not statistically significant after adjustment. Age-stratified results revealed that the detrimental impact of COMISA was most pronounced in middle-aged HF patients: for example, in patients <70 years old, COMISA was linked to a four-fold increase in MACE risk. In older HF patients (≥ 70), insomnia and OSA remained frequent, but the COMISA-related risk increment was more modest. These findings align with recent cohort data in non-HF populations showing that COMISA amplifies cardiac risk (e.g. doubling MACE incidence). Epidemiologically, the analysis confirmed that insomnia and OSA often coexist in HF: while only ~0.9% of Portuguese adults ≥ 25 are diagnosed with OSA (reflecting under-detection), estimates suggest up to 30% actually have clinically relevant sleep apnea, and many of these also report insomnia symptoms. Across all age groups, HF patients with COMISA reported poorer quality of life and sleep quality than those with one sleep disorder, highlighting an additive burden on daily functioning.

Conclusions: The data support our hypothesis that COMISA has a greater clinical impact on heart failure than either insomnia or sleep apnea alone. Patients with HF and COMISA experienced more frequent cardiac events and hospitalizations, suggesting a synergistic deleterious effect of concurrent sleep fragmentation and sleep-disordered breathing on the failing heart.

Co-morbid Insomnia and Obstructive Sleep Apnea Augments Cardiac Autonomic Burden to Increase All-cause Mortality

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Introduction: Co-morbid insomnia and sleep apnea (COMISA) is associated with increased mortality. It remains unclear whether COMISA has cumulative deleterious impact on autonomic regulation to augment risk of deaths compared to insomnia alone and OSA alone. This study aimed to evaluate an association of heart rate variability (HRV) as a marker of autonomic burden to all-cause mortality in patients with COMISA.

Materials and methods: 5225 participants from the Sleep Heart Health Study were included. The participants underwent unattended polysomnography and completed sleep questionnaires on insomnia and daytime impairment from which the diagnosis of COMISA was determined. The diagnosis of COMISA required the criteria for both insomnia (difficulties initiating sleep, maintaining sleep, and/or early morning awakenings on 16-30 times/month and daytime impairment) and sleep apnea (an apnea-hypopnea index [AHI] ≥ 15 events/h) to be met. HRV measures were computed from a 5-min ECG segment extracted during wakefulness prior to sleep and sleep using time-domain and frequency-domain methods, detrended fluctuation analysis, entropy, symbolic dynamics, deceleration capacity (DC) and acceleration capacity (AC). Analysis of covariance controlling for relevant covariates (age, body-mass index, gender, race, smoking status, AHI and prevalent cardiovascular disease) was used to compare differences in HRV characteristics among control, insomnia, OSA, and COMISA groups. Multivariable Cox analysis and ROC were used to estimate the association between HRV and in COMISA subgroup. Multivariable-adjusted Cox proportional hazards analysis were conducted to estimate the associations between HRV metrics and all-cause mortality in patients with COMISA.

Results: Of the 5255 participants, 2697 (51.6%) were controls without insomnia or OSA, 170 (3.3%) had only insomnia, 2221 (42.5%) had only OSA, and 137 (2.6%) had COMISA. 42 deaths occurred in COMISA (30.6%). By comparisons of HRV metrics among these 4 groups, patients with COMISA were associated with elevated autonomic burdens, showing decreased parasympathetic function during wakefulness and sleep compared to controls. In the Multivariable Cox model, DC during wakefulness and sleep were significantly associated with all-cause mortality in COMISA (hazard ratio [HR] per 1-SD, 0.91; 95%CI, 0.84-0.99; $P=0.026$ and HR, 0.86; 95%CI, 0.77- 0.96, $P=0.007$, respectively). DC demonstrated favorable performance in identifying mortality risk in COMISA during wakefulness (the area under the curve, AUC, 0.78) and sleep (AUC, 0.76).

Conclusions: COMISA proposed HRV impairments to be related to the increased risk of all-cause mortality through decreased parasympathetic function during wakefulness. HRV can provide information on underlying pathogenic mechanisms of alterations in the autonomic cardiac modulation associated with all-cause mortality in COMISA.

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Comparative Effectiveness of Digital CBT and MBSR for Insomnia in Cancer Survivors: Results from a Meta-Analysis

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Introduction: Insomnia is a prevalent complaint among cancer patients, with a significant impact on various aspects of their lives throughout the cancer continuum. The present study conducted a meta-analysis to evaluate the effectiveness of digital interventions in alleviating insomnia symptoms by intervention type: CBT vs. MBSR.

Materials and methods: Following PRISMA guidelines, a comprehensive search of the published literature from January 2009 and July 2023 was conducted across 10 major databases, including PubMed, EMBASE, Cochrane, Web of Science, PsycINFO, CINAHL, KoreaMed, MedRIC, KISS, and RISS. Eligible studies included adults (≥ 18 years) with cancer or cancer survivors who received digital psychological interventions and reported quantitative sleep-related outcomes before and after the intervention. Key outcomes included insomnia severity (ISI), overall sleep quality (PSQI), sleep onset latency (SOL), total sleep time (TST), and wake after sleep onset (WASO). Meta-analyses were conducted using a random-effects model, and effect sizes were reported as Hedges'g.

Results: A total of 17 studies were included in the meta-analysis. digital CBT demonstrated significant improvements across multiple outcomes: ISI (Hedges' g = -2.09, 95% CI [-3.63, -0.56]), sleep disturbance (g = -0.52, 95% CI [-0.72, -0.31]), total sleep time (TST) (g = 1.02, 95% CI [0.23, 1.82]), sleep onset latency (SOL) (g = -1.44, 95% CI [-2.69, -0.18]), and total PSQI score (g = -0.79, 95% CI [-1.51, -0.06]). In contrast, digital-based MBSR showed statistically significant improvement only in sleep disturbance (g = -0.33, 95% CI [-0.53, -0.13]), while other outcomes such as total PSQI score (g = -0.76, 95% CI [-1.56, 0.05]) did not reach statistical significance. Heterogeneity was higher among CBT studies ($I^2 = 81.1-96.7\%$) compared to MBSR ($I^2 = 0\%$).

Conclusions: Digital psychological interventions are effective in improving sleep problems among cancer patients. However, effectiveness varies by intervention type and sleep domain. Digital CBT showed robust effects across several sleep outcomes, while digital-based MBSR showed more limited benefits. These findings highlight the need to tailor digital interventions based on therapeutic mechanisms and targeted sleep problems.

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Consistency of Objective Results on Sleep Onset and Sleep Maintenance Parameters From Global Studies of Lemborexant

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Introduction: When selecting a hypnotic for patients, it is important to know whether there are differences in response based on age, sex, and/or race. For registration purposes and to increase patient diversity across the clinical development program for lemborexant (LEM), a dual orexin-receptor antagonist approved to treat adults with insomnia, 2 additional studies were conducted beyond the original Phase 3 studies that enrolled patients in North America, Europe, and Japan, but few from South Korea and none from China. Since studies have now completed in these latter countries, it is possible to compare results on polysomnography (PSG) from the 3 studies conducted globally with South Korea or China.

Materials and methods: Each study was 1-month, multiple-site, randomized, and placebo-controlled enrolling participants with insomnia disorder. Study E2006-G000-304 (Study 304) included females ≥ 55 years/males ≥ 65 years with confirmed sleep maintenance insomnia. Studies E2006-J086-311 (Study 311) and E2006-J082-204 (Study 204) enrolled adults ≥ 18 and 19–80 years, respectively, with confirmed sleep onset and/or maintenance insomnia. PSGs were obtained during the placebo run-in (baseline) and at end-of-treatment. Each study included LEM 10 mg (LEM10) and placebo. Study 304 also included zolpidem extended-release, and Studies 204 and 304 included LEM 5 mg (not discussed here). Change from baseline to Day 30 in latency-to-persistent-sleep (LPS), sleep efficiency (SE), and wake-after-sleep-onset (WASO) were calculated. Safety and pharmacokinetics were assessed.

Results: Results from the 3 PSG studies (204, 304, and 311) were compared using 95% confidence intervals (CIs). LEM10 led to larger changes from baseline in LPS, SE, and WASO compared to placebo. The CIs overlapped, demonstrating that the direction and magnitude of effect were similar. LEM pharmacokinetics from Studies 204 and 311 were comparable to Study 304. Based on the totality of LEM data from clinical trials, analyses show that oral clearance was not affected by race. In Studies 204 and 311, like global Study 304, overall incidence of LEM10 treatment-emergent adverse events was similar to placebo. In all studies, most TEAEs were mild/moderate.

Conclusions: These data support the view that LEM is an effective and well-tolerated treatment for patients with insomnia without influence by race/national origin.

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Co-occurrence of Dysfunctional Cognitions about Sleep and Excessive Daytime Sleepiness as a Psycho-behavioral Characteristic of Comorbid Insomnia and Sleep Apnea

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Introduction: Chronic Insomnia Disorder (CID) and Obstructive Sleep Apnea (OSA) are both common sleep disorders that frequently co-occur as Comorbid Insomnia and Sleep Apnea (COMISA). COMISA has worse clinical symptoms and poorer treatment outcomes than either condition alone. Despite the clinical importance of COMISA, little is known about how psychological and behavioral characteristics are similar to or different from those of each condition. Dysfunctional cognitions about sleep and excessive daytime sleepiness are not necessarily central to the clinical presentation of CID and that of OSA, respectively. However, patients with COMISA could simultaneously exhibit amplified psycho-behavioral characteristics. This study examined whether the co-occurrence of dysfunctional cognitions about sleep and excessive daytime sleepiness differentiates COMISA from CID and OSA.

Materials and methods: We analyzed data from 346 patients in the NCNP database, which is part of a polysomnography databank for sleep disorders in Japan, comprising three distinct groups: CID alone (n = 42, median age: 43.5), OSA alone (n = 166, median age: 51.0), and COMISA (n = 75, median age: 61.0), who didn't have other sleep disorders. Participants were categorized into 4 groups based on combinations of high and low scores on the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS) and Epworth Sleepiness Scale (ESS), with each measure dichotomized by a median split. We conducted two separate logistic regression analyses to examine the relationship between DBAS/ESS combinations and COMISA. One analysis compared COMISA to CID, and the other compared COMISA to OSA. The DBAS/ESS combinations served as the independent variables, and age and sex were included as the covariates.

Results: The high-DBAS/high-ESS groups were younger than the low-DBAS/low-ESS groups across all conditions (COMISA, CID, and OSA). Additionally, the conditions with sleep apnea (i.e., COMISA and OSA) had a higher proportion of males compared to CID. Analyzing logistic regression models adjusting for age and sex, significant associations emerged between the high-DBAS/high-ESS combination and COMISA in both comparative analyses: COMISA vs. CID (adjusted odds ratio [AOR] = 8.01; p = 0.001) and COMISA vs. OSA (AOR = 3.09; p = 0.008).

Conclusions: A concurrent worsening of dysfunctional cognitions about sleep and excessive daytime sleepiness may be a psycho-behavioral characteristic of patients with COMISA. These findings highlight

the need for comprehensive assessment and treatment approaches that address both cognitive and physiological aspects of COMISA.

Correlates between sleep architecture and sleep reactivity to stress in the context of cumulative adversities: Is REM sleep continuity a potential protective factor for sleep reactivity?

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Introduction: Stress is a well-known risk factor for sleep problems, particularly insomnia. While life stressors may induce high sleep reactivity and precipitate insomnia in some vulnerable individuals, some others demonstrate resilience. Thus, it is of significant interest to understand the underlying mechanisms involved in low sleep reactivity against life stressors and adversities. This study aimed to examine the associations of sleep architecture with sleep reactivity in the context of cumulative life stressors in adults.

Materials and methods: All participants received clinical interview, completed questionnaires measuring demographic, sleep characteristics, childhood trauma, and life stressful events, and underwent one-night polysomnography (either ambulatory or in a laboratory setting). The sleep reactivity was measured by the Ford Insomnia Response to Stress Test (FIRST) questionnaire, and other sleep characteristics were measured by the Insomnia Severity Index (ISI) and Pre-sleep Arousal Scale (PSAS). Usage of medications, including hypnotics, antidepressants, NSAIDs, Beta-blockers, antihistamines, anticonvulsants, and melatonin were recorded. Childhood trauma including emotional and physical neglect and abuse, and sexual abuse were self-reported. Life stressful events were grouped into 5 categories: job-related stress, death of a loved one, enormous change in relationship, severe injury or chronic illness, and sexual related uncomfortable experiences or assault. We calculated the level of sleep reactivity versus that of cumulative adversities (life stressful events and childhood trauma) by the standardized residual value in the regression model. We further dichotomized into 2 groups by the split-median value (Low sleep reactivity despite cumulative adversities vs High sleep reactivity with cumulative adversities). The associations of sleep characteristics and sleep architectures with sleep reactivity residuals were further examined, with covariates including age, sex, PSG measures type (Ambulatory or Laboratory), and medications adjusted.

Results: A total of 354 participants (Mean age: 39.16 years; 62.7% female) were included. Among them, 178 participants were grouped into high sleep reactivity and 176 participants into low sleep reactivity, in the context of cumulative adversities. The group with low sleep reactivity upon cumulative adversities showed lower insomnia severity, lower pre-sleep arousal, higher sleep efficiency, less wake time after sleep onset, and less REM sleep transitions to Wake stage (All p values <0.05). The findings remained the same after adjustment of covariates, that participants with low sleep reactivity (despite cumulative adversities) had lower insomnia severity (OR: 0.91; 95%CI: 0.87-0.94), lower pre-sleep arousal (Somatic: OR: 0.88; 95%CI: 0.83-0.93; Cognitive: OR: 0.87; 95%CI: 0.84-0.91), better sleep efficiency (OR: 1.03; 95%CI: 1.00-1.05), less wake time after sleep onset (OR: 0.99; 95%CI: 0.98-0.99) and lower chance of REM sleep transitions to Wake stage (OR: 0.92; 95%CI: 0.86-0.99).

Conclusions: The persistence of low sleep reactivity despite cumulative life adversities is associated with higher sleep continuity, particularly REM sleep continuity. These suggest that maintaining sleep continuity with focus on REM sleep may be potential prevention and intervention target for stress-related sleep pathology.

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Cortical and Autonomic Activity Characteristics During Sleep in Patients with Sleep State Misperception Insomnia: A Retrospective Polysomnographic Study

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Introduction: A subset of insomnia patients perceives their sleep as worse than what is objectively measured by polysomnography (PSG), a phenomenon known as sleep state misperception (SSM). In South Korea, the prevalence of SSM is estimated at 26.4%; yet its classification remains inconsistent. This study aimed to classify SSM subgroups by integrating PSG and self-reported indices, and we hypothesized that distinct SSM profiles may represent physiologically unique characteristics, particularly in cortical and autonomic activity during sleep.

Materials and methods: We retrospectively reviewed the medical records of adult patients (≥ 18 years) who underwent PSG at department of psychiatry of Seoul National University Hospital between May 2018 and August 2022. Participants with ≥ 5 on the Pittsburgh Sleep Quality Index were classified as insomnia patients ($n = 78$; 51.3% female; age = 40.3 ± 14.7), while those with scores < 5 as controls ($n = 34$; 82.4% females; age = 34.5 ± 12.1). Exclusion criteria included PSG-confirmed sleep disorders, major psychiatric disorders (e.g., schizophrenia), and severe medical conditions (e.g., cancer). SSM index was calculated and EEG/ECG power spectral analysis were performed. Latent class analysis (LCA) was conducted based on total sleep time (TST) misperception and anxiety severity. LASSO regression selected EEG and heart rate variability (HRV) features, followed by multinomial logistic regression to identify group-defining markers.

Results: LCA identified two insomnia subtypes: an SSM group ($n = 53$; 60.4% female; age = 42.9 ± 14.3) and a simple insomnia group (INS) ($n = 25$; 32.0% female; age = 34.9 ± 14.2). Compared to the INS group, the SSM group exhibited greater TST misperception (misperception index: -0.261 vs. 0.001 ; $t = 6.82$, $p < 0.001$) and higher anxiety and depression scores than both the INS and control groups (Beck Anxiety Inventory: 17.4 vs. 7.8 vs. 3.2 ; Beck Depression Inventory: 16.1 vs. 11.0 vs. 4.6 ; both $ps < 0.001$). Compared to controls, the SSM group showed decreased N3 sigma power in the right central region (coefficient = -87.5 , $z = -79.3$, $p < 0.001$), while the INS group showed a significant increase (coefficient = 92.9 , $z = 84.2$, $p < 0.001$). N2 beta power in the left frontal region also showed opposite patterns between the SSM and INS groups (SSM: coefficient = 80.4 , $z = 23.1$, INS: coefficient = -84.1 , $z = -24.2$, both $ps < 0.001$). Both groups exhibited reduced REM delta power in the left central region (SSM: coefficient = -44.1 , $z = -7.9$; INS: coefficient = -72.9 , $z = -13.1$, both $ps < 0.001$), reduced normalized high-frequency (HF) power of heart rate variability (HRV) during REM (SSM: coefficient = -35.3 , $z = -20.1$; INS: coefficient = -35.6 , $z = -20.2$, both $ps < 0.001$), and increased N1 sleep percentage (SSM: coefficient = 2.5 , $z = 7.9$; INS: coefficient = 2.3 , $z = 7.3$, both $ps < 0.001$).

Conclusions: Reduced sigma power and increased beta power during deep sleep may serve as a physiological marker of SSM.

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Cost-utility of fully automated digital cognitive behavioral therapy for insomnia: Trial-based economic evaluation with 2 year follow up

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Introduction: Introduction: Insomnia is a common condition that affects approximately one-third of the general population. Cognitive behavioral therapy for insomnia (CBTi) is the recommended first-line treatment; however, a shortage of trained healthcare professionals limits access and increases wait times. Fully automated, digitally delivered CBTi (dCBTi) presents a promising alternative, but there is limited evidence on its cost-effectiveness, particularly over the long-term. This study aims to address this gap by conducting a trial-based economic evaluation of fully automated dCBTi compared to an active control group receiving online patient education.

Study design: Participants were recruited from the general population through advertisement in outpatient clinics and social media. They were assessed for eligibility using an automated questionnaire in the study's website. Eligible participants were randomized 1:1 to the intervention and control arms without stratification. A cost-utility analysis was conducted from a public health service perspective, with evaluations performed at 6 months and 24 months post-treatment. Post-treatment was defined as 9 weeks after randomization.

Materials and methods: Methods: Health utility index scores were obtained from the Short Form 12 at baseline, post-treatment, and at 6 and 24 months post-treatment, using UK preference weights for SF-6D. Quality-adjusted life years (QALYs) were calculated using the area under the curve method. Total costs included the program costs of treatment and health service utilization in terms of sleep medication, GP visits and mental health outpatient visits. Program costs for dCBTi and online patient education were derived from license fees paid during the study period. Resource utilization and costs were assessed based on patients' self-reported questionnaires. Unit costs were obtained from the Norwegian Medicines Agency's costing guidelines and published literature. All costs were adjusted to 2020 Norwegian kroner, and a 4% discount rate was applied to health service utilization costs at the 24-month follow-up.

Cost-utility was expressed in terms of the incremental cost-effectiveness ratio (ICER). Probabilistic sensitivity analyses were performed to explore uncertainty via non-parametric bootstrapping. Given the uncertainty around the dCBTi's market price, threshold analyses were conducted to explore the maximum price per patient.

Results: Results: Preliminary analysis indicated a significant improvement in health-related quality of life post-treatment, which was sustained at both the 6- and 24-month follow-ups. Mixed linear models showed a significant between-group difference in health utility index scores at post-treatment, though this difference reduced at 6 months and further narrowed at 24 months. Patients in the dCBTi group reported fewer GP visits and less sleep medication use compared to the control group.

Conclusions: Conclusion: Fully automated dCBTi may represent a cost-effective solution for increasing access to insomnia treatment in the general population, with potential long-term benefits in both health outcomes and resource utilization.

Data-driven subtypes of youth insomnia: A mixed-feature clustering analysis

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Introduction: Insomnia is a heterogeneous sleep disorder and frequently co-occurs with depressive and other daytime symptoms. Insomnia is prevalent in adolescence and young adulthood, which represents a unique transitional period associated with various biological and psychosocial changes and challenges. Whilst previous research has explored different subtypes of insomnia, the findings were mainly limited to the adult population. The current study aimed to identify and characterize subtypes of insomnia in youth using a data-driven approach.

Materials and methods: This was a secondary analysis of the baseline data (N = 172) collected from two randomized controlled trials conducted in youths aged 12 to 24 years old with DSM-5 insomnia disorder. A series of demographic and clinical features, including age, gender, education, depression diagnosis, duration of insomnia, chronotype preference (as measured by the reduced Morningness-Eveningness Questionnaire, rMEQ), depressive and anxiety symptoms (as measured by Hospital Anxiety and Depression Scale, HADS-D/A), cognitive failures (as measured by Cognitive Failures Questionnaire, CFQ), fatigue (as measured Multidimensional Fatigue Inventory, MFI), and five actigraphy-based sleep parameters, were used as the feature set for clustering. Missing values ($\leq 35\%$) were imputed via missForest, then Gower distances were computed and Partitioning Around Medoids applied. The optimal cluster number ($k = 3$) was selected by majority vote across 23 NbClust indices and confirmed by bootstrap stability (Jaccard > 0.60). Insomnia severity (ISI) and subjective sleep efficiency based on prospective 7-day sleep diary were compared across the clusters using linear regression models adjusted for age and gender.

Results: Partitioning-Around-Medoids applied to the 15 standardized baseline variables produced three reproducible subtypes (Jaccard = 0.69, 0.75, 0.65) with average Silhouette widths of 0.283. There were 39 (23 %), 98 (57 %), and 35 (20 %) participants in Clusters 1-3, respectively. Cluster 1 was characterized with a Low-Distress-Burden profile with lower depression, anxiety, fatigue and cognitive failures, and slightly higher objectively-estimated TST and SE. Cluster 2 was characterized with a High-Distress-Fatigue profile, exhibiting the highest mood and fatigue related scores while objectively-estimated sleep parameters remained near average. Cluster 3 was characterized with a Young Evening-Chronotype profile, containing the youngest and more evening-typed participants, with more cognitive failures and fewer actigraphy-based awakenings. Regressed on above-identified cluster with adjusting for age and gender, cluster 2 (High-Distress/Fatigue subgroup) had significantly higher ISI ($p=0.004$) and lower subjective sleep efficiency based on sleep diary ($0=0.045$) than cluster 1 (Low-Distress-Burden subgroup) but there were no differences in these measure between cluster 1 and 3.

Conclusions: Three distinct insomnia subtypes were identified in youths using a novel data-driven approach. These clusters were mainly driven by mood, fatigue, circadian preference rather than objectively-estimated sleep parameters. Identification of different profiles of youth insomnia may help develop personalized intervention to target specific needs. Future studies should validate these subtypes in larger, more diverse samples and examine their biological markers, as well as treatment response of these subtypes.

Development of the Integrated Home Sleep Detection System Based on the Pathophysiology of Insomnia

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Introduction: The diagnostic criterions of insomnia are not based on pathophysiological etiologies, leading to high diagnostic instability and imprecise treatments of insomnia. The polysomnography has first-night effects, inconvenience and might impact original sleep quality. Wearable devices such as actigraphy are highly applied in insomniac disorder, but the correlation between different variables and sleep quality is controversial. These biological signals could stand for the physiology of sleep based on the three major physiopathologies of insomnia^[1]: dysregulation of the circadian system, homeostatic system, and arousal system. By using information engineering technology, we converted physiological signals into digital signals, and analyzed them into pathophysiological models for assisting clinicians in diagnostic evaluation.

Materials and methods: Self-developed wearable devices were used, including the eye-mask^[2] and actigraphy^[3]. The eye-mask was frontal EEG/EOG-based device, with high correlation coefficients between eye-mask and PSG. It was used for scoring sleep stage and EEG power spectrum before sleep. The actigraphy recorded circadian quotation(CQ), inter-daily stability(IS), intra-daily variability(IV), activity counts of the most active 10 hour period(M10) and of the least active 5 hour period(L5), midpoint daytime of M5 and L5(mM5, mL5) and relative amplitude(RA). The portable ANS test analyzed

heart-rate variability(HRV) included SDNN, RMSSD, LF/HF. The salivary melatonin were also collected. All these devices and examinations were applied at home as home sleep test(HST). The above variables contributed to the above three systems of sleep, showed as [Table 1](#).

The inclusion criteria of insomniac group was (1) Pittsburgh Sleep Quality Index>5 (2) DSM-5 defined insomniac disorder. Normal group were also enrolled by age-and-gender match participants from insomniac groups. All participants used the HST during their daily life as the following figure 2. The above biological signals were statistically analyzed by T-test between these groups.

Results: A total of 30 normal sleepers and 42 insomniac sleepers were enrolled. The average age 25.40 ± 5.65 year-old. Gender distribution showed 50% male and 50% female. In insomniac group, the average PSQI was 10.90 ± 2.95 and ISI was 13.05 ± 5.07 , indicating moderate insomniac severity. In circadian rhythm, mM10 was 2 hour earlier in the insomniac group, about 15:00. The melatonin onset was not detected before bedtime, possible due to night-time light exposure in naturalistic setting. Early rest time might cause misalignment with endogenous circadian rhythm. In homeostatic system, theta and delta wave power and stage III sleep were lower in insomniac group. Sleep pressure accumulated from mental and physical activity might be more specific with slow wave by EEG than activity counts by actigraphy. In arousal system, lower alpha wave power, higher beta wave and lower SDNN under stress state were noted in the insomniac group. The hyperarousal insomnia might be the over-sensitivity of stress reaction. These signals were translated to a visualized model as [figure 1](#) for proposing precise treatments by different pathophysiology.

Conclusions: This system could offer a poly-signal, more precise and personalized evaluation in the naturalistic setting for insomniac patients. By specifying the pathophysiology of insomnia, the precise interventions could be applied more efficiently. Furtherly, more sample size from community and elderly is needed to develop the norm.

Diagnostic stability of insomnia and obstructive sleep apnea in 8 years – implications for the prevalence and progression of COMISA

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Introduction: Co-morbid obstructive sleep apnea (OSA) and insomnia (known as COMISA) is associated with a worse prognosis when compared to each of its constituent disorders alone. Proper therapeutic and prevention approaches imply understanding the disease prevalence, incidence and progression over time. Previous studies have demonstrated that the prevalence of COMISA is 17.6% in the city of São Paulo, Brazil, with an incidence rate of 16.7% and a remission rate of 53.5% over a follow-up of eight years. Although the epidemiology of COMISA is increasingly understood, the contribution and diagnostic progression of each of its constituent disorders (OSA and insomnia) is not known.

Materials and methods: This study was based on the São Paulo Epidemiologic Sleep Study (EPISONO), a population-based study aimed at evaluating the prevalence of sleep disorders in São Paulo, Brazil. Data from EPISONO third edition (2007) and its follow up edition (2015) were considered for the analyses. All procedures were similar in both editions, and all participants underwent type-I polysomnography (PSG) and subjective sleep assessment through validated questionnaires. OSA severity was scored based on the apnea-hypopnea index (AHI) as ≥ 5 for mild, ≥ 15 for moderate, and ≥ 30 for severe cases. Insomnia was evaluated based on the Insomnia Severity Index (ISI) score as ≥ 8 for mild/subthreshold, ≥ 15 for moderate and ≥ 22 for severe insomnia. Diagnostic stability was considered as remaining with the same diagnostic status from baseline to follow-up, either considering the dichotomic diagnosis (yes or no), or the disease severity (no, mild, moderate, or severe).

Results: The final sample was composed of 585 individuals with valid AHI data and 690 individuals with valid ISI data for both editions. Regarding OSA, when all severity levels are considered, 307 (52.5%) participants remained stable, while 230 (39.32%) worsened and 48 (8.21%) improved OSA severity status. When only the dichotomous diagnosis is considered, 416 (71.11%) remained stable, while 142 (24.3%) worsened (OSA incident cases) and 27 (4.6%) improved (OSA remission cases). Regarding insomnia, when all symptom levels are considered, 384 (55.6%) participants remained stable, while 115 (16.7%) worsened and 191 (27.7%) improved. When only the dichotomous conditions are considered, 464 (67.2%) participants remained stable, while 88 (12.8%) worsened (insomnia symptoms onset) and 138 (20.0%) improved (insomnia symptoms remission).

Conclusions: Both insomnia and OSA are stable conditions in most cases, as more than half of the patients with either of these conditions remained with the same diagnostic statuses over a follow-up of eight years. However, when considered individuals who changed their diagnostic status, OSA follows a unidirectional progression, as most individuals evolve into more severe cases, while OSA remission is unlikely without treatment. Conversely, insomnia follows a bidirectional progression, as both increase and decrease in symptoms severity levels are observable. The more unstable progression of insomnia might contribute more to the incidence and remission of COMISA cases.

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Differential Efficacy of Online Group BBTI on Fatigue and Sleep in Depressed Patients with Insomnia Symptoms Based on Sleep Reactivity: A Pilot Study

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Introduction: Fatigue and insomnia symptoms are highly prevalent in patients with depressive disorder, severely impeding their quality of life and treatment outcomes. Behavioral-Based Therapy for Insomnia (BBTI) has potential in enhancing sleep quality and alleviating depressive symptoms, which may also relieve the fatigue symptom. This study aims to investigate the differential efficacy of online group BBTI on fatigue and insomnia symptoms in depressed patients with insomnia symptoms, based on their sleep reactivity as measured by the Ford Insomnia Response to Stress Test (FIRST) score.

Materials and methods: Participants meeting the criteria of the Mini-International Neuropsychiatric Interview 6.0 for major depressive episode and with Insomnia Severity Index (ISI) ≥ 8 were randomized into two online groups: the BBTI group ($n=33$) and the sleep education group ($n=16$). After excluding four participants due to missing FIRST scores, 33 and 12 participants respectively remained in the intervention and control groups. Measures included subjective assessments (insomnia severity, sleep quality, fatigue, mood) and objective testing with polysomnography (PSG). PSG was conducted for two consecutive nights at baseline (using the second night data to exclude first-night effects) and post-intervention. At baseline, 45 participants were categorized into high sleep reactivity (SR) ($n=24$) and low SR ($n=21$) groups based on FIRST scores (>21). Clinical and sleep characteristics were compared between these groups. Twenty-nine participants (13 in high SR group; 16 in low SR group) completed all follow-ups in the BBTI group. Repeated-measures ANOVA was used to compare intervention effects between high SR and low SR groups across baseline, post-intervention, and 3- and 6-month follow-ups.

Results: Among the 45 patients with depressive episodes and insomnia symptoms, high SR was associated with increased subjective depressive symptoms (measured by the Beck Depression Inventory, BDI), reduced subjective positive affect (measured by the Positive and Negative Affect Schedule, PANAS), elevated subjective negative affect (measured by the PANAS), and higher objective sleep microarousal indices (all $p < 0.05$). The interaction between time and SR was statistically significant for the Fatigue Severity Scale (FSS; $p = 0.010$, partial $\eta^2 = 0.358$) and the microarousal index (MAI; $p = 0.003$, partial $\eta^2 = 0.446$). For FSS, high SR patients exhibited higher initial fatigue that decreased significantly post-intervention ($p < 0.05$), while low SR patients showed minimal change. For MAI, high SR patients had higher baseline microarousal indices that decreased significantly post-intervention ($p < 0.05$), whereas low SR patients showed less change. The interaction for subjective sleep onset latency (SSOL) approached significance ($p = 0.056$, partial $\eta^2 = 0.185$), with high SR patients showing a trend toward longer initial SSOL that improved over time, though changes were not statistically significant. Other subjective and objective sleep parameters did not show statistically significant interaction effects differences between the high and low SR groups.

Conclusions: Depressed patients with insomnia symptoms and high SR are characterized by higher negative affect, lower positive affect, more severe depressive symptoms, and increased objective sleep fragmentation. The online group BBTI intervention significantly reduced fatigue and microarousals in this subgroup, although these improvements did not reach statistical significance at later follow-up time points.

Digital CBTi improves insomnia and reduces sleeping pill use in Australian primary care patients: Preliminary analysis of a randomised controlled implementation trial

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Introduction: Insomnia is a prevalent and debilitating disorder in Australian primary care. Only 1% of patients access the recommended first-line treatment for insomnia, Cognitive Behavioural Therapy for Insomnia (CBTi). Most are instead managed with sleeping pills. Digital CBTi (dCBTi) programs may improve CBTi access and reduce sleeping pill dependence in primary care. However, most clinical trials of CBTi have been conducted in specialist settings that have excluded those using sleeping pills. More research in primary care is therefore required to investigate; 1) the effectiveness of dCBTi in the presence of sleeping pill use, and 2) the effect of dCBTi on reducing sleeping pill use in primary care.

Materials and methods: An Australia-wide primary care randomised controlled implementation trial investigated the effects of dCBTi versus digital sleep education (control), in patients with insomnia symptoms referred by general practitioners (GPs). Participants were randomised 1:1 to a self-guided 5-session interactive dCBTi program (Bedtime Window), or 5-weeks of digital sleep education (control). No deprescribing guidance was provided. Insomnia Severity (ISI) and sleeping pill use (any medicine used 'for sleep') were assessed via questionnaire at baseline, 8-weeks, 16-weeks, and 24-weeks. The control group accessed dCBTi after 8-weeks. Linear mixed models (LMM) with bonferroni corrections and Chi-square analyses were used to investigate; 1) the effect of baseline sleeping pill use (y/n) on changes in ISI between the dCBTi and control group, and 2) between-group differences in sleeping pill use/cessation over time.

Results: Participants included 346 adults with insomnia (68% female, M age = 55.6yrs [SD=15.5]). Baseline sleeping pill use did not differ between the dCBTi and control groups (61.8% vs 59.1%; $p=.61$), with a range of medications used, including benzodiazepines, melatonin, antidepressants and sedating-antihistamines. Treatment-response to dCBTi versus control did not significantly differ based on baseline sleeping pill use (interaction $p=.63$). Instead, a statistically significant group-by-time interaction indicated larger ISI improvement in the dCBTi group (M reduction=7.4 [95% CI:6.4-8.5]) than the control group (M reduction=1.9 [0.8-3.1], interaction $p<.001$), regardless of baseline sleeping pill use. ISI improvements in the dCBTi group were sustained at 24-weeks, and the control group experienced similar improvements from 8-weeks to 24-weeks (i.e., after accessing the dCBTi program). At 8 weeks, the CBTi group reported significantly lower sleeping pill use compared to the control group (34.6% vs 50.9%; $p=.009$), representing a 44% rate of sleeping pill cessation from baseline to 8-weeks. After the control group subsequently accessed the dCBTi program, rates of sleeping pill use were similar between groups (16-weeks: 32.3% vs 35.6%; 24-weeks: 30.3% vs 34.8%), indicating similar levels of cessation after accessing dCBTi.

Conclusions: Among a diverse sample of Australian general practice patients with insomnia symptoms, this digital CBTi program led to large, sustained improvements in insomnia severity regardless of the presence/absence of sleeping pill use before treatment. Compared to digital sleep education, dCBTi was associated with a 44% rate of sleeping pill cessation by post-treatment, sustained at 24-week follow-up. These findings support recommending this dCBTi program to primary care physicians and patients to improve insomnia and facilitate reduced dependence on sleeping pills in primary care.

Disentangling Co-morbid Insomnia and Obstructive Sleep Apnea (COMISA): Evaluating the additive diagnostic value of extended features in polysomnographic data

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Introduction: Comorbid insomnia and sleep apnea (COMISA) is a highly prevalent and burdensome disorder, associated with an increased risk of mental health disorders and all-cause mortality. Disentangling COMISA from insomnia and obstructive sleep apnea (OSA) is critical for effective therapeutic intervention. However, overlapping symptoms and mixed findings regarding the clinical characteristics of COMISA – based on commonly used diagnostic approaches such as questionnaires and standard clinical polysomnography (PSG) – complicate its identification and classification. Extended PSG variables, including (neuro)physiological metrics extracted from EEG and ECG recordings, may offer additional insight.

Materials and methods: This study tested machine learning models using XGBoost to evaluate the discriminative value of four feature sets: questionnaire features, conventional PSG features, extended PSG features, and a combined multimodal set. Classification performance was assessed across three pairwise group comparisons: COMISA vs. insomnia, COMISA vs. OSA, and insomnia vs. OSA.

Results: COMISA and insomnia were accurately distinguished using conventional PSG features, whereas questionnaire features showed moderate discriminative value. For COMISA vs. OSA, conventional PSG features were not informative. Questionnaire features performed acceptably, but not good enough for clinical usability, confirming the challenge of distinguishing between COMISA and OSA. Across all comparisons, extended PSG variables did not enhance classification, either independently or in combination.

Conclusions: Extended PSG variables, despite being identified as promising biomarkers, did not show meaningful discriminative power between COMISA, insomnia, and OSA. This suggests that these diagnosis groups do not exhibit unique (neuro)physiological profiles during sleep that can aid diagnostic differentiation.

Does the increase or decrease in the patient's vigilance performance during sleep restriction reflect a build-up of sleep pressure that contributes to treatment success in chronic insomnia?

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Introduction: Cognitive behavioral therapy for insomnia (CBT-I) is the first-line treatment for chronic insomnia disorder (CID) and includes sleep restriction therapy (SRT) as a core component. SRT aims to consolidate sleep by reducing wake time in bed and reinforcing the sleep-wake cycle. Previous home-based CBT-I studies have reported increased daytime sleepiness and impaired vigilance during SRT in CID, indicating the patients have similar response to SRT induced sleep pressure as healthy populations. However, these findings may be confounded by poor protocol adherence at home due to the lack of professional supervision. To address this, we investigated changes in daytime sleepiness and vigilance during a two-week, tightly controlled in-lab CBT-I program in patients with CID.

Materials and methods: We retrospectively analyzed clinical data from 56 patients with CID (mean age: 49.5 ± 14.9 years; 23 female) who completed a standardized two-week CBT-I in house program with the SRT (sleep window: 5-6 hours/night) as the core component at the Clinic Barmelweid, Switzerland. Daily Stanford Sleepiness Scale (SSS), subjective sleep quality (SQ) and psychomotor vigilance tests (PVTs) were performed between 3–4 p.m. . A linear mixed-effects model (LMM) with random slopes and intercepts was used to predict changes in vigilance quantified by the inverse of the mean reaction time ($1/RT$) of PVT across 10 subsequent working days, adjusting for age, sex, SQ and SSS. Changes in daily SSS scores and SQ were modeled similarly. To assess robustness of subject-specific slope of $1/RT$ over days, we performed a subject-level (cluster) bootstrap: in each of 500 replicates we sampled 90% of patients with replacement to refit the LMM. Patients were classified as positive-slope (>95% of bootstrap slopes >0), negative-slope (>95% of bootstrap slopes <0), or uncertain otherwise.

Results: SSS negatively ($p < 0.001$) while SQ tends to positively ($p = 0.07$) associate with $1/RT$ in all patients; however, $1/RT$ did not significantly change over the 10 days ($p = 0.39$). Similarly, SSS scores showed no significant change across days ($p = 0.14$), but negatively associated with SQ ($p < 0.001$). Overall, SQ significantly improved in our patients over the whole CBT-I ($p < 0.001$). Bootstrap analysis showed that 26 and 19 patients had negative and positive slopes of $1/RT$ over days, respectively.

There was no difference in age ($p=0.71$) or gender ($p=1$) between these two subgroups. Notably, the positive-slope group showed significantly improving vigilance ($p < 0.001$) while the negative-group had significantly declining vigilance ($p < 0.001$) when LMM was fit in the two subgroups separately. In both subgroups, the negative association between SSS and $1/RT$ remained (both $p < 0.001$). SQ positively associated with $1/RT$ in positive-slope group ($p=0.03$), not in the negative-slope group ($p=0.31$).

Conclusions: Contrary to prior home-based studies, our supervised, in-lab CBT-I protocol did not lead to consistent declines in vigilance or increases in sleepiness during SRT. Instead, a considerable proportion of patients showed an improvement in PVT performance, which was associated with reduced sleepiness and improved sleep quality. Improved PVT performance with concomitant reduction in subjective sleepiness could therefore be explained by an improved recovery effect of SRT-induced sleep consolidation.

Ecological momentary assessment as an outcome measure in insomnia clinical trials: Preliminary results

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Introduction: Assessment of daytime insomnia symptoms has historically relied on clinical interview or retrospective questionnaires with varying recall periods. Ecological momentary assessment (EMA) is a data-rich approach to assessing participant experiences in real-time. Participants respond to queries multiple times per day in their own natural environments. The purpose of this study was to employ EMA methods as the primary outcome measure in a randomized clinical trial of insomnia medication among older adults. As an initial analytic step, we hypothesized that 1) prior night sleep is associated with next-day insomnia symptoms and 2) within-day mood is associated with same-night sleep.

Materials and methods: This was a double-blind, placebo-controlled randomized clinical trial employing a two-group parallel design among older adults with insomnia. All research procedures including medication administration were entirely remote. Interested volunteers were recruited via print, online, and other media in a tertiary academic medical center and completed diagnostic interview, validated questionnaires, and home sleep apnea testing. Eligible participants were then randomized 1:1 to suvorexant (SUV) or placebo (PBO) nightly for 16 days, including a two night at 10mg run-in period then 14 nights at 20mg (study dose). Throughout, participants subjective sleep diaries each morning and the Daytime Insomnia Symptom Scale (DISS) 4x/day (i.e., 64 survey administrations over 16 days) via a commercially available smart phone app. Finally, participants completed a post-treatment outcomes assessment. To test the hypothesis that prior night sleep is associated with next-day insomnia symptoms among older adults in an insomnia RCT, a series of mixed models (MM) were developed. Each model included a single prior-night sleep metric (e.g., total sleep time [TST, sleep onset latency [SOL], wake after sleep onset [WASO], sleep efficiency [SE] sleep quality [QUAL]) as the independent variable and a single DISS domain (e.g., Alert Cognition, Negative Mood, Positive Mood, and Fatigue/sleepiness) as the dependent variable, controlling for age and sex as covariates. To test the hypothesis that within-day mood predicts same-night sleep, a similar approach was used. To adjust for multiple testing, the Benjamini-Hochberg procedure for correcting false discovery rate (BH-FDR) was employed, with statistical significance set at 0.05.

Results: Forty older adults with insomnia participated (M age=67.9 years, SD=5.4; 90% women; 64.3% White, 30.9% Black, 2.4% American Indian, and 2.4% Asian race). No significant between-groups (SUV n=20, PBO n=20) differences were observed in demographic characteristics. Lagged MM analyses across the 16-day study period revealed that prior-night TST, WASO, SE and QUAL were significantly associated with all next-day insomnia symptoms. Within-day Positive Mood and Negative Mood both demonstrated significant associations with same-night sleep. Participants completed 93.3% of sleep diaries and EMA surveys. 86.5% of participants reported that they were “mostly satisfied” or “very much satisfied” with the remote study approach.

Conclusions: Among older adults with insomnia participating in an insomnia treatment clinical trial, the associations between prior-night sleep and daytime insomnia symptoms, as well as the associations between within-day mood and same-night sleep, were strong. These preliminary results support further evaluation of EMA as an outcome measure in insomnia treatment research.

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Effectiveness of Nurse-Led Web-Based and Face-to-Face Brief Behavioral Therapy for Insomnia in Stroke Survivors: A Pilot Randomized Controlled Trial

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Introduction: Insomnia is prevalent among stroke survivors and is associated with adverse outcomes such as increased fatigue, anxiety, and depression. Brief Behavioral Therapy for Insomnia (BBTI) is a structured, short-term intervention that has shown efficacy in managing insomnia. This study aimed to evaluate the effectiveness of nurse-led web-based and face-to-face BBTI compared to Sleep Hygiene Education (SHE) in reducing insomnia severity and associated symptoms in stroke survivors.

Materials and methods: An assessor-blinded, three-arm, parallel-group pilot randomized controlled trial was conducted in an outpatient clinic in Indonesia. Thirty stroke survivors experiencing insomnia were randomly assigned to one of three groups: web-based BBTI, face-to-face BBTI, or SHE. Each intervention comprised four sessions. Data were collected using paper-based questionnaires assessing insomnia severity, daytime sleepiness, anxiety, depression, and fatigue.

Results: All participants completed the study. Both web-based and face-to-face BBTI groups demonstrated significant improvements in insomnia severity, anxiety, depression, and fatigue compared to the SHE group. No significant changes were observed in daytime sleepiness across all groups. The effectiveness of web-based BBTI was comparable to that of face-to-face BBTI in alleviating insomnia and associated symptoms.

Conclusions: Nurse-led web-based BBTI is as effective as face-to-face BBTI in managing insomnia and related symptoms among stroke survivors. Given its accessibility and practicality, web-based BBTI offers a viable alternative for patients with limited access to in-person therapy. These findings support the integration of web-based BBTI into clinical practice for stroke survivors experiencing insomnia.

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Effectiveness of Stepped-Care Chinese Herbal Medicine and Psychotherapy on Improving Sleep in Adults with Insomnia: A Stepped-Wedge Cluster Randomized Trial

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Introduction: Insomnia is one of the most common sleep disorders in adults, with global prevalence rates ranging between 2.3% and 25.5%. Cognitive behavioral therapy for insomnia (CBT-I) and pharmacotherapy are recognized as common treatments for managing insomnia. However, access to CBT-I is often limited, while low acceptance rate of pharmacotherapy is also a well-known limitation. Therefore, it is imperative to identify alternative treatments that are accessible, effective and acceptable.

Traditional Chinese medicine (TCM), including Chinese herbal medicine (CHM), has been proved to be effective for treating insomnia and is particularly popular in Eastern Asia. In Hong Kong (HK), 34.5% of insomnia patients choose TCM, making it the leading treatment option and reflecting strong cultural acceptance. However, most previous Chinese medicine studies on insomnia were well-controlled randomized trials, and real-world evaluations are lacking. This study aims to examine the effectiveness of stepped-care CHM and psychotherapy intervention in treating insomnia in adults in four clinical centers.

Materials and methods: (1) Study design

This stepped-wedge, cluster randomized trial recruited 366 adults with insomnia in HK between April and November 2024. The 18 geographic districts in HK are grouped into 4 clusters of 4 to 6 districts each, with randomization conducted at cluster level. The intervention was implemented sequentially in one cluster at a time based on a pre-generated random number, while the other clusters remained unexposed. After four steps, all clusters received the intervention. The study was approved by HK Baptist University Research Ethics Committee and prospectively registered with the Chinese Clinical Trial Registry (ChiCTR2400083685).

(2) Population

Adults with an insomnia severity index (ISI) score ≥ 14 .

(3) Stepped-care intervention

The intervention consists of two levels. In level 1, the CHM treatment was based on TCM syndrome differentiation, classifying participants into three subtypes: excess syndrome, treated with Jia Wei Xiao Yao powder; deficiency syndrome, treated with Gui Pi decoction; and excess-deficiency complex syndrome, addressed with Huang Lian E Jiao decoction and Jiao Tai bolus. This level lasted 6 weeks, with participants taking a 5-gram herbal formula twice daily. Those without sleep improvement (ISI score ≥ 14 after level 1 treatment) progressed to level 2, which involved an 8-week personalized CHM intervention and 8-session psychotherapy.

(4) Outcome

Outcome assessments were conducted at baseline and post-intervention. The primary outcome was ISI. The acceptance rate was operationalized as adherence rate by counting unconsumed sachets. Participants' self-management skills for handling insomnia and awareness of sleep health were also measured.

Results: All participants (age [SD]: 45.50 [13.08]; female: 282 [77.05%]) received the level 1 treatment, among whom, 49 (age [SD]: 47.61 [12.83]; female: 34 [69.39%]) progressed to the level 2 treatment. Only level 1 treatment significantly reduced insomnia severity (mean difference [95% CI]: -3.38 [-4.03 to -2.73]; $p < 0.0001$; level 2: -0.90 [-2.49 to 0.69]; $p = 0.26$). The adherence rate was high, at 84.8%. 98.4% of participants reported improved self-management skills for handling insomnia, while 97.3% expressed increased awareness of their sleep health.

Conclusions: The stepped-care CHM and psychotherapy is effective and acceptable in treating insomnia, empowering participants in self-managing insomnia and increasing awareness of sleep health.

Effect of combined treatment with transcranial direct current stimulation and repetitive transcranial magnetic stimulation compared to monotherapy for the treatment of chronic insomnia: a randomised, double-blind, parallel-group, controlled trial

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Introduction: Chronic insomnia increases the risk of various health problems and mental illness. Existing research suggests promise for both transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) in treating chronic insomnia individually. However, the combined effects of tDCS and rTMS on this condition remain unclear. This study aimed to verify the efficacy and safety of tDCS combined with rTMS for the treatment of adult patients with chronic insomnia.

Materials and methods: This was a randomised double-blind parallel-group controlled study. Overall, 157 participants with chronic insomnia were randomly assigned to one of three neurotherapy regimens: tDCS + rTMS, sham tDCS + rTMS, or tDCS + sham rTMS. All groups received 20 treatment sessions over 4 consecutive weeks. The primary outcome was the change in patients' sleep as assessed by the Pittsburgh Sleep Quality Index (PSQI) at 2 weeks, 4 weeks, and 3 months of follow-up. The secondary outcome was the assessment of different dimensions of depression and anxiety in patients through the Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA), as well as the occurrence of adverse events.

Results: Throughout the intervention and after the 3-month follow-up, the tDCS + rTMS group had significantly reduced total PSQI scores compared with the other two groups [tDCS + rTMS, 9.21 vs. sham tDCS + rTMS, 10.03; difference – 1.10; 95% confidence interval (CI), – 1.82 to – 0.38; $p = 0.003$; tDCS + rTMS, 9.21 vs. tDCS + sham rTMS, 10.76; difference – 2.14; 95% CI, – 2.90 to – 1.38; $p < 0.001$; sham tDCS + rTMS, 10.03 vs. tDCS + sham rTMS, 10.76; difference – 1.04; 95% CI, – 1.82 to – 0.26; $p = 0.010$], indicating improved overall sleep quality. Total HAMD and insomnia factor scores were significantly lower in the tDCS + rTMS group than in the other two groups after treatment ($p < 0.05$). Notably, no adverse events or serious adverse reactions were observed during the study period.

Conclusions: Combining tDCS with rTMS effectively relieved insomnia symptoms, achieving a significant therapeutic effect after 2-week of intervention, and demonstrating the persistence of treatment effects in later follow-up, emphasising the advantages of combination therapy in improving treatment stability and long-term benefits, reflecting the rapid and effective augmentation of combination therapy. This combined therapy may serve as a safe and effective treatment for adults with chronic insomnia.

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Effect of daridorexant on wakefulness throughout the night and morning sleepiness in patients with insomnia disorder

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Introduction: Reducing wakefulness throughout the night without residual effects the next morning are essential characteristics for drugs for chronic insomnia disorder. In Phase 3 trials, daridorexant, a dual orexin receptor antagonist, significantly reduced wake after sleep onset (WASO) with rates of daytime somnolence similar to placebo. We now examine in more detail the effect of daridorexant on wakefulness throughout the night and next-morning sleepiness.

Materials and methods: Data from 930 patients with insomnia disorder randomized to daridorexant 50 mg ($n=310$), 25 mg ($n=310$) or placebo ($n=310$) for 3 months were analyzed. Polysomnography-determined WASO by quarter of the night (QoN: Q1 to Q4) at Month (M)1 and M3 of treatment, and morning sleepiness upon awakening by a visual analogue scale (VAS; range 0-100; higher score indicates less sleepiness) were assessed (full analysis set).

Results: Decreases in WASO in Q2-4 of the night were numerically larger in both daridorexant dose groups versus placebo. Baseline WASO in Q1 was low in all groups and thus there were no visible changes in WASO in Q1. At M1, placebo reduced WASO evenly across QoN (Q2-4): Q2: -3.3 min, Q3: -3.7 min, Q4: -3.9 min. Daridorexant 25 mg reduced WASO by -6.2 min, -7.2 min and -7.6 min and daridorexant 50 mg reduced WASO by -8.7 min, -9.6 min, -11.3 min in Q2, Q3 and Q4, respectively. Results were similar at M3.

Mean baseline VAS morning sleepiness scores were 37-38 across groups. Scores increased (i.e. improved) from Day 1 of treatment in all groups and continued to improve as treatment duration increased, with treatment numerically ranked as daridorexant 50 mg > 25 mg > placebo. Mean weekly scores at Week 4 increased by 5.2, 8.8 and 10.2 with placebo, daridorexant 25 mg and 50 mg respectively, and at Week 12, scores increased by 11.6, 14.6 and 15.3 respectively (p values <0.05 for comparison of daridorexant 25 mg or 50 mg vs placebo at Weeks 4 and 12).

Conclusions: In patients with insomnia disorder, daridorexant reduces wakefulness throughout the entire night including Q4, while decreasing morning sleepiness upon awakening.

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Effect of daridorexant on wakefulness throughout the night: Post-hoc analysis of a randomised, double-blind, active reference (zolpidem) study in patients with insomnia disorder

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Introduction: Daridorexant, a dual orexin receptor antagonist [DORA] which works by selectively reducing the orexin-induced wake signalling, has been shown to induce a dose-dependent reduction in wake time after sleep onset [WASO] in patients with insomnia disorder (Dauvilliers et al. Ann Neurol 2020; 87 347–356). This exploratory analysis examined the efficacy of daridorexant in reducing the duration of awakenings in each quarter of the night, when compared to placebo and to the GABA-receptor agonist zolpidem, which induces sleep through widespread CNS sedation.

Materials and methods: This was a multi-centre, double-blind trial (NCT02839200), including adult (18–64y) patients with insomnia randomized (1:1:1:1:1) to placebo, daridorexant (5, 10, 25, or 50mg), or zolpidem (10mg) for 30 days. Polysomnography [PSG]-determined WASO was evaluated using descriptive statistics by quarter of the night (Q1–Q4) i.e. every 2 hours over 8 hours at Days 1 & 2, 15 & 16, and 28 & 29. Baseline was defined as the mean of the two PSG nights during the run-in period and Days 1 & 2 as the mean of the first two PSG treatment nights; Days 15 & 16 and 28 & 29 were defined similarly.

Results: Dose-dependent decreases in mean change from baseline in Q1–Q4 WASO were observed with daridorexant (5–50mg) at Days 1 & 2. Whereas the approved doses of daridorexant (25mg and 50mg) provided similar response to zolpidem 10mg in the first half of the night, mean reductions from baseline in WASO were numerically greater with daridorexant 50mg versus zolpidem 10mg during the second half of the night – with the difference most pronounced in the fourth quarter (mean WASO change from baseline Q3: –13.49 min versus –9.73 min; Q4: –17.51 min versus –7.81 min). Similar effects were seen at Days 15 & 16, and Days 28 & 29.

Conclusions: In patients with insomnia disorder, daridorexant reduces the duration of awakenings throughout the entire night, including the last two quarters.

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Effect of Lemborexant in Patients With Insomnia Comorbid With Depressive Episodes (SELENADE Study)

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Introduction: The objective of this study was to examine the efficacy of lemborexant (LEM) in patients with insomnia associated with depressive episodes.

Materials and methods: This was a multicenter, collaborative, prospective intervention study in patients with insomnia diagnosed with either major depression disorder (MDD) or bipolar disorder (BD) receiving stable treatment for the depressive episodes. Participants with a prior medication for insomnia were enrolled into either the MDD add-on or BD add-on cohort, and those without concomitant hypnotic medication were enrolled into either the MDD mono or BD mono cohort. The starting dose of LEM was 5 mg and could be titrated up and down. The primary endpoint was the change from baseline (BL) in the Insomnia Severity Index (ISI) at Week 4. The changes in both insomnia (ISI) and depressive symptoms (Hamilton Depression Rating Scale [HAMD-17] total scores and Young Mania Rating Scale [YMRS] total score [BD cohorts only]) during 12 weeks of LEM treatment were evaluated as secondary endpoints. This study was conducted with the approval of the certified ethical review board and with the participants' written informed consent.

Results: In total, 83 participants were enrolled, and 82 were included in the full analysis set (MDD add-on, n=29 participants; MDD mono, n=23; BD add-on, n=15; BD mono, n=15). The average age was 47.2 years, and 64.6% were women. For MDD add-on, MDD mono, BD add-on, and BD mono cohorts, the mean ISI total score at BL was 14.5, 13.2, 13.5, and 11.8, respectively, and the mean change from BL (95% confidence interval) after 4 weeks of treatment was –2.3 (–3.9, –0.7), –3.2 (–5.0, –1.3), –5.2 (–7.9, –2.5), and –4.5 (–6.3, –2.6), respectively. Improvements in insomnia were maintained up to 12 weeks in all cohorts. The mean score on the HAMD-17 at BL was 13.6, 12.6, 13.9, and 11.4,

respectively, and the mean change from BL (95% CI) after 12 weeks of treatment was -6.4 (-7.8, -4.9), -6.2 (-7.7, -4.6), -5.2 (-8.4, -2.1), and -5.4 (-7.2, -3.5), respectively. The mean score on the YMRS at BL was 1.1 and 2.3 for the BD add-on and BD mono cohorts, respectively, and the mean change from BL (95% CI) after 12 weeks of treatment was -0.7 (-1.9, 0.5) and -1.5 (-2.8, -0.2), respectively. The incidence of adverse events (AEs) was similar across cohorts (41.4%, 43.5%, 37.5%, and 33.3%, respectively). Most common treatment-emergent AEs (≥ 5 participants in total) were somnolence (MDD add-on, $n=4$ [13.8%]; MDD mono, $n=4$ [17.4%]; BD add-on, $n=4$ [25%]; BD mono, $n=0$) and nightmares ($n=2$ [6.9%]; $n=1$ [4.3%]; $n=2$ [12.5%]; $n=1$ [6.7%], respectively). All adverse events were mild to moderate and consistent with the known profile of LEM; no serious adverse events were observed. Three patients (3.6%) discontinued LEM due to AEs, all from the MDD add-on group.

Conclusions: The results of this study suggest the effectiveness of LEM for insomnia comorbid with depressive episodes.

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Effect of Lemborexant on Subjective Sleep Parameters in Chinese Participants With Insomnia Disorder: Results From a Phase 3, Randomized Study in China

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Introduction: Approximately 16.8–30.8% of people in China experience symptoms of insomnia. This post hoc analysis investigated the efficacy and safety of lemborexant (LEM), a competitive dual orexin-receptor antagonist, on subjective sleep parameters compared with placebo (PBO) in participants with insomnia disorder in China.

Materials and methods: Study E2006-J086-311 (Study 311; NCT04549168), a phase 3, one-month, multicenter, randomized, double-blind, PBO-controlled, parallel group study, evaluated the efficacy and safety of LEM 10 mg (LEM10) in Chinese adults (≥ 18 years) who met the criteria for insomnia disorder per *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, and who had an insomnia severity score ≥ 15 . Participants were randomized (1:1) to receive LEM10 or PBO, which was taken immediately before bedtime. Participants completed a sleep diary within 1 hour of awakening each morning throughout the study. Subjective sleep onset latency (sSOL; min), wake after sleep onset (sWASO; min), and total sleep time (sTST; min) were evaluated using sleep diary data. Baseline means (7 nights during the approximately 7-day single-blind PBO run-in period) and least square mean (LSM) (standard error [SE]) changes from baseline for the first and last 7 nights of the treatment period were calculated for sWASO and sTST. sSOL data (log-transformed) are presented as median (quartile [Q1, Q3]) changes from baseline for the first and last 7 nights of the treatment period. Safety data were collected.

Results: The full analysis set comprised 193 participants (LEM10: 93; PBO: 100). Baseline mean (SD) values for LEM10 and PBO, respectively, were 93.13 (70.46) and 86.60 (45.39) for sSOL; 122.76 (84.72) and 116.32 (75.31) for sWASO; 308.69 (92.58) and 306.68 (82.69) for sTST. Decreases (improvements) from baseline in sSOL were larger and statistically significant with LEM10 versus PBO during the first 7 nights (median [Q1, Q3]: LEM10: -17.00 [-42.86, -2.14]; PBO: -11.86 [-25.00, 5.17]; $P=0.0010$) and the last 7 nights (LEM10: -29.29 [-57.14, -10.00]; PBO: -20.46 [-38.71, -3.43]; $P=0.0063$). Decreases (improvements) from baseline in sWASO were larger and statistically significant with LEM10 (LSM [SE]: -19.67 [7.75]) during the first 7 nights compared with PBO (-4.79 [6.90]; $P=0.0095$); during the last 7 nights, sWASO decreased from baseline with LEM10 (-30.04 [8.47]), but was not significantly different from PBO (-19.67 [7.63]; $P=0.1625$). Increases (improvements) from baseline in sTST were larger and statistically significant in the LEM10 group compared with PBO during the first 7 nights (LSM [SE]: LEM10: 34.93 [10.24]; PBO: 0.87 [9.09]; $P<0.0001$) and the last 7 nights (LEM10: 52.42 [11.44]; PBO: 29.78 [10.26]; $P=0.0300$). Treatment-emergent adverse events occurred in 30 (31.9%) and 21 (21.0%) participants in the LEM10 and PBO groups, respectively. LEM10 was well tolerated.

Conclusions: In this study, LEM consistently improved subjective sleep parameters (sSOL, sWASO, and sTST) compared with PBO in Chinese participants with insomnia. LEM was well tolerated and may be a potential treatment option for patients with insomnia in China.

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Effect of Scalp Acupuncture on Neurological Deficits and Insomnia in Patients with Stroke

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Introduction: The scalp acupuncture is a treasure of traditional Chinese medicine treatment. This study was to observe the effect of scalp acupuncture on neurological deficits and insomnia in patients with stroke.

Materials and methods: A total of 40 patients with neurological deficits and insomnia disorders after stroke who were hospitalized in the Department of Neurology were enrolled prospectively from November 2021 to November 2022. According to whether or not scalp acupuncture (SA) treatment was performed, it was divided into a SA group (n = 23) and a control group (n = 17). The observation group received scalp acupuncture therapy in addition to conventional internal medicine treatment. The control group did not receive any acupuncture treatment and only received conventional internal medicine treatment. The NIH Stroke Scale (NIHSS), Modified Rankin Scale (mRS), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI) were performed before and after treatment, and reassessed after 3 months and followed up for 6 months. Safety assessment was performed at beginning and at 4 weeks after the treatment.

Results: At 3 and 6 months after treatment, there were statistically significant differences in mRS improvement between the observation group and the control group ($P < 0.05$). After treatment and 3 months of follow-up, there was no significant difference in NIHSS between the two groups ($P > 0.05$), while there was a significant difference in NIHSS between the two groups after 6 months of follow-up ($P < 0.05$). After treatment, the insomnia symptoms of the two groups were improved ($P < 0.05$). After 3 to 6 months of follow-up, the PSQI and ISI scores of the observation group were lower than those of the control group ($P < 0.05$).

Conclusions: Scalp acupuncture has clinical therapeutic value and high safety in reshaping neurological function and improving insomnia symptoms after stroke.

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Effects and Influencing Factors of the Different Components in Cognitive Behavioral Therapy for Insomnia

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Introduction: This study, combining the psychological characteristics of Chinese patients with insomnia, aims to verify the efficacy of CBT-I in Chinese insomnia patients and explore the different therapeutic components of CBT-I as well as the related factors affecting its efficacy, so as to provide a basis for the further localization and individualization of CBT-I.

Materials and methods: 120 insomnia patients were recruited from the outpatient department and randomly assigned to four groups: Cognitive Behavioral Therapy (CBT), Cognitive Therapy (CT), Behavioral Therapy (BT), and Treatment as Usual (TAU) (n=30/group). All groups received weekly interventions for 8 weeks. The Insomnia Severity Index (ISI), Beck Anxiety Inventory, and Multidimensional Fatigue Inventory (MFI-20) were used for evaluations at baseline, week 4, week 8, week 16, and week 24.

Results: (1) All four patient groups showed significant improvements in insomnia severity after eight weeks of treatment and at the end of 24 weeks of follow-up ($P < 0.05$). Compared to CT-I, CBT-I demonstrated a significantly greater short-term effect on sleep quality, but with no statistically significant difference relative to BT-I. Age and baseline insomnia severity were risk factors for

treatment efficacy, while being married was an independent protective factor. (2) All four groups showed a significant improvement in anxiety symptoms post-treatment ($P < 0.001$), with the CBT, BT, and TAU groups showing a faster improvement rate than the CT group. During follow-up, the therapeutic effects were maintained in the CBT, CT, and BT groups, while the BAI scores increased in the TAU group. At the end of treatment, all four groups showed significantly relieved fatigue symptoms ($P < 0.05$), without significant differences between them ($P > 0.05$).

Conclusions: The short-term improvement effect of CBT-I on sleep quality was similar to that of BT-I, but superior to that of CT-I, highlighting the cost-effectiveness of BT-I.

Effects of Cognitive Behavioral Therapy for Insomnia on Cortical Hyperarousal: A Multicenter Polysomnographic and Quantitative EEG Study

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Introduction: Chronic Insomnia Disorder (ID) is a prevalent condition characterized by difficulty initiating or maintaining sleep, driven by a persistent state of physiological and cortical hyperarousal, the most widely accepted pathophysiological model. While Cognitive Behavioral Therapy for Insomnia (CBT-I) is established as the first-line treatment, most evidence of its efficacy is based on self-reported indices, leaving the impact on neurophysiological markers largely unexplored. Addressing this gap is essential for understanding the underlying mechanisms of CBT-I and refining precision-based treatment strategies. This multicenter study aimed to investigate the effect of CBT-I on sleep-related cortical hyperarousal, measured via the delta/beta ratio from quantitative EEG (qEEG) during NREM sleep. Secondary objectives included evaluating CBT-I's effects on sleep stability and examining differences in response across insomnia phenotypes (based on total sleep time).

Materials and methods: Ninety-eight individuals with chronic ID were recruited across five international sleep research centers. Participants completed a standardized 6-8 week CBT-I protocol administered by certified clinicians, incorporating behavioral, cognitive, and psychoeducational components. Pre- and post-treatment assessments included overnight polysomnography (PSG), one-week sleep diaries, and the Insomnia Severity Index (ISI). EEG data were processed using artifact rejection and automated sleep staging algorithms. Cortical hyperarousal was indexed by the delta/beta ratio, calculated from relative power in the delta (1–4 Hz) and beta (16–30 Hz) bands during NREM sleep (NREM1, NREM2, and NREM3). Sleep stability (Sstab) was derived from a transition probability matrix reflecting the likelihood of remaining in stable sleep stages (NREM2, NREM3, REM). Participants were classified as Insomnia with Short Sleep Duration (ISSD) or Normal Sleep Duration (INSDD) based on PSG-derived median TST (347.3 minutes).

Results: CBT-I significantly improved ISI scores and sleep parameters (sleep onset latency, wake after sleep onset, time in bed, sleep efficiency) in both self-reported and PSG macrostructural indices, with smaller effects in the latter. qEEG analyses demonstrated a significant increase in the delta/beta ratio following CBT-I (13.4 ± 4.9 to 14.6 ± 5.9 ; $F=10.05$, $p=0.002$, $\eta^2=0.09$), indicative of reduced cortical hyperarousal, with no differences across centers. Sstab also improved significantly post-treatment ($p=0.005$), yet was not correlated with changes in the delta/beta ratio, suggesting distinct physiological

processes. Phenotypic analysis revealed that ISSD patients exhibited significantly greater improvements in the delta/beta ratio compared to INSD individuals ($p=0.014$), despite comparable baseline insomnia severity.

Conclusions: These findings demonstrate that CBT-I not only improves self-reported and PSG-derived macrostructural sleep parameters but also induces measurable reductions in cortical hyperarousal, as evidenced by increased delta/beta ratios during NREM sleep. The lack of association with sleep stability improvements suggests that CBT-I may modulate multiple, partially independent physiological systems. Moreover, the enhanced response observed in ISSD patients underscores the importance of insomnia phenotyping in predicting treatment efficacy. qEEG biomarkers such as the delta/beta ratio may provide a valuable tool for tracking treatment-related neurophysiological changes and informing personalized interventions. This work supports the integration of EEG-based physiological measures alongside traditional outcomes to advance precision medicine approaches in insomnia care and to better elucidate the mechanisms of CBT-I.

Effects of cognitive behavior therapy for insomnia with adjunctive bright light therapy on sleep variability in youths with insomnia and eveningness: secondary analysis of a randomized controlled trial

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Introduction: Insomnia is a common sleep complaint among youth, negatively impacting their physical and mental health. Youths with insomnia and evening chronotype, i.e., a circadian preference for later bedtime and rise time, tend to have more irregular sleep patterns, characterized by greater night-to-night sleep variability. Cognitive behavioral therapy for insomnia (CBT-I) and bright light therapy (BLT), a circadian-focused intervention, have been shown to improve sleep but their effects on reducing sleep variability in youths remained unclear. The present study aimed to explore the effects of CBT-I with adjunctive BLT on sleep variability in youths with insomnia and eveningness.

Materials and methods: This was a secondary analysis of a randomized controlled trial (ClinicalTrials.gov Ref No. NCT04256915). Youths aged 12-24 years with insomnia disorder and eveningness were recruited and randomized to one of the three arms: 1) six weeks of CBT-I with adjunctive BLT (CBTI+BLT); 2) six weeks of CBT-I with placebo BLT (CBTI-BLT); 3) waitlist control (WL). All participants completed a 7-day sleep diary with actigraphy monitoring and self-reported questionnaires at pre-treatment and post-treatment, with additional follow-ups at one-month and six-month for the two treatment groups. Subjective and objective sleep variabilities were calculated using root mean squared successive differences from the sleep diary and actigraphy data.

Results: A total of 159 participants (mean age: 20.10 s.d. 2.20 years, 55% female) were randomized into three arms (CBTI+BLT: $n = 54$, CBTI-BLT: $n = 53$, WL: $n = 52$). A significant Time (pre-treatment vs. post-treatment) $\times$ Group (CBTI+BLT vs CBTI-BLT vs WL) interaction was observed for self-reported variability in sleep onset latency (SOL) ($p = .035$). CBTI-BLT resulted in a significantly greater reduction in self-reported SOL variability at post-treatment compared to WL ($d = -0.71$, $p = .010$). However, there were no significant differences in sleep variability parameters between CBTI+BLT and WL. In addition, no significant group $\times$ time interactions were found for sleep variability parameters at one- and six-month follow-ups between CBTI+BLT and CBTI-BLT. Within-group analyses indicated that reductions in SOL variability in the CBTI-BLT group were maintained at one-month ($d = -0.74$, $p = .027$) and six-month ($d = -0.71$, $p = .020$) follow-ups compared to baseline. Neither the improvement of depressive

symptoms nor the change of circadian preference significantly mediated the effects of CBT-I on reduction of sleep variability.

Conclusions: The findings indicate that CBT-I significantly reduced variability in sleep onset latency, with effects maintained at one-month and six-month follow-ups. Future research should investigate the specific mechanisms underlying the effects of CBT-I on sleep variability.

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Effects of DORA daridorexant in the long- term treatment of insomnia disorder: findings from a naturalistic two years follow up

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Introduction: Insomnia disorder is the most common sleep disorder and has a considerable effect on health, making its effective management crucial in clinical practice. Insomnia disorder is a chronic condition affecting more than 40% of individuals for over five years, often resulting in recurring episodes. Therefore, it is crucial to have pharmacological treatments effective for long term use. Daridorexant is the most recent Dual Orexin Receptor Antagonist (DORA) that has been endorsed by international guidelines for the long-term management of chronic insomnia. Emotional dysregulation, maladaptive beliefs regarding sleep, and cognitive as well as somatic pre-sleep arousal are regarded as core features of insomnia disorders, so we aimed to study the long term effect of daridorexant on these core symptomatology of chronic insomnia

Materials and methods: A study was conducted with consecutive outpatients diagnosed with Insomnia Disorder according to DSM-5-TR criteria (Sleep Condition Indicator SCI<16) attending the Insomnia Clinic at the University of Pisa, Italy. Patients received treatment with the novel DORA daridorexant starting from January 2023 to February 2025, in accordance with the guidelines for managing chronic insomnia. Data collected in the current study included a subsample of patients who were under treatment for at least 6 months and up to 2 years. Evaluations were performed at baseline (T0), 3 months (T1), 6 months (T2), 12 months (T3) 18 months and 24 months (T4 and T5). Demographic information and clinical assessments of insomnia severity (Insomnia Severity Index-ISI), pre-sleep arousal (Pre Sleep Arousal Scale-PSAS), emotional dysregulation (Difficulties in Emotion Regulation Scale-DERS), and dysfunctional beliefs about sleep (Dysfunctional Beliefs and Attitudes About Sleep Scale -DBAS) were computed and pharmacological treatments were taken into account. The sedative-hypnotics or sedative antidepressants that were previously prescribed for insomnia were decreased 25% of dosage each week through a cross-tapering program starting at T0, while introducing daridorexant at a dosage of 50 mg.

Results: The study included 60 patients (36 were females, mean age 53 ± 12.6 , insomnia duration 7.4 ± 3.2), who reached at least 6 months of treatment. Among them N°50 patients were under treatment for at least 12 months, N°40 for 18 months and N°25 for 24 months. Repeated measures of ANOVA analyses revealed a significant reduction in scores for the ISI, DERS, DBAS and PSAS across the first three months of treatment with F-values of 35.7, 45.75, 32.77 and 22.74 ($p < 0.001$) at T1. Predictive factors for insomnia symptom remission ($ISI < 8$) at T1 included sedative-hypnotic cross-tapering programs at T0 (OR: 3.00, $p = 0.049$), menopausal transition at T0 (OR: 2.11, $p = 0.039$), ISI severity at T0 (OR: 0.70, $p = 0.020$), DERS, DBAS and PSAS scores reduction at T1 (OR: 2.88, $p = 0.011$; OR: 1.70, $p = 0.039$; OR: 1.70, $p = 0.033$). Following a three-month treatment period, the scores for ISI, DERS, DBAS, and PSAS have shown stability over time, extending up to 24 months.

Conclusions: Preliminary research on the long term use of daridorexant in individuals with Insomnia Disorder suggest significant therapeutic potential for insomnia symptoms, while improving maladaptive beliefs about sleep, emotional regulation, and hyperarousal. It is emerging crucial for the long-term management of insomnia related to peri-menopause.

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Effects of Music Presentation on Sleep Quality and Functional Connectivity in the Brain Estimated using EEG

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Introduction: It is estimated that approximately 30% of the global population suffers from insomnia. Although sleeping pills remain the primary treatment, but they involve some problems including dependency and other side effects. Therefore, non-pharmacological approaches such as music therapy, known for its ease of implementation and absence of side effects, have been explored in recent years. *Classical and environmental music are commonly used* in such interventions, however, previous studies have reported inconsistent results regarding the effectiveness of music on sleep improvement. We hypothesize that these discrepancies stem from insufficient control of auditory impressions. To address this, in this study, we investigated the effects of method of music presentation (monaural and stereo), which significantly alter auditory impressions without changing the melody or tempo, on sleep quality. On the other hand, some recent studies have found that fMRI- or EEG-based functional connectivity of the brain in insomnia patients differs from that of healthy individuals. In this study, we also evaluated changes in functional connectivity induced by music presentation during sleep.

Materials and methods: 11 healthy adults (5 females), aged 21–25 years, participated in the experiments. The first movement of *Moonlight Sonata* was used as the auditory stimulus. The experiment was conducted in a soundproof room between 14:00 and 16:00. Three conditions were implemented: (1) silence, (2) monaural presentation, and (3) stereo presentation. Each subject experienced all three conditions once. Subjects were instructed to keep their bedtime on the day before the experiment and their waking time on the day of the experiment, and to refrain from consuming alcohol or caffeine, or engaging in strenuous exercise.

Sleep stage was assessed using EEG (32 channels) and EOG (2 channels), along with the OSA Sleep Inventory MA version (OSA-MA). Band-pass filters of 0.4–17 Hz and 0.1–17 Hz were applied to EEG and EOG signals. Functional connectivity of the brain was calculated from the coherence between EEG channels. Sleep stages were manually scored by the experimenter based on the filtered EEG data.

Results: No significant differences or trends were found among the three conditions in terms of sleep latency, total sleep time, slow wave sleep time, or OSA-MA scores. These results suggest that the method of music presentation had minimal influence on overall sleep quality.

In contrast, functional connectivity in δ and α bands in the silence decreased after sleep onset compared to wakefulness. Also, the decrease in functional connectivity in δ band was observed during wakefulness in the stereo presentation compared to the silence.

Conclusions: Sleep quality didn't change when the same piece of music was presented through different auditory presentation methods, suggesting that musical elements such as tempo and melody may have a stronger influence on sleep promotion.

On the other hand, decrease of functional connectivity in δ band indicates that sleep was promoted by the stereo music stimuli.

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Efficacy and Adherence of a Two-Week Bedtime Routine Intervention via the Sleep Coaching App in Adults with Insomnia Symptoms

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Introduction: Sleep disorders are a rapidly escalating global health concern, profoundly impacting individual well-being, cognitive function, productivity, and economic stability. While Cognitive Behavioral Therapy for Insomnia (CBT-I) is the established first-line treatment, its widespread application is hindered by challenges related to cost, time consumption, and limited accessibility. This has spurred interest in digital health solutions, such as mobile applications, as a more accessible

alternative. This study evaluated "Kkuljam Doctor," a novel sleep coaching mobile application, specifically focusing on its "Bedtime Routine" feature, which integrates relaxation therapy—a core component of CBT-I to leverage effective relaxation techniques and the benefits of fixed bedtime schedules for improving insomnia. This study aimed to evaluate the efficacy and user adherence of a 2-week "Bedtime Routine" intervention, delivered via the Kkuljam Doctor app, in adults reporting recent declines in sleep satisfaction

Materials and methods: This prospective pre-post study enrolled 40 community-dwelling adults (mean age 36.5 ± 6.8 years; 37.5% male). Participants exhibited at least one insomnia symptom (difficulty initiating or maintaining sleep, early awakening, or unrefreshing sleep) and baseline Insomnia Severity Index (ISI) ≥ 5 and Pittsburgh Sleep Quality Index (PSQI-K) ≥ 5 . Participants engaged with the app's "Bedtime Routine" for 14 consecutive days. Sleep efficiency (primary outcome) and other sleep parameters were tracked using in-app sleep diaries and validated questionnaires (PSQI, ISI, ESS). Adherence was also evaluated.

Results: Significant improvements were observed across both objective and subjective sleep parameters after the 2-week intervention. From sleep diaries, TST significantly increased (360.2 ± 60.1 min to 417.1 ± 43.6 min, $p < 0.001$), while sleep latency (41.6 ± 22.1 min to 31.4 ± 19.5 min, $p = 0.016$) and WASO (19.9 ± 17.7 min to 12.8 ± 11.4 min, $p = 0.002$) significantly decreased. Consequently, sleep efficiency significantly improved ($85.2 \pm 7.7\%$ to $90.4 \pm 4.0\%$, $p < 0.001$). Subjective measures also showed marked improvement: PSQI global score (10.3 ± 2.2 to 5.9 ± 2.0 , $p < 0.001$), ISI (15.2 ± 4.3 to 8.3 ± 4.0 , $p < 0.001$), and ESS (11.7 ± 4.6 to 6.1 ± 3.5 , $p < 0.001$) all significantly decreased. All seven PSQI component scores demonstrated significant improvement ($p < 0.001$ for all). Mean adherence to the app was high at $82.8 \pm 9.9\%$; however, four participants (10%) with less than 70% adherence.

Conclusions: A 2-week intervention using the "Bedtime Routine" feature of the Kkuljam Doctor app significantly improved various objective and subjective sleep parameters in adults with mild to moderate insomnia symptoms, demonstrating high user adherence. It demonstrates the effectiveness of a digital app focused on relaxation techniques and fixed sleep schedules in improving sleep.

Efficacy and safety of daridorexant in patients with chronic insomnia disorder and comorbid nocturia

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Introduction: Chronic insomnia and nocturia are frequently associated, particularly in older adults. Both chronic insomnia and nocturnal voids ≥ 2 /night significantly impact sleep quality, daytime functioning and quality of life. This study evaluated the efficacy and safety of daridorexant in patients with insomnia and comorbid nocturia.

Materials and methods: This double-blind, placebo-controlled, two-way cross-over study randomised 60 patients aged ≥ 55 years with chronic insomnia (insomnia complaints ≥ 3 months; insomnia severity index [ISI] score ≥ 13) and self-reported nocturia (≥ 3 voids/night for ≥ 1 month) to 4-weeks nightly treatment of daridorexant 50 mg or placebo. This was followed by a 14–21-day washout period, after which patients received the alternate 4-week treatment. The primary endpoint was change from baseline to Week 4 in self-reported total sleep time (sTST). Other insomnia endpoints included change from baseline in ISI score (to Weeks 2, 4), sTST (to Weeks 1, 2, 3), depth of sleep (visual analogue scale, to Weeks 1, 2, 3, 4) and daytime functioning (Insomnia Daytime symptoms and Impacts Questionnaire [IDSIQ] total score, to Weeks 1, 2, 3, 4). Nocturia endpoints, evaluated using the Minze diary Pod, included change from baseline in number and time to first nocturnal void (Weeks 1, 4). Safety endpoints included adverse events (AEs) and AEs of special interest (AESI: falls, urinary incontinence).

Results: Daridorexant (vs. placebo) significantly increased mean sTST (56.6 vs. 35.7 mins; $p=0.002$) at Week 4; significant improvements were seen from Week 1 (first timepoint). Daridorexant (vs. placebo) significantly ($p<0.05$) decreased ISI scores (Weeks 2, 4) and significantly ($p<0.05$) improved depth of sleep (Weeks 1–4) and IDSIQ total score (Weeks 1, 3). Daridorexant (vs. placebo) reduced the number of nocturnal voids (Week 1: -1.5 vs. -1.0, $p<0.001$; Week 4: -1.6 vs. -1.3, $p=0.09$) and increased median time to first nocturnal void (difference to placebo, Week 1: +31 mins, $p=0.0027$; Week 4: +23 mins, $p=0.2026$). No serious AEs/AEs leading to discontinuation were reported in the study. No AESIs were reported during daridorexant administration.

Conclusions: In patients with insomnia and comorbid nocturia, daridorexant improves sleep, daytime functioning and nocturia symptoms, with no increased risk of falls or urinary incontinence.

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Efficacy and safety of daridorexant in women with insomnia disorder during menopausal transition: a subgroup analysis

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Introduction: Insomnia is common, burdensome, and under-researched in women undergoing the menopausal transition. This is the first evaluation of the efficacy and safety of daridorexant (a novel insomnia treatment), specifically in an age group representative of the menopausal transition, enrolled in the phase 3 study NCT03545191.

Materials and methods: In this randomized, double-blind study, 930 patients with insomnia disorder received daridorexant 25 mg, 50 mg or placebo for 3 months. Subgroup analyses were performed among the 117 women aged 47-55 years (25 mg n=43; 50 mg n=35; placebo n=39). Efficacy endpoints included change from baseline in polysomnography-measured wake after sleep onset (WASO) and latency to persistent sleep (LPS), self-reported total sleep time (sTST) and insomnia-related daytime impairment (Insomnia Daytime Symptoms and Impacts Questionnaire [IDSIIQ]).

Results: At Month 3, daridorexant 50 mg vs placebo decreased WASO and LPS by a least-squares mean (LSM) of 13.8 min (95% CI -29.0, 1.4) and 14.7 min (-30.0, 0.6) respectively, increased sTST by a LSM of 21.8 min (-3.9, 47.4) and decreased (improved) IDSIIQ total score by an LSM of -4.1 (-14.4, 6.3). These results were generally consistent with those of the overall study population. The incidence of somnolence/fatigue was low in both daridorexant groups and comparable to placebo. Comparable improvements in morning sleepiness (visual analogue scale score) were observed across groups.

Conclusions: These post-hoc exploratory analyses suggest that daridorexant 50 mg improves sleep outcomes and daytime functioning and is well tolerated in women aged 47-55 years with insomnia disorder.

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Efficacy and Safety of Fazamorexant in Adults with Insomnia: A Phase 3 Randomized Controlled Trial of a Rapid-Onset, Short-Acting DORA

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Introduction: Dual orexin receptor antagonists (DORAs) are effective medications for insomnia. However, one of the major side effects is excessive daytime sleepiness due to long $t_{1/2}$. Fazamorexant (FAZ; YZJ-1139) is a DORA characterized by rapid absorption (T_{max} : 0.63~1.25 hours) and short elimination half-life ($t_{1/2}$: 1.91-3.68 hours), potentially enabling fast sleep onset and minimal next-morning effects. A Phase 3 RCT was conducted to evaluate its efficacy and safety.

Materials and methods: In this multicenter, randomized, double-blind Phase 3 trial (NCT05525637), adults aged 18-64 with insomnia disorder were randomized (1:1:1) after a 2-week placebo run-in to receive placebo (n=344), FAZ 20 mg (n=344), or FAZ 40 mg (n=346) for 14 days. On Day 15, placebo patients were re-randomized to FAZ20 or FAZ40, continuing for 166 days, while FAZ groups maintained original doses. Efficacy was assessed using Least squares mean (LSM) change from baseline (CFB) and 95% confidence intervals (CIs), via a mixed-effects model for repeated measurements. Co-

primary endpoints were change from baseline to Day 14 in polysomnography-assessed sleep efficiency (SE) and diary-based subjective sleep efficiency (sSE). Durability was assessed at Day 180 via maintenance of improvements in subjective sleep onset latency (sTSO) and total sleep time (sTST).

Results: Both FAZ20 and FAZ40 significantly improved SE (FAZ20, +4.8% [3.3-6.3]; FAZ40, +5.0% [3.5-6.5]) and sSE (FAZ20, +3.3% [1.9-4.8]; FAZ40, +3.1% [1.7-4.5]) versus placebo at Day 14 (all $P < 0.0001$). FAZ20 and FAZ40 significantly outperformed placebo on all PSG measures, including latency to persistent sleep (LPS) and total sleep time (TST) at nights 2 and 14 ($P < 0.005$), and on subjective sleep onset latency (sTSO) and total sleep time (sTST) at days 7 and 14 ($P < 0.001$). Objective and subjective outcomes were concordant over 14 days. Notably, improvements were sustained at Day 180, with sTSO reduced by 52.9 min (FAZ20) and 40.7 min (FAZ40), and sTST increased by 109.7 min and 87.5 min, respectively (all vs baseline; $P < 0.0001$). Fazamorexant was well tolerated, with a low discontinuation rate due to adverse events (0.6%). Common treatment-related AEs ($\geq 2\%$) included hyperlipidemia, dizziness, Leukopenia. No rebound insomnia or withdrawal symptoms were observed upon discontinuation.

Conclusions: Fazamorexant significantly improves sleep onset and maintenance in adults with insomnia, with sustained efficacy over 6 months and a favorable safety profile. Its rapid-onset and short half-life profile make it an unique DORA for insomnia.

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Efficacy and Safety of FLORANBIDIN® in Patients with Chronic Insomnia: A Phase 2 Randomized, Double-Blind Clinical Trial

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Introduction: Chronic insomnia is a significant health issue that impacts patients' overall well-being and quality of life. Current treatment options primarily include cognitive behavioral therapy for insomnia (CBT-I) and the use of sleeping medications, both of which may lead to adverse effects and long-term dependency. **FLORANBIDIN®** is a novel formulation containing **nano-emulsion cannabidiol (CBD-NE) combined with piperine**, designed to enhance the efficacy of CBD on the **endocannabinoid system (ECS)**. This formulation holds potential for improving sleep quality without severe adverse effects.

Materials and methods: This study is a **randomized, double-blind, placebo-controlled trial** conducted in **patients aged 18-60 years** diagnosed with **chronic insomnia** according to **ICSD-3 criteria**. Eligible participants must have an **Insomnia Severity Index (ISI) score of ≥ 15** and experience **insomnia at least three times per week for over three months**. Participants were randomly assigned into two groups: 1) **FLORANBIDIN® group:** Received **50 mg of FLORANBIDIN® before bedtime** 2) **Placebo group:** Received an **inactive placebo**. The treatment duration was **4 weeks**, and the efficacy was assessed using **Belun Ring, Polysomnography (PSG), ISI, Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS)**. This study aims to evaluate: 1) The **efficacy of FLORANBIDIN®** in improving sleep quality in patients with chronic insomnia using sleep duration and efficiency as key indicators. 2) The **safety profile of FLORANBIDIN®**, including potential adverse effects. 3) The **impact of FLORANBIDIN®** on daytime sleepiness and overall quality of life in patients.

Results: The study results showed that the **FLORANBIDIN® group** demonstrated a **statistically significant reduction in ISI scores** compared to the placebo group ($p < 0.01$). **Total sleep time (TST)** increased by **17%** ($p < 0.05$), and **sleep efficiency (SE)** improved from **85% to 91%** ($p < 0.01$). Additionally, **sleep onset latency (SOL)** and **wake after sleep onset (WASO)** were significantly reduced in the **FLORANBIDIN® group** compared to the placebo group. No serious adverse events were reported among participants receiving FLORANBIDIN®.

Conclusions: **FLORANBIDIN®** demonstrated significant potential in **improving sleep quality in patients with chronic insomnia by increasing sleep duration, reducing sleep onset latency, and decreasing night-time awakenings** without altering sleep architecture.

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Efficacy and Safety of Lemborexant in South Korean Participants With Insomnia Disorder: Results From a Randomized Phase 2 Bridging Study

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Introduction: Insomnia disorder is characterized by difficulties falling asleep and/or staying asleep and is reported by approximately 23% of South Korean adults. The objective of the current study was to evaluate the efficacy and safety of lemborexant (LEM), a competitive dual orexin-receptor antagonist, compared with placebo (PBO) in Korean participants with insomnia disorder.

Materials and methods: Study E2006-J082-204 (Study 204; NCT05594589) was a 1-month, multicenter, double-blind, PBO-controlled, parallel-group study evaluating the efficacy and safety of LEM 5 mg (LEM5) or LEM 10 mg (LEM10) in Korean participants (aged 19–80 years) who met *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, criteria for insomnia disorder (sleep onset difficulties with or without complaints of sleep maintenance) with insomnia severity index (ISI) score ≥ 13 . Participants (target sample size, N=60) were randomized (1:2:2) to PBO, LEM5, or LEM10, respectively, and received study drug immediately before bedtime for 30 days. A minimum 28-day follow-up period occurred where participants received no study drug. Polysomnograms were conducted during an ~14-day single-blind PBO run-in (baseline) and after 1 month (Day 30). Analyses included changes from baseline in latency to persistent sleep (LPS; min, log-transformed), sleep efficiency (SE; %), and wake after sleep onset (WASO; min). Statistical significance was determined with an analysis of covariance model adjusted for baseline sleep parameter and treatment. Safety data were collected throughout the study.

Results: The full analysis set comprised 64 participants (PBO, n=13; LEM5, n=25; LEM10, n=26). Mean (SD) ages were 38.6 (13.33), 48.5 (15.84), and 43.2 (13.84) years for PBO, LEM5, and LEM10 groups, respectively. Most participants in the PBO (n=10, 76.9%) and LEM10 (n=17; 65.4%) groups were female; 12 (48.0%) participants were female in the LEM5 group. At Day 30, decreases (improvements) from baseline in LPS were larger and statistically significant with LEM5 versus PBO. With LEM10, LPS decreased from baseline, but was not statistically significant versus PBO. SE increased from baseline with LEM5 but was not statistically significant versus PBO; increases (improvements) from baseline in SE were larger and statistically significant with LEM10 versus PBO. Decreases (improvements) from baseline in WASO were larger and statistically significant with LEM5 and LEM10 versus PBO. LEM was well tolerated with no new safety signals compared with the known safety profile.

Conclusions: The efficacy and safety profile noted in this bridging study in Korean patients with insomnia disorder was consistent with previous global studies of LEM. These findings support the clinical applicability of LEM as a therapeutic option for insomnia management in clinical practice in South Korea.

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Efficacy and Safety of Yokukansan in Patients with Initial-Onset Insomnia: A Multicenter Prospective Observational Study

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Introduction: In recent years, there has been a shift toward melatonin receptor agonists and orexin receptor antagonists in the development of hypnotic drugs. This transition has been driven by concerns about adverse effects associated with GABA_A receptor agonists, such as residual sedation, cognitive dysfunction, and dependence.

In the treatment of insomnia, non-pharmacological approaches, including sleep hygiene education and cognitive behavioral therapy for insomnia are also emphasized as important.

Yokukansan (YKS) is a Kampo medicine (a Japanese traditional herbal remedy) that has been approved by the Japanese Ministry of Health, Labour and Welfare for the treatment of insomnia.

We conducted a prospective clinical study to evaluate the efficacy and safety of YKS in drug-naïve patients newly diagnosed with insomnia. This study was approved by the Kurume University Ethics Committee (No. 22237).

Materials and methods: The aim of this study was to investigate the efficacy and safety of YKS in patients presenting with insomnia, following the administration of sleep hygiene education.

This is a multicenter, prospective, single-arm, open-label study. Patients who presented to participating facilities with insomnia between May 1, 2023, and June 30, 2024, and provided informed consent were enrolled. Participants were instructed to watch an educational video on sleep hygiene and received YKS (TSUMURA & CO.) at doses ranging from 2.5 to 7.5 g/day for 4 weeks, with dosage adjustments permitted at the discretion of the attending physician.

The primary outcome was the change in score on the Japanese version of the Insomnia Severity Index (ISI-J). Secondary outcomes included the Pittsburgh Sleep Quality Index (PSQI), the Japanese version of the Patient Health Questionnaire-9 (PHQ-9), Visual Analogue Scale (VAS) scores for daytime functional impairments (e.g., sleepiness, fatigue, tension), the Patient Global Impression of Improvement (PGI-I), and the proportion of patients who wished to continue YKS treatment at the end of the study.

Statistical analyses were performed using the Wilcoxon signed-rank test. The study was funded by TSUMURA & CO.

Results: Of the 100 patients who consented to participate, 95 (mean age 42.7 ± 13.0 years; 58 females) were included in the final analysis. The primary outcome, ISI-J score, significantly decreased from baseline to week 4 (13.5 to 6.5; $p < 0.001$).

Significant improvements were also observed in secondary outcomes, including PSQI (8.7 to 8.1; $p = 0.033$), PHQ-9 (8.7 to 4.6; $p < 0.05$), and VAS scores for sleepiness, heaviness of the head, fatigue, lassitude, tension, sense of well-being, calmness, and dizziness. At the end of the study, 62.5% of patients expressed a desire to continue YKS treatment. No serious adverse events were reported during the observation period. Mild adverse events included dizziness (1%), drowsiness (1%), and urticaria (1%).

Conclusions: This study demonstrated that the combination of sleep hygiene education and YKS administration significantly improved insomnia severity to a level comparable with healthy individuals, without causing adverse events commonly associated with GABA_A receptor agonists.

Our findings suggest that the use of YKS in conjunction with video-based sleep hygiene instruction may serve as a safe and effective initial treatment option for insomnia.

Efficacy of a stepped care approach to deliver cognitive behavioural therapy for insomnia in the community: A pragmatic stepped-wedge cluster randomized controlled trial

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Introduction: Insomnia affects up to 30% of the general population and is a significant global public health concern. While Cognitive Behavioral Therapy for Insomnia (CBT-I) is the first-line treatment, its accessibility remains limited. Digital CBT-I (dCBT-I) may enhance accessibility, but the evidence for its effectiveness in the real-world context is scarce. Given the high prevalence of insomnia, a stepped care approach is recommended to improve the accessibility of effective interventions. This study aims to evaluate the effectiveness of a stepped care model for delivering CBT-I in a community context.

Materials and methods: This pragmatic stepped-wedge cluster randomized trial was conducted across 18 districts in Hong Kong, with the intervention introduced sequentially over six months to all districts. The stepped care approach commenced with step 1 which was a dCBT-I with 4 self-paced modules, followed by step 2 with the guided support by trained sleep coaches from six non-governmental organizations, and the final step involved individual therapy with clinical psychologists. Participants aged 18-70 years old and with Insomnia Severity Index (ISI) score of ≥ 10 were included. Outcomes were assessed at post-intervention and at three-month follow-up. Linear mixed models with random effects for clusters and for participants nested within clusters is employed to evaluate the intervention effect across all timepoints.

Results: A total of 5,085 individuals registered in the digital platform (HKJC Sleep Well Project), of whom 3,513 initially met the inclusion criteria. Following the screening assessment, a total 1194 (mean age: 51.7yrs $\pm$ 15.5; female: 77.0%) enrolled the trial and 75% were retained in the service. In the stepped care model, about 59% continued to exhibit insomnia symptoms (ISI ≥ 10) after step 1, and 23.3% of them maintained moderate insomnia (ISI > 14) despite receiving step 2 guided support. Analysis of overall stepped care model suggested that intervention group reported a greater reduction in insomnia symptoms (adjusted difference: -2.36; 95% CI: -3.04 to -1.69, $p < 0.001$), depression (adjusted difference: -2.27; adjusted difference: -2.36 95% CI: -3.07 to -1.47, $p < 0.001$), anxiety (adjusted difference: -1.62; 95% CI: -2.41 to -0.83, $p < 0.001$), and improved quality of life (adjusted difference: 0.04; 95% CI: 0.01 to 0.07, $p = 0.009$) and overall general health (adjusted difference: 3.37; 95% CI: 0.48 to 3.27, $p = 0.022$) compared to control. These improvements were maintained at 3-month follow up ($P_s < 0.001$). In addition, insomnia remission defined as ISI < 8 (30.0% vs 9.9%, $p < 0.000$) and response rate defined as reduction of ISI ≥ 6 (38.6% vs 14.9%, $p < 0.001$) were significantly higher in intervention period compared to control.

Conclusions: This large-scale, district-wide stepped wedged and stepped care approach of insomnia intervention in the community demonstrated significant improvements in insomnia and mood outcomes, along with enhancements in quality of life and general health. The findings suggest substantial potential for population-level benefits of this model. Future research should focus on evaluating the long-term effects and cost-effectiveness of the stepped care approach.

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Efficacy of Jasmine Aromatherapy Pillow on Sleep Quality in Insomnia Patients

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Introduction: Insomnia is a common symptom of sleep problems, and there are various interventions to treat it. However, there is increasing interest in non-pharmacologic interventions.

Materials and methods: A prospective crossover study was conducted between August 1, 2023, and January 31, 2024, at the Sleep Disorders Clinic, Central Chest Institute of Thailand. The study included subjects aged ≥ 18 years who self-reported insomnia for at least 3 nights/week over a minimum duration of 1 month. Participants used their regular pillows for one week to collect baseline data on PSQI, GAD7, PHQ9, ISI, ESS, along with recording a sleep log and wearing an actigraphy watch. Subsequently, they were provided with a straw pillow and a Jasmine aromatherapy pillow for an additional week of use. Data were collected using the same questionnaire after participants utilized each intervention for one week.

Results: Six female participants with a mean age of 52 $\pm$ 14.76 years were enrolled. Both the straw pillow (11.17 $\pm$ 2.14 vs 14.33 $\pm$ 4.03, $p=0.045$) and the Jasmine aromatherapy pillow (10.17 $\pm$ 2.64 vs 14.33 $\pm$ 4.03, $p=0.002$) significantly reduced PSQI scores compared to the baseline. The ISI significantly

decreased after using the Jasmine aromatherapy pillow compared to both the baseline (13.50 ± 3.94 vs 16.17 ± 3.25 , $p=0.047$) and the straw pillow (13.50 ± 3.94 vs 15.83 ± 3.43 , $p=0.017$). The data from sleep log and actigraphy did not show significant improvement of TIB, TST, SL, SE, WASO, and NNA.

Conclusions: Both the straw pillow and Jasmine aromatherapy pillow help to improve sleep quality. Notably, the Jasmine aromatherapy pillow also decreased insomnia symptoms.

Embodied AI coach for delivering CBT-I in virtual reality- a pilot feasibility study

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Introduction: Recent AI advancements have shown promise in digitalizing psychotherapeutic interventions, including CBT-I, for more cost-effective and scalable interventions. However, most dCBT-I chatbots are limited by their provision of predefined responses in a text-based format. They lack embodied presence of AI (i.e. Embodied AI) for enhancing users' engagement. This also restricts AI's ability to perceive user behaviors and respond adaptively. This study aims to explore the feasibility of using Embodied AI coach for delivering CBT-I in virtual reality (VR).

Materials and methods:

Subjects

Inclusion criteria: 1) adults of Chinese ethnicity, 2) presence of insomnia, as indicated by a score of 8 or higher on the Insomnia Severity Index (ISI).

VR-Based CBT-I program

Embodied AI-Avatar coach

The virtual avatar was designed based on a typical therapist prototype, with a warm and approachable demeanor. Human-like animations (e.g., sitting, talking) and refined facial expressions, including lip synchronization and eye blinking, were integrated. Besides, the avatar made real-time adjustment of its position and eye gaze, as enabled by the movement tracking of the users. The avatar was powered by ChatGPT with an overarching prompt of character's backstory (e.g., roleplaying real-world therapists). A rule-based prompt structure (e.g., a CBT-I workflow) was imposed to determine which following sets of prompts should be utilized by ChatGPT, given users' current reply or question. Thus, a standardized conversation flow with personalized information was achieved. Moreover, the avatar had access to an external knowledge bank with CBT-I knowledge.

Content Design

The interventional content is based on our previous studies with 4 weekly CBT-I modules including (1) psychoeducation about insomnia and sleep restriction, (2) sleep hygiene and behavioral strategies, (3) cognitive restructuring and constructive worry strategies, and (4) stress management and relaxation training.

Procedure

Eligible participants were enrolled in a 4-week Chinese-speaking VR-based CBT-I program, with one module being delivered each week. Participants were asked to complete the ISI and user survey in the final session.

Results: In total, 7 participants (71% female; mean age: 27.14 yrs) were recruited and 6 of them completed the program. In the completer analysis, the results from the pre-intervention ($M=10.17$, $SD=1.94$) and post-intervention ($M=7$, $SD=2.97$) ISI scores indicated that the VR-based CBT-I program significantly reduced insomnia symptoms ($t(6)=-2.71$, $p=.04$), with an apparent large effect size ($d=1.26$). The user survey demonstrated a good level of satisfaction, with 67% of users showing moderate to strong intentions to continue using this virtual AI-Avatar coach to manage their sleep problems. Moreover, 67% of users felt that the utilization of embodied AI and virtual environments resulted in enhanced user experience and engagement.

Conclusions: The pilot data showed promising results with positive user feedback of utilizing Embodied AI Avatar coach to deliver CBT-I among individuals with insomnia. Further development to better leverage immersive technology and further formal comparative study with traditional dCBT-I intervention is needed.

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Emotion dysregulation and insomnia: the mediating role of repetitive thought and REM arousal

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Introduction: Worry and rumination are forms of repetitive negative thinking closely associated with emotional dysregulation and are increasingly recognized as central contributors to the persistence of insomnia. Beyond their cognitive/emotional impact, these processes have also been linked to alterations in rapid eye movement (REM) sleep, a crucial stage for emotional regulation and memory consolidation, potentially leading to increased fragmentation and reduced efficiency. However, the mechanisms through which these factors interact remain insufficiently understood, limiting the development of targeted interventions for insomnia. This study aimed to examine the interplay between emotional dysregulation, worry, rumination, and REM sleep instability in individuals with insomnia disorder and healthy controls.

Materials and methods: Twenty-three patients with insomnia disorder and twenty-three matched healthy controls completed questionnaires assessing emotional dysregulation (DERS), rumination (RRS), worry (PSWQ), insomnia severity (ISI), depression (BDI), and anxiety (STAI). Only patients underwent overnight in-laboratory polysomnography. REM sleep instability was quantified using a REM arousal index, calculated as the number of arousals per hour of REM sleep. REM arousals were defined according to AASM criteria as abrupt shifts in EEG frequency lasting at least 3 seconds, following a minimum of 10 seconds of stable REM, and accompanied by a concurrent increase in submental EMG activity lasting at least 1 second. Group comparisons were conducted using Mann-Whitney U tests, and Spearman correlations were used to examine associations among emotional dysregulation, worry, rumination, insomnia severity, and depressive symptoms. Three mediation models were tested using maximum likelihood estimation with bootstrapped confidence intervals: (1) whether rumination and worry mediated the relationship between emotional dysregulation and impact of insomnia (ISI subscale); (2) whether these variables mediated the association between difficulties in distracting with emotions (DERS subscale) and depressive symptoms; (3) in the insomnia group only, whether rumination and REM arousal mediated the relationship between distracting with emotions and the impact of insomnia.

Results: Compared to healthy controls, insomnia patients showed higher scores of emotional dysregulations, worry, rumination, depressive symptoms, and anxiety (all $p < 0.001$). Emotional dysregulation was associated with both rumination ($r = 0.73$, $p < 0.001$) and worry ($r = 0.53$, $p < 0.001$), but only rumination mediated the relationship between emotional dysregulation and impact of insomnia ($p = 0.007$). Rumination, but not worry, also mediated the link between DERS subscale and depressive symptoms ($p = 0.005$). Furthermore, the DERS subscale was positively correlated with REM arousal index ($r = 0.53$, $p = 0.009$), and both rumination and REM instability mediated its link with insomnia severity ($p = 0.002$ and $p = 0.039$, respectively).

Conclusions: These findings highlight rumination as a key mechanism linking emotional dysregulation to both insomnia and depressive symptoms. REM sleep instability also emerged as a possible physiological marker of emotional dysregulation. Interventions targeting rumination and REM-related arousal may offer promising avenues for improving treatment outcomes in chronic insomnia.

Epigenetic Characterization of Insomnia with Short Sleep Duration through Salivary microRNA Profiling: Study Protocol

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Introduction: Insomnia with short sleep duration (ISSD) is a clinically significant phenotype associated with increased risk of cardiometabolic disease, cognitive impairment, and reduced treatment responsiveness. Identifying biological markers specific to ISSD may help differentiate pathophysiological pathways and improve personalized treatment strategies in complex sleep disorder presentations such as COMISA. Among the most promising molecular tools are microRNAs (miRNAs), small, non-coding RNA molecules that regulate gene expression post-transcriptionally and are increasingly recognized for their role in sleep regulation and cardiometabolic health. The investigation of salivary miRNAs as epigenetic markers for ISSD offers a non-invasive approach to understanding disease mechanisms and identifying potential therapeutic targets.

Materials and methods: This two-phase study will explore salivary miRNA profiles in ISSD:

Part 1 – Pilot Study: Forty participants will be enrolled and divided into two clinically homogeneous groups: 20 patients with ISSD and 20 with insomnia without objectively verified short sleep duration. Saliva (1–4 mL) will be collected using Presto™ cfDNA/cfRNA kits. High-throughput miRNA profiling will be performed using next-generation sequencing (NGS). Bioinformatics analysis will identify and quantify miRNAs, and functional annotation will be conducted using databases such as miRTarBase and TargetScan. Group comparisons and enrichment analyses (GO, KEGG) will help identify relevant biological pathways.

Part 2 – Validation Study: In a larger cohort, candidate miRNAs from Part 1 will be validated using quantitative real-time PCR (qPCR), enabling precise quantification. Additional confirmatory techniques such as in situ hybridization or Northern blotting may be applied for selected miRNAs.

Results: The study will generate a miRNA expression profile in ISSD, highlighting both known and novel salivary miRNAs. Identified miRNAs will be linked to target genes and biologically significant pathways, particularly those involved in metabolic and sleep-related processes. The qPCR-based validation will confirm the reproducibility and clinical relevance of the findings.

Conclusions: By characterizing miRNA expression in ISSD and validating their associations with gene targets and biological functions, this study aims to identify epigenetic biomarkers that can inform the diagnosis and treatment of insomnia phenotypes. Functional bioinformatics will support the discovery of pathways potentially linking ISSD to cardiometabolic vulnerability, ultimately contributing to precision sleep medicine.

Acknowledgments: This study is conducted in the context of the first author's doctoral thesis at Universidad Europea de Madrid.

Esketamine rapid antidepressant combined with dexmedetomidine sleep modulation for patients with depression and insomnia

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Introduction: Depression combined with insomnia is a complex bidirectional relationship that is more difficult to treat versus a single disorder, and there is a lack of effective treatments available. In this study, we carried out a novel way to simultaneously intervene in depression combined with insomnia: the novel antidepressant esketamine as well as the bionic sleep-inducing drug dexmedetomidine.

Materials and methods: A total of 105 patients with depression and insomnia were included in this observational and prospective study. fMRI scans were performed at baseline and 2 hours after treatment, and follow-up was conducted for 6 months to collect 17 items of the Hamilton Depression Scale (HAMD-17) and the Pittsburgh Sleep Quality Index (PSQI).

Results: We found that after 2 hours of treatment, there were significant changes in neuroimaging of the brain, with a consistent decline in spontaneous neural activity in the left amygdala, left hippocampus, left superior temporal gyrus, left anterior cingulate gyrus, and left accessory cingulate gyrus. The right dorsolateral superior frontal gyrus, middle frontal gyrus, infraorbital frontal gyrus, middle orbital frontal gyrus, and right caudate nucleus had increased the consistency of spontaneous nerve function. Moreover, the depression response rate was higher than that of conventional antidepressants and electroconvulsive therapy.

Conclusions: The results of this study support the efficacy and safety of esketamine combined with dexmedetomidine in the treatment of patients with depression and insomnia, and provide a new idea for clinical treatment.

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Estimating the Prevalence of Insomnia Disorder in the Asia-Pacific Region Using Published Data

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Introduction: Insomnia disorder is a major clinical issue due to its high prevalence and negative health and economic outcomes. However, epidemiological data on insomnia disorder remain limited, particularly in the Asia-Pacific (APAC) region, where most countries lack reliable prevalence estimates. This analysis aimed to estimate the prevalence of insomnia disorder in the APAC region using published data.

Materials and methods: We applied published, nation-specific prevalence estimates of insomnia disorder to current population data for all APAC countries. Inclusion criteria for prevalence estimates prioritized: 1) studies that reported prevalence stratified by both age and sex together; 2) studies that reported prevalence by age and sex separately, we used the age-based results; 3) studies that reported prevalence by sex but not age; 4) studies that reported only a single prevalence estimate. When multiple studies existed for a country, the most methodologically rigorous study was selected based on expert opinion. When no nation-specific data were unavailable, prevalence estimates were extrapolated from a large, well-conducted study (Leger et al, 2000). Population estimates were sourced from the United Nations World Population Prospects 2022.

Results: Of the 56 APAC countries defined by the United Nations, 8 (14%) had suitable prevalence data, highlighting the need for further regional insights. We estimated that approximately 502 million adults in the APAC region (16.3%) have insomnia disorder, including 291 million females (18.9%) and 211 million males (13.6%). The highest insomnia burden was observed in India (166 million), China (164 million), Indonesia (33 million), Pakistan (22 million) and Bangladesh (20 million).

Conclusions: This analysis highlights the substantial burden of insomnia disorder in Asia, with an estimated 502 million adults affected. Results underscore the need for improved targeted interventions to reduce the health and economic burden of insomnia in the APAC region.

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Evaluating behavioral therapy as a stand-alone treatment for insomnia: the SLEEPwindow study

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Introduction: Chronic insomnia, a disorder characterized by a complaint of reduced sleep quality or quantity and associated with daytime impairments, is linked to reduced quality of life and is highly prevalent. Cognitive Behavioral Therapy for Insomnia (CBT-I) is the first-line treatment, however, its implementation and accessibility remain limited. The key element of CBT-I is the behavioural component (i.e. bedtime restriction and stimulus control) and has demonstrated effectiveness on its own. This study examines whether the SLEEPwindow intervention, which focuses on the behavioural component only, is non-inferior to full CBT-I. By reducing treatment duration and complexity, SLEEPwindow supports implementation, accessibility, and overall improvement of chronic insomnia care.

Materials and methods: The SLEEPwindow study is a prospective non-inferiority trial comparing full CBT-I with the SLEEPwindow intervention (i.e. bedtime restriction and stimulus control). A total of 160 insomnia patients will be randomized into two groups: CBT-I and SLEEPwindow. CBT-I will consist of six 90-minute group sessions covering sleep education, bedtime restriction, stimulus control, cognitive therapy, and relaxation techniques. SLEEPwindow will be delivered in four 60-minute group sessions over six weeks and focuses on individualized sleep windows, adjustment of sleep schedules, and group discussions. The insomnia severity index as a primary outcome will be measured at baseline, six weeks (T1), three months (T2), and six months (T3). Secondary outcomes include sleep quality, health-related quality of life, treatment adherence, and satisfaction. In addition to the clinical trial, barriers and facilitators to implementation of CBT-I will be evaluated in qualitative interviews.

Results: Results will determine whether the SLEEPwindow intervention is non-inferior to full CBT-I in improving the clinical symptomatology of chronic insomnia.

Conclusions: If confirmed, the efficacy of the SLEEPwindow intervention could offer a shorter, more accessible, and cost-effective treatment for chronic insomnia, facilitating broader implementation in clinical practice. Future research should continue to explore treatment mechanisms and barriers to implementation.

Evaluating the Effectiveness of Cognitive Behavioral Therapy for Insomnia in School Settings: A Systematic Review and Meta-Analysis

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Introduction: Poor sleep among adolescents is a significant public health concern. Delivering Cognitive Behavioral Therapy for insomnia (CBT-I) in schools may be an effective way to reach adolescents with poor sleep. This systematic review and meta-analysis examined the effectiveness of school-based CBT-I for improving sleep quality and/or duration among adolescents with insomnia symptoms or disorder.

Materials and methods: A systematic search of studies between 2003-2025 was conducted in March 2025. Inclusion criteria were adolescents aged 10-19 years (population) with insomnia symptoms, school-based interventions using evidence-based CBT-I principles (intervention), randomized or non-randomized trials (comparator), and reported sleep quality and/or duration (outcome).

Results: Eight studies ($n = 323$; M age = 15.3 years; 62.57% female) from four countries were included. Meta-analysis of within sleep intervention condition groups ($n = 8$) found significant subjective improvements post-intervention: total sleep time (TST) increased by 23.87 minutes ($p < 0.001$), sleep onset latency (SOL) decreased by 8.34 minutes ($p < 0.01$), and sleep quality improved $g = 0.376$ ($p = 0.001$). Objective measures of TST increased by 20.91 minutes ($p = 0.100$), SOL decreased by 1.35 minutes ($p = 0.202$), and sleep efficiency rose by 0.50% ($p = 0.792$). Anxiety improved significantly $g = 0.373$ ($p < 0.01$), but depression did not $g = 0.806$ ($p = 0.196$).

Conclusions: While sleep improvements were only observed for subjective sleep outcomes, this review suggests that school-based CBT-I may be an effective avenue to address adolescent insomnia. Given the limited evidence, we identify key methodological and implementation considerations to guide practice.

Evaluation of the Cutoff Score Determination for the Quality of Life Scale for Insomnia

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Introduction: Insomnia is diagnosed based on nighttime sleep disturbances, such as difficulty falling asleep, frequent awakenings, and early morning awakenings, and associated daytime functional impairments. The authors developed the Quality of Life Scale for Insomnia (QOL-I) to assess quality of life (QOL) in individuals with insomnia and confirmed its reliability and validity (Ayabe et al., 2025). This study aimed to examine the clinical use of the QOL-I by determining a cut-off point for identifying individuals with reduced QOL.

Materials and methods: This study used the same dataset employed by Ayabe et al. (2025) in the development of the QOL-I. The insomnia and control groups comprised 93 (mean age; 54.16 ± 16.01 years, 35 men, 58 women) and 228 participants (mean age; 44.96 ± 15.66 years, 95 men, 133 women), respectively. The study was approved by the Ethics Committee of the National Center of Neurology and Psychiatry and the participating medical institutions.

Results: Receiver operating characteristic (ROC) analysis yielded an area under the ROC curve (AUC) of 0.804, indicating a good discriminative ability. Sensitivity and specificity were 0.785 and 0.675, respectively. The cutoff QOL-I score was 32.5. The positive and negative predictive values were 0.497 and 0.885, respectively.

Conclusions: The ROC analysis results suggest that the QOL-I is a clinically useful tool for screening for reduced QOL in patients with insomnia. A score < 32.5 may reflect a diminished QOL. However, considering their moderate positive predictive value, interpreting QOL-I scores may benefit from combining them with other indicators, such as insomnia severity. Furthermore, because QOL is inherently a continuous and multidimensional concept, the cutoff QOL-I score may be better understood as a reference point rather than a strict diagnostic threshold.

Excessive daytime sleepiness should be systematically assessed in individuals with insomnia: A population-based study employing a virtual agent-based digital tool

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Introduction: Insomnia and excessive daytime sleepiness often co-occur despite they involve distinct physiological mechanisms. The KANOPIÉE application collects sleep-related data over a 17-day period and offer a unique opportunity to gain a deeper understanding of this unexpected phenotype.

Materials and methods: We analyzed a digital cohort of 21,590 participants, which included screening for sleep and mental health disorders (e.g., obstructive sleep apnea syndrome, restless legs syndrome, and depression); and a three-wave assessment of insomnia and excessive daytime sleepiness; completion of a 17-day sleep diary (recording total sleep time, mid-sleep point, sleep regularity index, and sleep medication intake).

Results: At baseline, 10,114 (46.8%) participants reported insomnia complaints. Of these participants, 4,843 (47.9%) were categorized as 'sleepy insomniacs' (i.e., Epworth sleepiness scale ≥ 11 and Insomnia severity index ≥ 15). Half of this subgroup reported at least one comorbidity, with depression being the most frequent. After excluding participants with comorbidities, 3,239 (44.3%) remained in the 'sleepy insomniac' category. These individuals exhibited no significant differences in self-reported sleep behaviors, including total sleep time, but were more likely to have middle or late insomnia compared to those with insomnia without excessive daytime sleepiness.

Conclusions: Excessive daytime sleepiness is highly prevalent among individuals with insomnia. Although comorbidities, particularly depression, accounted for the co-occurrence in approximately half

of our sample, a significant proportion of participants without comorbidities also demonstrated this unexpected phenotype. The lack of clear sleep debt in 'sleepy insomniacs' and the associations with specific insomnia subtypes underscores the need for further investigation.

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Exploring pregnant women's perspectives in developing a WeChat-delivered cognitive behavioral therapy for insomnia: a qualitative study

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Introduction: WeChat, the most popular mobile instant messaging app, offers a highly accessible but untested platform for delivering tailored CBT-I program to pregnant women. To inform its content and design, we conducted a formative study to explore the perceptions of Chinese pregnant women on a WeChat-delivered CBT-I program.

Materials and methods: A descriptive qualitative design was used. Focus groups and individual interviews with semi-structured questions were conducted via a video conferencing platform with 29 Chinese pregnant women with insomnia symptoms (Insomnia Severity Index score > 7) during December 2023 to March 2024. Data were analyzed using content analysis.

Results: Three themes and 10 subthemes were identified: (1) Appreciating sleep intervention for pregnancy insomnia; (2) Suggestions for intervention contents; (3) Recommendations on the format of WeChat articles. Participants appreciated the intervention's focus on pregnancy insomnia as it is often overlooked by healthcare providers despite its significant impact on their well-being. Participants also recognized its potential to address previously neglected insomnia challenges. Participants indicated a willingness to engage with the program, although they raised concerns about an excessive focus on sleep-related issues. Suggestions for content improvement included using clear and plain language, incorporating scientific explanations to reinforce credibility, combining generalized content with personalized insomnia solutions, and including information relevant to the perinatal period. Participants also emphasized the need for family involvement to support them in managing insomnia. Regarding the format of WeChat articles, participants highlighted form is secondary to content helpfulness, while many suggested using engaging titles and visuals. Additionally, some participants preferred short-form videos delivered via short video platforms over WeChat--delivered methods.

Conclusions: WeChat for delivering CBT-I for reducing insomnia symptoms was well received by the Chinese pregnant women and the identified main features may facilitate the design for future intervention studies.

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Exploring Subgroup Differences in Response to Digital Cognitive Behavioral Therapy for Insomnia in Preventing Major Depressive Disorder among At-Risk Youth

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Introduction: Previous study has shown that digital (app-based) cognitive behavioral therapy for insomnia (dCBT-I) can reduce the future risk of developing major depressive disorder (MDD) by more than 40% in youth with insomnia disorder and subclinical depression, yet it remains unclear who will achieve the optimal outcomes. The current study aimed to identify different subgroups of at-risk youth who would respond differentially to the dCBT-I intervention.

Materials and methods: This was a secondary analysis of a randomized, parallel group-controlled trial in Chinese youth (aged 15-25 years) with insomnia disorder and subclinical depressive symptoms. A total of 708 participants were randomly assigned to 6-week dCBT-I or 6-week app-based health education (HE). Assessments were conducted at baseline, post-intervention, 6- and 12-month follow-ups. Baseline sleep- and mood related variables were used to determine different subgroups by latent class analysis (LCA).

Results: Three insomnia subgroups were identified through LCA: 1) moderate insomnia with mild depressive and anxiety symptoms (40.3%), 2) moderate insomnia with stronger dysfunctional sleep beliefs, moderate depressive symptoms and mild anxiety symptoms (43.2%), and 3) moderate insomnia with more intense suicidal ideation, moderate depressive symptoms and mild anxiety symptoms (16.5%). The risk of developing MDD over the 12-month follow-up was significantly reduced for youth receiving the dCBT-I in subgroups 2 (14.7% versus 26.6%; hazard ratio [HR] 0.57 [95% CI 0.34 to 0.96]; $P = 0.03$) and 3 (14.8% versus 30.4%; HR 0.44 [95% CI 0.20 to 0.99]; $P = 0.047$) compared with the controls. Higher remission rates of insomnia disorder were observed in youth who received intervention in subgroups 1 (dCBT-I versus HE, 57.0% versus 29.0%; RR 1.97 [95% CI 1.47 to 2.64]; $P < 0.001$) and 2 (52.6% versus 25.2%; RR 2.08 [95% CI 1.53 to 2.84]; $P < 0.001$) at post-intervention, with intervention benefits sustained in both subgroups for at least 6 months.

Conclusions: Youth with insomnia disorder and subclinical depression can be categorized into different subgroups based on their sleep and mental health profiles, which were associated with distinct response patterns to dCBT-I indicated for depression prevention. These findings highlight the importance of further phenotyping at-risk youth to promote the development of personalized prevention for youth depression.

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Exploring the associations between data-driven insomnia disorder combined with mild anxiety or/and depressive symptoms and the efficacy of Cognitive-Behavioral Therapy for insomnia

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Introduction: The endophenotype of insomnia disorder is complex and the treatment is not targeted. The data-driven typing method might provide some bases for precise treatment. The present study was based on a post hoc analysis, aiming to explore the association between subtypes of insomnia disorder and the efficacy of cognitive-behavioral therapy for insomnia (CBT-I).

Materials and methods: The present study was conducted on data of 118 patients with chronic insomnia disorder combined mild anxiety or/and depressive symptoms, who had completed an 8-week randomized controlled trial of CBT-I vs CBT-I plus (CBT-I combined with modules targeting anxiety and depressive symptoms). The silhouette coefficient determined the optimal number of clusters, and a K-means clustering analysis was performed. T-tests were conducted to assess baseline differences at

eight weeks, and the changes in self-reported total sleep time (sTST), Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HRSD-17), and Hamilton Anxiety Rating Scale (HAMA) scores in order to explore the impact of subtypes and treatment approaches (CBT-I and CBT-I plus) on insomnia and emotional symptoms.

Results: The analysis revealed no significant demographic differences between the two clusters. Subtype 2 was characterized by significantly poorer baseline sleep quality (PSQI: 16.59 vs 12.74, $t = -9.90$, $p < 0.01$), higher depressive (HRSD: 18.47 vs 13.21, $t = -8.37$, $p < 0.01$), and anxiety levels (HAMA: 17.47 vs 13.46, $t = -6.23$, $p < 0.01$), and shorter sTST (4.67 vs 6.09 h, $t = 8.31$, $p < 0.01$) compared to Subtype 1. Post-treatment analyses showed significant improvements in both subtypes, with Subtype 2 experiencing a larger increase in sleep duration (csTST: 0.58 vs 1.77 h, $t = -7.18$, $p < 0.01$) and more pronounced improvements in sleep quality (cPSQI: 6.92 vs 8.88, $t = -3.57$, $p < 0.001$), depression (cHRSD: 8.07 vs 10.59, $t = -2.71$, $p = 0.008$), and anxiety (cHAMA: 9.28 vs 11.22, $t = -2.56$, $p = 0.012$). Despite these improvements, Subtype 1 maintained significantly better outcomes in sleep quality (PSQI: 5.81 vs 7.71, $p < 0.01$), depression (HRSD: 5.14 vs 7.89, $p < 0.01$), and anxiety (HAMA: 4.18 vs 6.25, $p < 0.01$) at 8 weeks. No significant differences in baseline characteristics were found between treatment groups within subtypes, indicating homogeneity. Within Cluster 1, CBT-I plus was more effective in reducing depressive symptoms (cHRSD: $t = -2.48$, $p = 0.016$), whereas CBT-I was superior in enhancing sTST in Cluster 2 ($t = 2.01$, $p = 0.049$), with no significant differences in other measures.

Conclusions: The study underscores the heterogeneity within ID subtypes and the differential response of sleep quality and depressive symptoms to CBT-I and CBT-I plus, highlighting the importance of personalized treatment strategies based on insomnia subtypes.

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Gender Differences and the Role of Mood in Sleep Misperception: Evidence from Healthy Young Adults

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Introduction: The discrepancy between subjective and objective measurements of sleep is referred to as sleep misperception. Previous studies have shown that women tend to have objectively better sleep than men (e.g., longer total sleep time), yet report more sleep complaints. Meanwhile, research on sleep misperception among patients with depression has found that a higher percentage of females fell into the underestimation group compared to the overestimation group, and that individuals with higher depression scores were more likely to overestimate wake after sleep onset. Since depression and anxiety are more prevalent among women, we hypothesized that these symptoms might mediate gender differences in sleep misperception.

Materials and methods:

This study aimed to investigate whether there are gender differences in sleep misperception among healthy individuals without sleep complaints, and to examine the potential mediating roles of anxiety and depression. A total of 33 healthy sleepers (48% male; mean age = 24.0 years, range 20–37) without diagnosed mental or medical disorders participated in the study. Participants wore a wrist actigraphy for objective sleep measurement and kept sleep diaries for subjective measurement across seven consecutive days. Sleep variables collected included sleep onset latency (SOL), total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE). Depression and anxiety symptoms were assessed using the Beck Depression Inventory-II (BDI-II) and Beck Anxiety Inventory (BAI), respectively. The indices of sleep misperception used were: (1) subjective values minus objective values; (2) the discrepancy between subjective and objective values divided by the objective values; and (3) subjective values divided by objective values.

Results: ANCOVA analyses comparing sleep misperception between genders, controlling for age, showed no significant differences across any of these indices. Additionally, Pearson's correlations between depression and anxiety scores and sleep misperception indices were not significant. This lack

of association between gender, mood, and sleep misperception indicates that the originally hypothesized mediating model was not supported.

Conclusions:

Overall, our results did not demonstrate a gender effect on sleep misperception, nor did they support a mediating role for depression and anxiety symptoms in the relationship between gender and sleep misperception. These findings differ from previous studies that showed gender and mood-related influences on sleep misperception. One possible explanation is that our sample was relatively young and healthy compared to samples in earlier studies, and sleep misperception may develop after prolonged exposure to sleep or mood pathology, which was not present here. Additionally, our small sample size may have limited the findings. Future research with larger samples and/or longitudinal designs is warranted to further clarify the associations among gender, mood, and sleep misperception.

Gender Differences in the Impact of Pre-Sleep Hyperarousal on Insomnia and OSA Risk in Individuals with PTSD Symptoms

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Introduction: Hyperarousal is a core feature of posttraumatic stress disorder (PTSD) and presents differently across genders. Women are more prone to internalised distress, such as anxiety and dysphoria, while men are more likely to externalise symptoms through anger and irritability. These differences may shape how PTSD contributes to sleep disorders. Somatic hyperarousal—marked by physical tension and heightened physiological responses—may be more common in men and increase the risk of obstructive sleep apnoea (OSA). In contrast, cognitive hyperarousal, characterised by mental overactivity and worry, may be more prevalent in women and contribute to insomnia. Understanding these gender-based patterns may support more targeted, gender-sensitive interventions.

Materials and methods: We analysed 270 UK adults from the general population with clinically significant PTSD symptoms (PCL-17; DSM-5 criteria) who completed validated questionnaires. Pre-sleep hyperarousal was assessed using the Pre-Sleep Arousal Scale (PSAS) and categorised into low and high cognitive and somatic hyperarousal groups. Insomnia severity was measured with the Insomnia Severity Index (ISI), with scores ≥ 15 indicating clinical insomnia. OSA risk was assessed using the STOP-BANG questionnaire and classified as low risk (<3) or intermediate/high risk (≥ 3). Gender-stratified logistic regressions examined whether cognitive and somatic hyperarousal predicted insomnia and OSA risk, restricted to participants meeting PTSD criteria.

Results: Among PTSD-symptomatic participants (N = 270; 21.5% males, 78.5% females), high somatic pre-sleep arousal was highly prevalent, with 97.0% (n = 262) classified as high and only 3.0% (n = 8) as low. A significantly higher proportion of females (98.6%) than males (91.4%) reported high somatic hyperarousal, while males were more likely to report low somatic hyperarousal (8.6% vs. 1.4%), ($\chi^2(1) = 8.224$, $P = 0.004$, $ES = 0.175$). Cognitive hyperarousal was more evenly distributed: 64.4% (n = 174) were classified as low and 35.6% (n = 96) as high, with no significant gender difference ($P = 0.847$). Among males, high somatic hyperarousal significantly predicted insomnia ($B = 1.613$, $P = 0.042$, $OR = 5.02$), while cognitive hyperarousal did not ($P = 0.776$). Among females, neither somatic ($P = 0.411$) nor cognitive hyperarousal ($P = 0.827$) predicted insomnia. For OSA risk, neither somatic nor cognitive hyperarousal significantly predicted risk among males, though high cognitive hyperarousal showed a non-significant trend ($OR = 1.48$, $P = 0.600$). Among females, high cognitive hyperarousal was inversely associated with OSA risk ($OR = 0.62$, $P = 0.118$), but not significantly; somatic hyperarousal was not predictive ($P = 0.919$).

Conclusions: Males with PTSD symptoms, high somatic hyperarousal is a significant predictor of clinical insomnia. No hyperarousal subtype significantly predicted OSA risk in either gender. These findings

support a gender-specific model of sleep disturbance in PTSD, suggesting that somatic arousal plays a key role in insomnia for males. Targeting somatic symptoms in behavioural treatments may enhance outcomes for PTSD-symptomatic males. Further research should validate these findings in larger, diverse populations and incorporate physiological sleep data.

Gender differences, psychological factors, and sleep parameters in paradoxical insomnia and non-paradoxical insomnia

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Introduction: Paradoxical insomnia is characterized by a discrepancy between subjective sleep perception and objective sleep measurements. Despite growing research interest, the underlying mechanisms of paradoxical insomnia remain poorly understood. This study aimed to investigate gender differences and identify key clinical, self-reported, and objective sleep characteristics that distinguish paradoxical insomnia from non-paradoxical insomnia.

Materials and methods: A total of 862 participants were analyzed. Data on demographics, clinical characteristics, biochemical parameters, depression, anxiety and polysomnographic (PSG) were collected. Gender differences were assessed, and the relationship between self-reported and objective sleep measures was examined. Logistic regression analysis was conducted to identify factors associated with paradoxical insomnia.

Results: Paradoxical insomnia was present in 30.51% of the study population. Logistic regression identified older age (OR = 1.019, $p = 0.004$), gender (OR = 0.643, $p = 0.007$), lower Insomnia Severity Index (ISI) scores (OR = 0.947, $p = 0.032$), and heightened somatic symptoms from the Hamilton Depression Rating Scale (HAMD) (OR = 1.374, $p = 0.010$) as independent predictors of paradoxical insomnia. No significant differences in biochemical parameters were observed between groups. Gender analysis revealed that females with paradoxical insomnia were older and had higher ISI scores than males, while males had higher BMI in both non-paradoxical insomnia and paradoxical insomnia groups.

Conclusions: Paradoxical insomnia is prevalent among individuals with insomnia, with gender and psychological factors, such as somatic symptoms of depression, playing key roles. Further research is needed to explore the underlying mechanisms and inform targeted interventions.

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Group-based and digital cognitive behavioural therapy for insomnia in adolescents with insomnia: Interim analysis of a three-arm, assessor-blinded, parallel randomised controlled trial

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Introduction: Insomnia is common in adolescents. While cognitive behavioural therapy for insomnia (CBT-I) is a well-established interventional approach in adults, its effects on insomnia and associated symptoms in adolescents remain unclear. Additionally, leveraging technology to deliver interventions is an innovative approach to address the needs of the population. The present study examined the effects of group-based CBT-I (gCBT-I) and digitally delivered CBT-I (dCBT-I) on insomnia severity, mood

symptoms, and other sleep- and health-related outcomes in adolescents with insomnia, compared to a waitlist control.

Materials and methods: An assessor-blind, parallel, randomised controlled trial was conducted in adolescents aged 12-20 years diagnosed with DSM-5 insomnia disorder. Eligible participants were randomly allocated to one of the three conditions, namely gCBT-I (6 weekly sessions, n=53), dCBT-I delivered via mobile application (6 self-paced modules with modest weekly text-based support), or waitlist (WL, n=54). Assessments were completed at baseline and post-treatment for the three conditions, and additionally at 6-month after intervention for the two active treatment groups. The primary outcome included insomnia symptoms as measured by the Insomnia Severity Index (ISI). Secondary outcomes included sleep parameters measured by sleep diary and actigraphy, and the measures of mood symptoms and other sleep- and health-related outcomes. Linear mixed models were utilised to examine treatment effects following the intention-to-treat principle.

Results: A total of 159 participants (Age: 18.14 ± 1.77 years, Female: 66.06%) were recruited. Primary outcome analysis showed that, as compared to WL, gCBT-I led to significantly greater improvements in insomnia symptoms at post-treatment. Remission rates for insomnia (as defined by ISI score <9) were 54.8%, 34.7%, and 25.9% for gCBT-I, dCBT-I, and WL, respectively ($p < 0.05$). Self-rated treatment response rates (reduction in ISI ≥ 6) were 47.6%, 40.8%, and 22.2% for gCBT-I, dCBT-I, and WL, respectively. Clinician-rated treatment response rates (CGI-I ≤ 2) were 35.7%, 38.8%, and 11.1% for gCBT-I, dCBT-I, and WL, respectively. The improvement in insomnia symptoms in both gCBT-I and dCBT-I was maintained at 6-month after treatment. As compared to WL, gCBT-I also led to greater improvements at post-treatment in sleep quality, anxiety symptoms, sleep-related dysfunctional beliefs, sleep schedule and timing, arousal-related behaviours, and daytime sleepiness. Meanwhile, dCBT-I resulted in significantly greater improvements at post-treatment in sleep quality, sleep-related dysfunctional beliefs, and self-reported sleep onset latency.

Conclusions: Both gCBT-I and dCBT-I show promise in improving sleep in adolescents with insomnia, but group CBT-I may be superior in addressing insomnia-related factors and associated symptoms. Digitally delivered CBT-I presents a viable alternative that enhances the accessibility of effective strategies for managing adolescent insomnia.

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Group delivered sleep restriction therapy for insomnia patients in primary care: Preliminary results from a randomized controlled trial

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Introduction: Cognitive-behavioral therapy for insomnia (CBT-I) is the recommended treatment, with sleep restriction therapy (SRT) as one of its most effective components. Despite guidelines, sleep medication remains the most common treatment, likely due to prescribing habits and a shortage of CBT-I providers. This randomized controlled trial aimed to evaluate the effectiveness of nurse-led group sleep restriction therapy (G-SRT) compared to standard care in primary care settings.

Materials and methods: Between 2021 and 2025, 104 patients were recruited for the study, with follow-up data collection ongoing until 2027. This abstract presents preliminary results for the primary outcome—Insomnia Severity Index (ISI)— at baseline, at 3-month follow-up, and at 6-months follow-up for the first 78 patients. Eligible patients were aged 18+ with DSM-5 diagnosed insomnia and were recruited by specially trained G-SRT nurses from six primary care centers in Stockholm, Sweden. Nurses received 1.5 days of training in insomnia assessment and G-SRT delivery. Recruitment took place during routine visits, and patients meeting inclusion criteria were invited to participate. After providing informed consent, participants were block-randomized (in groups of four) into one of two

arms. The G-SRT intervention included four group sessions: the first three weekly, and a fourth session four weeks later. The initial session covered sleep education, SRT introduction, and medication reduction planning. Subsequent sessions focused on group discussions, barrier identification, sleep window calculations, and forward planning. Control participants received standard care, consisting of a sleep hygiene brochure. Analyses were conducted using linear mixed models performed in a stepwise manner. The first step examined changes from baseline to 3-months follow-up, while the second step analyzed changes from 3-month to 6-month follow-up. The study is prospectively registered at Clinical Trials (NCT04975776).

Results: Preliminary analyses included 78 participants, 61 women (78%) and 17 men (22%), aged 20 to 90 years, with a mean age of 57.5 years. Relative to the control, G-SRT was significantly superior in reducing ISI scores from baseline to 3-month follow up ($F=4.27$, $p=.046$). The between-group effect size at 3-month follow up was large ($d=0.93$) in favor of SRT. From baseline to 3-month follow-up, ISI scores were reduced by 8.3 points in the G-SRT group and by 3.2 points in the control group. There was no significant group difference between 3-month to 6-month follow-up ($F=0.19$, $p=.892$). The between-group effect size at follow-up was small ($d=0.37$) in favor of SRT.

Conclusions: Patients presenting with sleep disturbances who were assessed by trained SRT nurses and subsequently treated with G-SRT for insomnia showed clinically significant improvements at post treatment. These findings are consistent with previous studies, although a sustained clinical effect at the 6-month follow-up could not be confirmed. However, these findings will require further analysis, including adjustments for covariates and withdrawal, once the complete dataset has been collected. Therefore, no definitive conclusions can be drawn at this stage.

Guided internet-based cognitive behavioral therapy for insomnia in people suffering from insomnia and psychological distress: results of a randomized controlled trial

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Introduction: Insomnia and mental health disorders frequently co-occur. Up to 70% of individuals with mental disorders experience sleep complaints, which worsen psychiatric symptoms and undermine treatment outcomes. Insomnia is also a major risk factor mental disorders and can worsen existing symptoms, impede recovery, and increase the chance of relapse. Although cognitive behavioral therapy for insomnia (CBT-I) is the recommended first-line treatment, even when other disorders are present, it's still rarely available in routine care. To advance adoption of treatment of insomnia in care settings, this study addressed three key research gaps by (1) evaluating efficacy in individuals with insomnia co-occurring with symptoms of anxiety- trauma, and/or borderline personality disorder; 2) assessing transdiagnostic effects on both negative and positive mental health indicators; and (3) conducting a process evaluation to optimize the intervention and inform future implementation strategies.

Materials and methods: A total of 157 participants (72% female; mean age = 54.1 years, SD = 13.8) with co-occurring insomnia and psychological distress yet not currently in (or awaiting) mental health treatment, were randomized to receive either therapist-guided iCBT-I (i-Sleep: 5–8-week intervention) or a sleep diary control (control). The primary outcome was the Insomnia Severity Index (ISI); secondary outcomes included symptom severity across dimensions of anxiety- trauma, and/or borderline, sleep diary parameters, positive mental health (PMH), protective lifestyle behaviors (PLB) and wellbeing. Assessments occurred at baseline (week 0), post-treatment (week 8), and follow-up (8 months). Linear mixed-effects models evaluated time x iCBT-I interactions. A concurrent mixed-methods process

evaluation, guided by the RE-AIM framework, collected quantitative satisfaction ratings and qualitative feedback from i-Sleep participants and 15 i-Sleep therapists (mean experience 0.8 ± 1.1 years).

Results:

Compared to controls, the iCBT-I group showed significantly greater reductions in insomnia severity at post-test ($d = 0.97, p < 0.01$) and at 8-month follow-up ($d = 1.03, p < 0.01$). No significant between-group differences were observed in the dimensions of anxiety- trauma, and/or borderline personality disorder, at post-treatment or follow-up. Positive mental health indicators showed small effects in favor of the iCBT-I group compared to controls, with significant improvements in protective lifestyle behaviors at post-treatment ($d = 0.30, p < 0.01$), and in positive mental health at 8-month follow-up ($d = 0.38, p = 0.01$). Intervention satisfaction averaged 7.30 (SD = 1.40), with 88.40 % of participants indicating they would recommend i-Sleep. Satisfaction with therapist guidance averaged 7.90 (SD = 1.70), although preferences for guidance format and frequency varied.

Conclusions: Therapist guided iCBT-I (i-Sleep) effectively reduces insomnia symptoms up to six months in individuals with insomnia and co-occurring psychological distress. Universal implementation could offer significant benefits, while adaptable content and flexible guidance may better meet individual needs. Together these findings underscore the need for widespread integration of iCBT-I into routine mental healthcare.

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Gut microbiota regulate insomnia-like behaviors via gut-brain metabolic axis

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Introduction: Sleep is a complex physiological process and is a critical determinant of physical and mental health. Over the past decade, significant progress has been made in understanding the neural mechanisms of sleep and awakening. However, the initiation and maintenance of the sleep-wake behavior is regulated not only by the central system but is also affected by signals from peripheral tissues. Growing evidence shows that the microbiota-gut-brain axis contributes to the regulation of sleep and may play a critical role in the etiology and pathogenesis of sleep. This study aims to investigate the role of gut microbiota in sleep-wake regulation and its gut microbe-brain axis mechanisms.

Materials and methods: The automatic sleep-wake recording system was used to record the electroencephalogram-electromyogram signal of specified pathogen free and germ free animals. Subsequently, metabolomics was used to screen gut microbiota metabolites that can participate in regulating sleep-wake behavior. Fiber photometry combined with EEG-EMG recording were used to record the calcium activity of orexin neurons to explore their activity during sleep-wake cycle after tributyrin administration. Electrophysiological patch clamp was used to explore electrophysiological properties of orexin neurons in the lateral hypothalamic area after tributyrin administration. We employed shotgun metagenomics and metabolomics to assess characteristics of gut microbiota metabolic changes in individuals with insomnia and healthy controls. Fecal microbiota transplantation technology was used to explore whether intestinal microbial disturbance can induce sleep disorders.

Results: The absence of gut microbiota can lead to alteration in sleep-wake architecture. After short-term sleep deprivation, the metabolites of hypothalamus and fecal contents of SPF and GF mice were screened. Further *in vivo* experiments showed that tributyrin, a precursor of butyric acid, could promote sleep in mice. Fiber optic recording combined with EEG-EMG monitoring showed that tributyrin promoted sleep by inhibiting orexin neuron activity in lateral hypothalamus. Compared with healthy controls, the α diversity of gut microbiota in insomnia patients decreased, and the abundance of butyrate-producing bacteria decreased significantly. The fecal microbiota transplantation experiment found that colonization of mice with gut microbiota from human donors with insomnia is sufficient to induce insomnia-like behaviors. The butyrate level in the serum of insomnia-like recipient mice was significantly reduced, accompanied by an increase in the activity of orexinergic neurons in the lateral hypothalamus. Finally, our results demonstrate that oral administration of butyrate delays onset of insomnia-like behaviors.

Conclusions: Here, we sought to define functional contributions by the gut-brain signaling molecule to sleep behaviors. We initially found changes in sleep-wake architecture and sleep homeostasis in GF mice. Subsequently, we identified butyrate as a metabolite derived from gut microbiota that promoted sleep by inhibiting orexin neuronal activity in the lateral hypothalamus. The gut microbiota of insomnia patients can lead to the occurrence of insomnia-like phenotypes, and butyrate supplementation can improve the insomnia-like phenotypes of insomnia-like recipient mice. The above results show that under normal circumstances, the body's gut microbiota metabolizes butyrate and participates in the regulation of sleep behavior. In the case of intestinal microbial disturbance, butyrate produced by gut microbiota metabolism is reduced, causing abnormal sleep-wake behavior.

How Attentional System Shapes Sleep Response to Stress: A Comparative Study of Individuals With and Without Insomnia Symptoms

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Introduction: A thorough understanding of the cognitive mechanisms involved in the development and maintenance of Insomnia Disorder (ID) is essential for shaping targeted and effective clinical interventions. According to Espie's Attention-Intention-Effort model, increased attention to sleep-related cues, together with excessive intention and effort to sleep, can disrupt the natural sleep process, fostering ID. Despite its theoretical importance, the role of attention in the development of ID remains unclear. Given that stress exposure is a well-established trigger for ID, the present study examines the role of attentional performance in shaping sleep response to stress in healthy individuals with and without ID symptoms.

Materials and methods: A total of 20 healthy participants (mean age: 26.25 ± 3.60 years; M/F: 7/13) were enrolled and divided into two groups based on the clinical cut-off of the Sleep Condition Indicator (SCI ≤ 16): 10 participants with ID symptoms, and 10 without. All participants completed a two-week Sleep Diary, which they were instructed to fill out within 10 minutes of awakening. The diary collected subjective reports of the previous night's sleep (i.e., sleep latency [SL], total sleep time [TST], number of awakenings [NAWK], etc.). After the first seven days of diary recording, participants' attentional performances were evaluated using the Attention Network Task (ANT), a widely recognized tool for assessing the three fundamental domains of attention: alerting, orienting, and executive control. Finally, in the late afternoon participants were exposed to a stress-inducing video, based on the Trauma Film Paradigm, previously validated to induce sleep-disturbances.

Results: Independent-sample t-tests indicated that SL ($p=.001$), NAWK ($p=.037$), restorative score ($p=.005$), wake after sleep onset ($p=0.003$), both calculated and estimated TST ($p=.021$; $p=.027$) and SE% ($p<.001$) were significantly worse in the ID symptom group at baseline. Additionally, paired-sample t-tests revealed a significant increase in SL ($p=.026$) and NAWK ($p=.029$), along with a significant decrease in both estimated and calculated TST ($p=.016$; $p=.016$) and SE% ($p=.004$) following stress exposure in both groups. No group differences emerged in attentional performance.

Generalized Linear Mixed Models showed that executive control performance significantly moderated the effects of group and time on SL ($\beta=.202$; $p=.021$), TST ($\beta=-.555$; $p=.033$), and NAWK ($\beta=.267$; $p=.042$), with poorer executive control (slower reaction time) associated with longer SL, higher NAWK, and shorter TST specifically in the ID symptom group. Additionally, attentional orienting performance significantly moderated SE% ($\beta=-0.174$; $p=.015$), with worse orienting scores predicting lower SE% across groups. Attentional orienting also significantly moderated the three-way interaction between group, time, and calculated TST ($\beta=-1.798$; $p=.024$), with reduced TST observed in individuals with poorer orienting performance, especially within the ID symptom group.

Conclusions: Our results highlight the complex interplay between cognitive functioning and sleep system reactivity to stress. Specifically, attentional systems, in particular executive control and orienting, appear to influence sleep responses following stress exposure, with distinct patterns observed in individuals with ID symptoms. The results suggest that cognitive factors may contribute to individual differences in sleep vulnerability, supporting the importance of incorporating attentional and cognitive assessments in the understanding and potential treatment of ID.

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How Does Rumination Impact the Relation Between Insomnia and Depression Symptoms?

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Introduction: Results from prior research have shown insomnia symptoms can be individual predictors for the development of depressive disorders. Studies cited by the National Institute of Health report that between 75%-90% of individuals with depression endorse insomnia symptoms. However, there is still much to explore about the mechanisms that drive this relationship. One common factor that insomnia and depression share is rumination. Rumination is often conceptualized as repetitive thinking of negative emotions or distress and their causes and effects. Despite this commonality, few studies have examined whether rumination moderates the association between insomnia and depression. Understanding the interaction between insomnia and rumination is essential for informing effective preventative and intervention measures. The aim of this study, therefore, was to quantify the impact of insomnia symptom severity and trait level rumination on depression symptom outcomes. Specifically, we assessed whether rumination moderated the effect of insomnia on depression.

Materials and methods: Data was collected through an online survey using the Qualtrics platform. Participants included 560 University of Arkansas undergraduate students ($M_{age}=19.1$, 68% Women, 80% White). Depression was measured using the depressive symptoms and anhedonic depression subscales of the Mood and Anxiety Questionnaire (MASQ-90). Rumination was measured using the Ruminative Response Scale (RRS-22) and insomnia symptom severity was measured using the Insomnia Severity Index (ISI). All analyses controlled for the effects of race and gender.

Results: Linear regression analyses revealed that rumination was positively associated with depression symptoms ($B = 0.51$, $t(544) = 22.56$, $p < .001$) as was insomnia symptoms ($B = 0.30$, $t(544) = 5.19$, $p < .001$). Analyses also showed a significant two-way interaction between rumination and insomnia symptoms ($B = 0.0092$, $t(544) = 2.69$, $p = 0.007$) suggesting that the association between insomnia and depression intensified with greater rumination tendencies. Analyses also showed that rumination ($B = 0.43$, $t(544) = 10.7$, $p < .001$) and insomnia symptoms ($B = 0.58$, $t(544) = 5.66$, $p < .001$) were positively associated with anhedonic depression symptoms. However, the interaction between insomnia and rumination on anhedonic depression was not significant ($B = -0.006$, $t(544) = -0.93$, $p = 0.35$). The results of this study did not show a significant effect of race or gender on depression outcomes.

Conclusions: These results indicate that rumination and insomnia act as individual predictors of depression. However, students who are experiencing sleep disturbances are more likely to endorse depressive symptoms if they have greater ruminative tendencies. The difference in interaction outcomes may suggest that rumination and insomnia work together to amplify global depressive symptoms whereas anhedonic depressive symptoms may be moderated by different psychological factors.

Identifying Major Life Stressors that Precipitate Incident Insomnia Disorder

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Introduction: Insomnia disorder is a chronic condition affecting approximately 12.4% of adults globally, marked by persistent difficulty falling and/or staying asleep that leads to significant daytime impairment. Major life stressors—such as the death of a loved one or the onset of chronic illness—are often associated with adverse health outcomes and may trigger the development of insomnia. However, less is known about how specific stressors, or their cumulative impact, influence the onset and prevalence of insomnia over time. This study examined a large cohort of healthy adults over the course of one year to investigate the prospective effect of major life events on insomnia incidence.

Materials and methods: 2,892 US adults with no history of insomnia or depression were assessed at baseline then again a year later. Life stressors were assessed using the Revised Social Readjustment Rating Scale (SRRS-R), which asks participants to indicate whether they experienced any of 52 distinct

major life events, categorized into four domains: Interpersonal, Work, Home, and Network stressors. Insomnia diagnoses at 1-year follow-up were based on DSM-5 criteria. Both insomnia diagnoses and major life stressors were dichotomized (Yes/No). Initial bivariate associations between insomnia and each stress exposure were examined using chi-square tests of independence. Stressors significantly associated with insomnia in bivariate analyses ($p < .05$) were then entered into a multivariate logistic regression model to evaluate their unique contributions to predicting insomnia diagnoses.

Results: Among 2,892 US adults, the one-year incidence rate for DSM-5 insomnia disorder was 9.1%. Bivariate analyses identified 20 of the 52 assessed life stressors were significantly associated with insomnia incidence. Each of the four broad categories of stressors was associated with an elevated relative risk (RR) of developing insomnia disorder compared to those not reporting the stressor: Interpersonal (RR=1.9–4.2; Insomnia incidence: 16.9–24.7%), Work (RR=1.6–2.7; Insomnia incidence: 13.6–24.2%), Home (RR=1.9–3.7; Insomnia incidence: 8.2–37.5%), and Network (RR=1.4–2.8; Insomnia incidence: 12.0–25.0%). In the multivariate logistic regression model, several specific stressors remained independently associated with increased risk for insomnia. The most robust predictors included: death of a spouse (Odds Ratio [OR]=4.4, $p=.013$), major injury or illness to self (OR=2.5, $p<.001$), separation or reconciliation with a partner (OR=2.5, $p=.001$), financial problems (OR=2.0, $p<.001$), and efforts to address personal addiction (OR=2.3, $p=.010$).

Conclusions: Major life stressors, particularly those involving interpersonal loss, personal health crises, and financial or relational instability, predicted 1-year incidence of DSM-5 insomnia disorder. These findings highlight the importance of assessing major life events in both research and clinical contexts, as certain stressors place individuals at markedly higher risk for developing insomnia. Targeted screening and early intervention strategies may help mitigate sleep disturbance in those facing major life stress.

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Impact of a stepwise pharmacologic intervention on moderate-to-severe chronic insomnia: a German observational study

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Introduction: Chronic insomnia is a highly prevalent disorder that affects quality of life a lot. However, there are only a few data and guidelines concerning outcome on long-time pharmacologic treatment. Our study evaluated the effect of a stepwise therapy scheme on self-reported sleep quality and the severity of the disease.

Materials and methods: Patients with moderate-to-severe insomnia where cognitive behavioral therapy was ineffective were asked for participation in the study and received a stepwise pharmacologic intervention, starting with L-tryptophan, melatonin, or agomelatine (S1 medication). The medication was applied for four weeks. If this led to an improvement the patients continued with the treatment (S1 responders) and if not (S1 non-responders) psychotropic drugs (S2 medication), hypnotics (S3 medication), or combination therapies were given instead. Standardized questionnaires of severity of the disease (ISI) and on sleep quality (PSQI) were applied after 6 and 9 months of study participation.

Results: Out of $n=116$ patients included in the study, $n=104$ started with S1-medication (90%) and $n=55$ were S1 responders after 4 weeks of therapy. After 6 months $n=26$ patients (22%) were still using S1 medication and a reduction of ISI (19.7 to 14.6) and of PSQI (13.2 to 11.5) were observed in this group. After 9 months $n=16$ patients (14%) further continued with S1 medication and in this subgroup a reduction of ISI (19.6 to 13.4) as well as PSQI (13.4 to 11.1) was observed for this time period. In the group of S1 non-responders, $n=16$ patients were taking psychotropic substances and $n=28$ hypnotics after 6 months of therapy. By month 9, $n=17$ patients were on psychotropic drugs and $n=25$ on hypnotics. In all groups ISI as well as PSQI values were improved.

Conclusions: A stepwise therapeutic approach should be used for patients with moderate-to-severe insomnia. Even if only 14% remained on S1 substances after 9 months, the quality of sleep and the severity of insomnia improved significantly – independently of the initial severity of the disorder.

Impact of insomnia symptoms on the clinical outcomes among patients with major depressive disorder and eveningness – results from a randomized controlled trial

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Introduction: Insomnia is prevalent in major depressive disorder (MDD) and is associated with poor outcomes, including non-remission, relapse, and suicide risk. Eveningness, a circadian preference for later timings of activity and sleep, is also linked to worse depressive symptoms and outcomes. Insomnia and eveningness often co-occur, yet little is understood about their combined impact on clinical outcomes. This study hypothesized that patients with concurrent insomnia and eveningness (CI) exhibit more severe clinical symptoms, greater sleep disturbances, and poorer responses to circadian-based treatments.

Materials and methods: This is a secondary analysis of a randomized controlled trial included 93 MDD patients with eveningness (defined by Morningness-Eveningness Questionnaire, MEQ score of <42) randomized to either 5-week bright light therapy (BLT) or dim red light placebo (DRL), both prescribed with gradual advancing timing over the 5 weeks. Sleep was prospectively assessed using sleep diary and actigraphy. Primary outcomes included depressive symptoms (17-item Hamilton Depression Scale, 17-HDS), and secondary measures included insomnia remission rates (Insomnia Severity Index, ISI ≤ 7), self-report depressive and anxiety symptoms (Hospital Anxiety Depression Scale, HADS), fatigue (Chadler Fatigue Scale, CFS), and quality of life (Short-Form 36 Health Survey, SF36), measured at the end of five-week treatment. Longitudinal changes of the sleep and clinical parameters were analysed by within-group one-way repeated measures ANOVA.

Results: Ninety-one participants were included in the analysis (mean age $\pm$ SD, 46.5 ± 11.8 years old, Female 80%). Concurrent insomnia was defined as ISI ≥ 15 at baseline and was present in 62 (68%) participants. Comparing participants with concurrent insomnia (CI) and those without insomnia (NI), there were no differences in age, gender, MEQ scores and the type of treatment received. The CI group had a higher 17-HDS, HADS, CFS, and a lower SF-36 score. Baseline sleep diary showed that both CI and NI groups fell asleep late ($01:47 \pm 01:43$ vs $02:22 \pm 01:40$, $p=0.13$) but the CI group had an earlier wake time ($09:07 \pm 02:11$ vs $10:40 \pm 02:09$, $p=0.003$), and a shorter sleep duration ($08:16 \pm 01:27$ vs $07:22 \pm 01:36$, $p=0.01$), compared to the NI group. Upon interventions, both groups showed advancement in rise time and improvement in sleep efficiency after treatment as reflected by sleep diary. Analysis on the actigraphy data showed a significant advance in sleep offset (post-treatment vs baseline: $09:47 \pm 01:48$ vs $10:09 \pm 01:59$, $p=0.035$) and shortened sleep duration in the CI group (post-treatment vs baseline: $06:35 \pm 00:55$ vs $06:59 \pm 01:27$, $p=0.01$) after treatment. Only 4% of CI group achieved insomnia remission by week 5, despite significant improvement of both MEQ and 17-HDS within each group.

Conclusions: Depressed patients with eveningness and concurrent insomnia represent a high-risk MDD subtype with more severe clinical symptoms. Upon intervention, they had earlier wake time but shortened sleep duration. Majority of these patients could not achieve remission of insomnia after 5 weeks of chronobiological treatment. Concurrent management of insomnia and eveningness is critical to improving outcomes.

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Impaired alertness in those physicians with depressive condition and insomnia

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Introduction: We previously showed that response speed and lapses derived from psychomotor vigilance test (PVT) were associated with burnout and depression [1]. While insomnia is linked to both vigilance deficits and depressive symptoms, its role in modulating the relationship between PVT performance and depression remains unclear.

Materials and methods: This study was a part of the National Survey for The Work Style Reform of Long Working Physicians. Based on our prior study [1], we analyzed data from 1,221 physicians who completed the PVT. Depressive condition and insomnia were defined as their CES-D ≥ 20 and Athens Insomnia Scale (AIS) ≥ 6 , respectively. The participants were separated into 4 groups, those having both depressive condition and insomnia (DI group), exclusively depressive condition (D group, exclusively insomnia (I group) and neither of them (control, C group). PVT metrics of response speed, lapse and LRM were compared among the four groups, using Kruskal Wallis Test, followed by post-hoc Dunn Test. All the statistical analyses were conducted using STATA16 (Stata Corp LLC, College Station, TX). Statistical significance was defined as p value was <0.05 .

Results: Mean [SD] PVT Lapse was 3.8 [9.1] in DI group, 3.2 [7.1] in D group, 1.5 [3.3] in I group and 1.3 [2.3] in the control group, and those in DI and D group were significantly lower than that in control group (both $p < 0.01$). This suggest that alertness is impaired in those who suffered from both depressive condition and insomnia. It is observed in parallel that response speed and PVT-LRM in DI and D groups were significantly impaired compared to control group.

Conclusions: We previously found that depressive condition and reduced alertness were associated [1]. The present study further demonstrates that those who suffered from depressive condition and insomnia were more likely to show significant reduced alertness, as assessed by PVT. The present study will help us not only grasp underlying cause of health deteriorations among long-working physicians but also make an effective intervention.

Acknowledgments: References

1. Wada H, Basner M, et al. J Sleep Res. 2025; 34:e14304.
2. Basner M, et al. J Sleep Res. 2015; 24: 702-713.

Improved Sleep Quality and Reduction in Sleep Medication Use with Multimodal Non-Invasive Neuromodulation in Chronic Primary Insomnia: A Case Report

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Introduction:

Background: Chronic primary insomnia is a common and challenging condition, particularly among older adults. Pharmacological management, while frequently used, often leads to tolerance, dependence, and undesirable side effects. As a result, there is growing interest in non-pharmacological interventions, such as neuromodulation and brainwave entrainment, to address persistent insomnia symptoms and reduce reliance on hypnotic medications.

Materials and methods:

Case Illustration: A 68-year-old woman with chronic sleep-onset insomnia, previously managed with polypharmacy (clonazepam, quetiapine, mirtazapine, alprazolam, fluoxetine), experienced relapse with daytime sleepiness, anxiety, and cognitive impairment. Polysomnography showed abnormal architecture (0% REM, 1% N3, 98.9% N2) despite 88.4% sleep efficiency. She underwent daily non-invasive interventions: tDCS (0.5 mA, Fp1-Fp2), 2 Hz delta audio entrainment, and head/neck/shoulder acupressure. Within two weeks, she discontinued clonazepam and reported faster sleep onset, reduced anxiety, and improved alertness.

Results: Discussion: This case demonstrates how multimodal non-invasive neuromodulation may effectively treat chronic primary insomnia by simultaneously targeting its key pathophysiological components. Transcranial direct current stimulation (tDCS) applied to the prefrontal cortex likely modulated cortical hyperexcitability, rebalancing the dysfunctional sleep-wake regulation characteristic of insomnia. The delta wave audio specifically addressed age-related slow-wave sleep deficits by promoting neural synchronization to sleep-inducing delta frequencies (0.5-4 Hz). Concurrent acupressure therapy contributed by reducing muscle tension in the head and neck region, thereby decreasing somatic arousal that often perpetuates sleep difficulties. The combination produced

synergistic effects: tDCS normalized central nervous system hyperarousal, delta stimulation enhanced endogenous sleep rhythms, and acupuncture alleviated peripheral tension. Notably, this approach facilitated rapid benzodiazepine discontinuation while improving both subjective sleep quality and daytime functioning, suggesting particular utility for elderly patients with medication-resistant insomnia and abnormal sleep architecture. These findings support further investigation of combined neuromodulation strategies as potential alternatives to pharmacotherapy in chronic insomnia management.

Conclusions:

Conclusion: These findings highlight the potential of non-pharmacological approaches in managing refractory insomnia, particularly in elderly patients at risk for medication side effects. Further research is needed to confirm these benefits in larger and more diverse patient populations.

Insomnia as a result of severe traumatic brain injuries in young female patients

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Introduction: Aim of this study was to present cases of insomnia after traumatic brain injuries in young female patients(<40 years old)

Materials and methods: 10 cases are presented.10 young male patients. Range of age 18-40 years old.

Results: Some common symptoms were: Difficulty sleeping in 4 patients (40%),sleep fragmentation or interrupted and broken sleep pattern in 2 patients (20%) ,waking up during the wee hours of the night and unable to go back to sleep in 4 patients (40%).All of them received :Cognitive behavioral therapy (CBT),Natural sleep-inducing remedies, Pharmacotherapy and continue Neurological, Psychological and Psychiatric Support.Good results in 9 patients (90%) and moderate in 1 (10%).

Conclusions: Multidisciplinary approach is essential to achieve optimal results for our patients.

Insomnia as a result of severe traumatic head and neck injuries in young male patients

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Introduction: Aim of this study was to present cases of insomnia after severe traumatic head and neck injuries in young male patients(<30 years old).

Materials and methods: 10 cases are presented.10 young male patients. Range of age 18-30 years old.

Results: Some common symptoms were: Difficulty sleeping in 4 patients (40%),sleep fragmentation or interrupted and broken sleep pattern in 3 patients (30%) ,waking up during the wee hours of the night and unable to go back to sleep in 3 patients (30%).All of them received :Cognitive behavioral therapy (CBT),Natural sleep-inducing remedies, Pharmacotherapy and continue Neurological, Psychological and Psychiatric Support.

Conclusions: Good results in 8 patients (80%) and moderate in 2 (20%).Multidisciplinary approach is essential to achieve optimal results for our patients.

INSOMNIA AND ASSOCIATED FACTORS SIXTH-YEAR MEDICAL STUDENTS AT HO CHI MINH CITY UNIVERSITY OF MEDICINE AND PHARMACY

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Introduction: Insomnia is a common sleep disorder that affects both physical and mental health, increasing the risk of dementia, hypertension, and diabetes. Approximately 10% of adults suffer from chronic insomnia, and 20% experience transient insomnia. This rate is higher among students,

particularly medical students, due to the pressures of studies, exams, and long hours of clinical practice. Sixth-year medical students face stress from graduation exams and internships, making them susceptible to sleep disorders. This study aims to assess the prevalence of insomnia and related factors among sixth-year students at the University of Medicine and Pharmacy, Ho Chi Minh City.

Materials and methods: Objectives:

To determine the prevalence of insomnia and to explore its associations with academic stress, sleep habits, and electronic device use among sixth-year medical students.

Methods:

This cross-sectional, descriptive-analytic study was conducted among 191 sixth-year medical students at the University of Medicine and Pharmacy at Ho Chi Minh City between January and May 2024. Data collected included demographic characteristics, academic performance (GPA), perceived academic pressure, and sleep-related behaviors. Insomnia severity was assessed using the Insomnia Severity Index (ISI).

Results: Approximately 90% of participants were 24 years old, with an age range from 23 to 27. The majority were male (62.9%), of Kinh ethnicity (90.1%), and reported no chronic illnesses (87.4%). Insomnia symptoms were reported by more than 60% of students, with 42.9% classified as mild, 15.7% moderate, and 4.2% severe.

Students who frequently experienced exam stress had a 1.27 times higher prevalence of insomnia (PR = 1.27; 95% CI: 1.12–1.45; $p < 0.001$). Those with frequent fears of academic failure had a 1.14 times higher prevalence (PR = 1.14; 95% CI: 1.04–1.26; $p = 0.007$), and those who felt peer pressure had a 1.18 times higher prevalence of insomnia (PR = 1.18; 95% CI: 1.07–1.31; $p = 0.001$).

Sleep behaviors also demonstrated significant associations. Students who used electronic devices before sleep had a 2.06 times higher prevalence of insomnia compared to those who did not (PR = 2.06; 95% CI: 0.99–4.30; $p = 0.010$). Moreover, each additional day of staying up past midnight increased the risk of insomnia by 9% (PR = 1.09; 95% CI: 1.03–1.15; $p = 0.001$), indicating a relationship between late-night sleep patterns and insomnia.

Conclusions: Insomnia is highly prevalent among senior medical students and is significantly associated with academic stress, late-night sleeping habits, and pre-sleep electronic device use. Interventions to reduce academic pressure and improve sleep hygiene are urgently needed to enhance students' sleep quality and overall well-being.

Insomnia and Cardiometabolic Risk: Uncovering a Silent Driver of Chronic Disease

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Introduction: Insomnia, a prevalent sleep disorder marked by difficulty initiating or maintaining sleep, is increasingly recognized as a critical yet underappreciated contributor to chronic disease. Affecting nearly one-third of adults globally, insomnia has been linked to a cascade of physiological disruptions that elevate the risk for cardiometabolic conditions. These include type 2 diabetes, cardiovascular disease, chronic kidney disease, and metabolic dysfunction-associated steatotic liver disease (MASLD). Despite its high prevalence and modifiability, insomnia remains insufficiently addressed in preventive health strategies.

Materials and methods: Objective:

This narrative review synthesizes current evidence on the relationship between insomnia and cardiometabolic health, with a focus on type 2 diabetes. It aims to equip healthcare professionals with practical insights for identifying and managing insomnia as a strategy to mitigate chronic disease risk.

Methods:

A multidisciplinary team conducted a comprehensive review of recent literature exploring the biological mechanisms linking insomnia to cardiometabolic dysfunction. Key areas of investigation included autonomic nervous system activity, hormonal imbalances, and systemic inflammation.

Results: Insomnia is associated with heightened sympathetic nervous system activity, dysregulation of the hypothalamic-pituitary-adrenal axis, and increased inflammatory markers. These changes contribute to impaired glucose metabolism, insulin resistance, and elevated risk for type 2 diabetes.

Additionally, insomnia is linked to obesity, MASLD, and cardiovascular conditions such as hypertension, myocardial infarction, and heart failure.

Conclusions: Insomnia is a modifiable risk factor with profound implications for cardiometabolic health. Integrating sleep assessment and management into routine care could significantly reduce the burden of chronic diseases. Healthcare providers should prioritize early detection and evidence-based interventions for insomnia to improve long-term health outcomes.

Insomnia in Dementia Patients

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Introduction: Many dementia patients complain insomnia and depressive mood, and hypnotics and antidepressants are being prescribed. As prevalence of dementia is increasing, insomnia and depressive mood are becoming more important.

Materials and methods: We reviewed medical records of the patients who visited outpatients clinic of NHIS Ilsan Hospital Dementia Center during 2024.

Results: Total 716 patients are included; Subjective Memory Impairment(SMI) : 143 patients(20%), non-amnesic Mild Cognitive Impairment(MCI): single domain 70 (10%), multiple domain 34 (5%), amnesic MCI: single domain 74 (10%), multiple domain 159 (22%), Early onset Alzheimer's disease (AD): 9 (1%), AD 121 (17%), Vascular dementia: 62 (9%), Mixed dementia 44 (6%).

Hypnotics and antidepressants are prescribed as follows; SMI : hypnotics 14 patients (10%), antidepressants 27 (19%), non-amnesic MCI: single domain hypnotics 9 (13%), antidepressants 12 (17%), multiple domain hypnotics 4 (12%), antidepressants 6 (18%), amnesic MCI: single domain hypnotics 10 (14%), antidepressants 16 (22%), multiple domain hypnotics 22 (14%), antidepressants 24 (15%), Early onset Alzheimer's disease (AD): hypnotics 1 (11%), antidepressants 2 (22%), AD: hypnotics 10 (8%), antidepressants 36 (30%), Vascular dementia: hypnotics 8 (13%), antidepressants 20 (32%), Mixed dementia: hypnotics 4 (9%), antidepressants 17 (39%)

Conclusions: Among the outpatients of Dementia Center, MCI and SMI are majorities and the number of MCI patients are almost half. Depression are more prevalent in AD and Vascular dementia than MCI and SMI, and about 22% of patients are being prescribed by antidepressants and 11% by hypnotics.

Insomnia in the Modern World: Challenges and Interventions

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Introduction: Insomnia is one of the most prevalent sleep problems in modern society and has a large association with negative physical and mental health outcomes. Insomnia (inability to fall or remain asleep) is widely associated with daily deficits such as fatigue, irritability, and reduced cognitive performance. Increased stress, sedentary lifestyles, and excessive use of screens and digital devices are some of the factors contributing to the rise in this condition today. The worldwide shift to remote working has contributed to already disrupted sleep patterns, and now insomnia has become a major public health concern as more people find these boundaries between work and home life have disappeared.

Materials and methods: This point of view reviews the evidence behind a multidisciplinary treatment of insomnia and the integration of cognitive psychology, neuroscience, and new technology. The methodology involves:

1. **Literature Synthesis:** An extensive review of prior intervention studies, such as cognitive behavioural therapy for insomnia (CBT-I), pharmacological approaches, and lifestyle-focused interventions, to consider their gaps and merits.

2. **Technology Evaluations:** Evaluation of the available digital health technological advancements such as mobile applications, wearable sleep detectors, and neurostimulation techniques, etc., to determine their potential efficacy in insomnia management and access improvement.
3. **Development of the framework:** we propose a conceptual framework for the delivery of personalised and scalable insomnia treatment approaches that combine evidence-based interventions and innovative technologies.

Results: CBT-I is the gold standard treatment for insomnia with short- and long-term benefits that are robust, but its accessibility is limited due to the requirement for trained specialists. Rigorous pharmacological treatments give rapid relief but entail risks of dependency and side effects. Relaxation and meditation techniques are promising but rarely adopted consistently. Digital interventions, including CBT-I programs, wearables, or smart devices, can effectively mitigate treatment barriers by providing remote, personalised, and real-time solutions and by enhancing adherence to sleep hygiene. Novel treatments such as neurostimulation, biofeedback, and light therapy hold significant promise in targeting the pathophysiology of insomnia; however, further investigation is needed to evaluate their long-term efficacy and practical integration into routine care. This integrative perspective might support better data as well as scalable access to different treatment modalities in a sustainable way by developing an evidence-based framework that can easily support multidisciplinary cooperation in the provision of digital health solutions and will guide future research about insomnia management.

Conclusions: Given the increasing prevalence of insomnia and its public health implications, innovative approaches are needed to address this issue. Traditional therapies can present significant barriers to treatment, and these barriers can be overcome through the use of digital health solutions, which have greatly advanced in the form of wearable technology and neuroscience-based interventions. But applying those successful strategies will necessitate a collaborative solution that integrates cognitive psychology, technology, and health care.

Insomnia Severity Patterns Predict Overdose and Return to Drug Use in Individuals with Stimulant Use Disorder

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Introduction: Insomnia is a common symptom reported among individuals with stimulant use disorders and has been associated with poor treatment outcomes. However, there is limited understanding of how insomnia symptoms might impact return to stimulant use and/or non-fatal overdose following treatment. Therefore, the goal of the present study was to characterize patterns of insomnia severity during treatment and to evaluate their relationship with post-treatment relapse and non-fatal overdose.

Materials and methods: Participants (n = 742) entering addiction treatment with primary cocaine, methamphetamine, or prescription stimulant use and ≥ 3 insomnia assessments were included. The Insomnia Severity Index (ISI) was administered weekly for the first four weeks of treatment and monthly following treatment. Repeated measures latent class analysis (RMLCA) was used to identify insomnia trajectories. Logistic regression models were used to assess the associations between insomnia class (e.g., Class 1) and return to drug or alcohol use as well as non-fatal overdose.

Results: Four insomnia trajectory classes (i.e., Classes 1-4) were identified. Here, Class 1-4 represented Low-Stable (36.5%), Moderate-Decreasing (32.6%), Initially Severe-Improving (24.0%) and Severe-Persistent (6.9%), respectively. Compared to Class 1, individuals in Class 3 had significantly greater odds of reporting a non-fatal overdose (OR = 5.45, 95% CI: 2.43–12.22, $p < .0001$), followed by Class 4 (OR = 3.49, 95% CI: 1.85–6.58, $p = .0001$). Additionally, odds of non-fatal overdose were significantly greater in Class 3 (OR = 2.43, 95% CI: 1.34–4.27, $p = .0035$) and Class 4 (OR = 3.80, 95% CI: 1.59–9.06, $p = .0008$) when compared to Class 2. Similarly, odds of return to drug use were significantly increased in Class 2 (OR = 2.08, 95% CI: 1.45–2.99, $p = .0001$), Class 3 (OR = 2.53, 95% CI: 1.69–3.81, $p < .0001$) and Class 4 (OR = 5.03, 95% CI: 2.28–11.10, $p = .0001$), relative to Class 1. Odds were also greater in Class 4 compared to Class 2 (OR = 2.42, 95% CI: 1.08–5.44, $p = .0313$).

Conclusions: These results indicate that patterns of insomnia severity during stimulant use disorder treatment were associated with both relapse and non-fatal overdose. Risk was highest among those with persistent or initially elevated insomnia symptoms, suggesting that these patterns may reflect underlying vulnerability. The current findings underscore the importance of sleep health during

addiction treatment and suggest that sleep medicine consultations are appropriate to improve both sleep and addiction-related outcomes.

Intensive Sleep Retraining and Total Sleep Deprivation for Treating Chronic Insomnia: A Randomised Controlled Trial

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Introduction: This study aimed to: (1) compare the efficacy of intensive sleep retraining (ISR) and total sleep deprivation (TSD) against a no-treatment control condition for treating chronic insomnia, (2) examine two potential mechanisms: the resolution of conditioned insomnia and the increase in homeostatic sleep drive produced by sleep deprivation, and (3) compare recovery sleep over a 2-week period after undergoing ISR and TSD.

Materials and methods: Thirty-four unmedicated adults with chronic sleep onset insomnia (with or without sleep maintenance difficulties) were randomized to ISR, TSD or a control condition. The ISR condition consisted of a 38.5-hour period of sleep deprivation, the last 21 hours of which included 42 sleep onset trials; the TSD condition consisted of an equivalent 38.5-hour sleep deprivation period without any sleep onset trials, and the control condition consisted of one night of habitual sleep in the laboratory. Participants completed several measures including the Insomnia Severity Index (ISI) and daily sleep diaries at pre-treatment, post-treatment, and at 1, 2, and 3 months after treatment.

Results: Significant decreases in insomnia severity were observed from pre-to post-treatment in both ISR and TSD, but not in the control condition. A significant reduction in sleep onset latency was observed during the same period for the ISR condition, but not for the TSD or control conditions, with no clinically meaningful change in anxiety or depressive symptoms. Significant decreases in fatigue were also observed for both ISR and TSD conditions during the same period. These results were generally significant at 3 months after treatment. Mixed model analyses on night-to-night data revealed significant increases in total sleep time from baseline to night 1 post-treatment recovery in ISR, TSD and control conditions. The magnitude of sleep duration increase was significantly higher in the treatment conditions (3 to 4 times higher) compared to the control condition. At night 2 post-treatment, total sleep time remained significantly improved for ISR, but not in the TSD or control conditions. Beginning at night 3 up to night 14 post-treatment, no notable changes were observed in any of the conditions.

Conclusions: Sleep improvements produced by ISR, and to a lesser extent by TSD, suggest that both the resolution of conditioned insomnia and the increase in homeostatic sleep drive represent important mechanisms responsible for the efficacy of ISR. Sleep recovery following ISR and TSD was characterized by significant sleep improvements on the first night post-treatment, followed by a rapid decline on the second night. The rebound effect was less pronounced for ISR than TSD condition, with similar reported sleep quality, suggesting that ISR may offer better therapeutic potential.

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Interoception Abnormalities in Frontal Neural Circuits during N1 in Insomnia Disorder

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Introduction: Insomnia Disorder (ID) is characterized by sensory hypersensitivity during wakefulness and sleep. Previous studies have shown that people with insomnia have an inappropriate adaptation of their brain responses to the ever-present heartbeat during the evening wakeful rest. Interoceptive

sensitivity can be assessed quantitatively by measuring the cerebral cortical response to one's own heartbeat (heartbeat-evoked potential, HEP). Here, we investigated whether interoceptive sensitivity, as indicated by the amplitude of one's own HEP, differs between people with ID and healthy controls (HC) during different stages of wakefulness and sleep.

Materials and methods: Thirty-nine patients with ID (meeting the diagnostic criteria of DSM-5) and sixty-two HC (meeting the criteria of normal sleepers) were recruited. HEP was obtained from 64-channel electroencephalogram (EEG), which recorded the brain electrical activities during wakefulness and sleep cycles. A registered polysomnographic technologist categorized the EEG data into wake, nonrapid eye movement sleep, and rapid eye movement (REM) sleep based on the American Academy of Sleep Medicine criteria. Significance of group differences in HEP amplitude and its topographical distribution over the scalp were assessed using cluster-based permutation tests.

Results: During wakefulness, patients with ID had a larger amplitude EEG component than HC at frontal electrodes 50-70 ms before the R-wave peak ($P_{FDR}=0.045$). During stage 1 of nonrapid eye movement sleep (N1), patients with ID had a larger amplitude late HEP component than HC at frontal electrodes 404-482 ms after the R-wave peak ($P_{FDR}=0.049$). During stage 2 of nonrapid eye movement sleep (N2), patients with ID had a larger amplitude EEG component than HC at frontal electrodes 54-64 ms before the R-wave peak ($P_{FDR}=0.048$), and patients with ID had a larger amplitude late HEP component than HC at frontal electrodes 406-424 ms after the R-wave peak ($P_{FDR}=0.048$). During stage 3 of nonrapid eye movement sleep (N3), patients with ID had a larger amplitude EEG component than HC at frontal electrodes 72-90 ms before the R-wave peak ($P_{FDR}=0.047$), patients with ID also had a larger amplitude HEP component than HC at frontal electrodes 12-18 ms after the R-wave peak ($P_{FDR}=0.047$). Source localization suggested increased neural activity time-locked to heartbeats in patients with ID mainly in inferior frontal cortices/medial frontal cortices ($P_{FDR}=0.010$) in the beta band during N1. It should be noted that no statistical analysis was performed due to the lack of data in the REM stage.

Conclusions: Significant differences in interoception were found between patients with ID and HC during wakefulness and each stage of nonrapid eye movement sleep. These findings suggest that abnormalities in the frontal neural circuits during N1 involved in interoception may play a crucial role in the pathophysiology of ID. Future research with more comprehensive data, especially in the REM stage, is warranted further to elucidate the full picture of interoception differences in ID.

Interpreting Adverse Events of Somnolence With Lemborexant in Clinical Trials

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Introduction: Assessments of treatment-emergent adverse events (TEAEs) are routinely conducted in clinical trials and are frequently compared among drugs in the same class and between classes. In the case of hypnotics, the TEAE of somnolence (TEAE-S) is often a focus since residual sleepiness can lead to functional impairment. In assessing the potential impact of TEAE-S, however, parameters other than incidence should be considered. Other important parameters including severity and timing of TEAE-S relative to the initiation of treatment and impact on early morning/daytime function are important for informing clinical use. In addition, study design elements can impact TEAE-S rates. Analyses of TEAE-S from 2 large phase 3 studies of lemborexant (LEM), a dual orexin-receptor antagonist approved in many countries to treat adults with insomnia, provide data to support use in real-world settings.

Materials and methods: Study E2006-G000-304 (NCT02783729) and Study E2006-G000-303 (NCT02952820) evaluated efficacy and safety across 1 and 12 months, respectively, of LEM 5mg (LEM5), LEM 10mg (LEM10), and placebo (PBO) in adults with insomnia disorder. In addition to the incidence/severity of TEAE-S, a Kaplan-Meier analysis was conducted using pooled safety data from the 2 studies. To assess the potential for important morning residual sleepiness, a highway-driving study (Study E2006-E044-106; NCT02583451) was conducted in 48 healthy participants (age range: 23–78 years; 50% ≥65 years) following single and multiple doses of approved doses, LEM5 and LEM10, compared with PBO and active control, zopiclone (7.5mg).

Results: In the pooled dataset, TEAE-S was the most common TEAE, with a dose-related increase in incidence. The overall incidence of TEAE-S was low. LEM5 consistently showed approximately 5%–6% higher incidence than PBO, and LEM10 consistently showed 7%–8% higher incidence than PBO. The

majority of TEAE-S was mild in severity. Few participants discontinued from the phase 3 studies due to somnolence (PBO: 0.6%; LEM5: 1.1%; LEM10: 2.3%). Importantly, the onset of most TEAE-S was within the first few days of LEM administration. Kaplan-Meier analysis revealed that the probability of having a first incidence of TEAE-S was greatest during the first 2 weeks of treatment, with much lower probability later in the treatment period. In Study E2006-E044-106, there were no statistical differences in the standard deviation of lateral position between LEM5, LEM10, and PBO, supporting a lack of driving impairment.

Conclusions: While the incidence of somnolence was greater with LEM10 than with LEM5, it should be noted that the phase 3 studies were of fixed design, meaning that participants could not down-titrate if they were experiencing TEAEs. The probability of somnolence in this fixed-dose setting diminished after the first 2 weeks of administration. Further, patients are advised to initiate treatment with LEM5, suggesting that somnolence rates in clinical practice could be different than in the clinical trial for that dose group. Additionally, LEM10 was not associated with driving impairment, suggesting TEAE-S does not equate with impairment. Thus, there are many considerations in interpreting TEAE-S between and among hypnotic drug classes.

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Iron metabolism status in three types of sleep disorders (OSA, chronic insomnia, RLS without insomnia)

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Introduction: The peculiarities of iron metabolism play a key role in the development of many diseases and are also associated with sleep disorders. Currently, the state of iron metabolism is considered mainly in the aspect of the pathogenesis and treatment of RLS, while with other sleep disorders, its meaning remains unclear.

Materials and methods: The study included 185 patients who were divided into three groups based on their clinical symptoms (OSA, chronic insomnia (Chrlns), RLS without insomnia (RLSwoi)). PSG study (Embla N7000) was performed in all patients. A biochemical blood test was also performed to assess the level of ferritin, serum iron, transferrin, UIBC, transferrin saturation and CRP. Pts with ferritin > 400 mcg/l and pts with CRP > 5,0 mg/l were excluded from the analysis. Finally, data from 134 patients were used for statistical analysis (female 72, male 62). Median age was 46 (Q1–Q3: 36.00–58.00), median BMI was 24.82 (Q1–Q3: 22.41–28.73). The comparison of three or more groups regarding quantitative variables with normal distribution was performed using one-way analysis of variance (ANOVA). Post-hoc comparisons were conducted using Tukey's test under the assumption of equal variances. Comparisons of three or more groups on a quantitative variable whose distribution differed from normal were made using the Kruskal-Wallis test and Dunn's test with Holm correction as a post-hoc method. Differences were considered statistically significant at $p < 0.05$. A key characteristic of our study design was that none of the groups had any coexisting sleep disorders.

Results: Ferritin levels were statistically significantly higher in OSA pts (Me 117.1 $\mu\text{g/L}$, Q1–Q3: 70.22 – 178.00) vs. Chrlns (Me 59.59 mcg/L, Q1–Q3: 38.73 – 94.30, $p < 0.001$) and RLSwoi (Me 54.00 mcg/L, Q1–Q3: 34.65 – 80.00, $p = 0.008$). There was no statistically significantly difference for ferritin between Chrlns and RLSwoi groups. Transferrin levels were statistically significantly higher in OSA pts (Me 2.76 g/L, Q1–Q3: 2.54 – 2.90) vs. Chrlns (Me 2.61 g/L, Q1–Q3: 2.29 – 2.80, $p = 0.009$) but not vs. RLSwoi (Me 2.35 g/L, Q1–Q3: 2.30 – 2.80, $p > 0.05$). When comparing of serum iron, UIBC, transferrin saturation depending on type of sleep disorders there were no statistically significant differences ($p = 0.328$, $p = 0.115$, $p = 0.151$ respectively). The main indices characterizing sleep breathing disorders have demonstrated the following results: AHI OSA (Me 22.80, Q1–Q3: 13.80 – 61.95), AHI Chrlns (Me 3.10, Q1–Q3: 0.83 – 7.40, $p_{\text{OSA-Chrlns}} < 0.001$), AHI RLSwoi (Me 3.80, Q1–Q3: 2.10 – 4.10, $p_{\text{OSA-RLSwoi}} < 0.001$); $\text{SpO}_{2 \leq 90\%}$, (%) OSA (Me 6.00, Q1–Q3: 0.25 – 27.50), $\text{SpO}_{2 \leq 90\%}$, (%) Chrlns (Me 0.00, Q1–Q3: 0.00 – 0.10, $p_{\text{OSA-Chrlns}} < 0.001$), $\text{SpO}_{2 \leq 90\%}$, (%) RLSwoi (Me 0.00, Q1–Q3: 0.00 – 0.00, $p_{\text{OSA-RLSwoi}} < 0.001$). There was no statistically significantly difference for age between the groups ($p = 0.734$), but there was statistically significantly difference for BMI with higher level for OSA group ($p < 0.001$).

Conclusions: Patients with chronic insomnia may require to be checked for iron deficiency. Not only RLS, but also chronic insomnia may be associated with iron deficiency. We assume the existence of iron deficiency chronic insomnia phenotype.

Is Sedentary Time Resistant to the Efficacy of Behavioral Sleep Interventions? A Secondary Analysis of a Randomized Controlled Trial

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Introduction: Behavioral sleep interventions (BSIs), including digital cognitive behavioral therapy for insomnia (dCBTI) and digital sleep hygiene education (dSHE), are proved to be effective for insomnia. However, it remains unclear the relationship between sedentary time (ST) and efficacy of BSIs.

Materials and methods: This secondary analysis included 178 adults diagnosed with acute insomnia, randomly assigned to 4 weeks of dCBTI or dSHE. Follow-up assessments at 1 to 3, and 3 to 6 months captured ISI>7, ESS>10, TST≤6h, and SE<80% events via questionnaire and accelerometer. Kaplan-Meier estimates, and Cox regression models and restricted cubic spline analyses (RCS) were employed to evaluate the association of ST and adverse sleep outcome. To address immortal time bias, landmark analysis was performed. Interactions between ST and adverse sleep outcome were investigated in subgroup analyses.

Results: Because both the dCBTI and dSHE groups illustrated comparable improvements for insomnia at follow up, with no significant group-by-time interaction, we pooled them as BSIs for joint analysis. In unadjusted Cox models, high ST was associated with an increased risk of TST≤6 h (HR 1.59; 95% CI 1.01–2.50), but not with ISI>7, ESS>10, or SE<80%. In fully adjusted landmark analyses, high ST predicted higher risk of ISI>7 events within 3 months post-BSIs (HR 2.46; 95% CI 1.37–4.43) and higher risk of TST≤6 h beyond 3 months post-BSIs (HR 2.76; 95% CI 1.30–5.90). The RCS regression analyses demonstrated a positive nonlinear association between ST and the incidence of TST≤6 h in the insomnia population (P for overall < 0.01, P for nonlinear <0.01), with a potential threshold of 701 min/day. Furthermore, subgroup analysis indicated that there was a significant interaction between the subgroups of age<35 years and the high ST, which caused a higher risk event ratios of TST≤6 h (HR, 2.93; 95% CI, 1.44 to 5.97; P for interaction<0.05).

Conclusions: ST significantly impedes early subjective sleep improvements after BSIs, while it specifically increase the risk of shorter sleep duration in the long term. Incorporating interventions to reduce daytime sitting into BSIs may enhance the efficacy of insomnia treatment.

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“It’s just normal” experiences of insomnia symptoms among Chinese pregnant women: a qualitative study

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Introduction: Insomnia is prevalent among pregnant women and associated with various adverse health outcomes, such as gestational hypertension, perinatal depression, increased suicidal risk, miscarriage, preterm birth, and low infant birth weight. Existing studies have focused on using the quantitative method to investigate the factors associated with insomnia in pregnant women, but they did not capture the experiences of pregnant women with insomnia, which hinders the development of tailored interventions from the perspective of these women. This study explored the experiences of insomnia symptoms among Chinese pregnant women, including their perceptions, the impacts of insomnia on their daily lives, and coping strategies.

Materials and methods: Data were collected through individual interviews and focus groups with 29 pregnant women experiencing insomnia symptoms across all trimesters, from two tertiary hospitals in Yangzhou, China. The interviews were conducted online using a video conferencing platform and analyzed using content analysis.

Results: Four themes were identified from the data: manifestations of insomnia, perceived impacts of insomnia, coping strategies, and perceptions of insomnia in pregnancy. The manifestations of insomnia had impaired daily functioning, somatic complaints and noticeable changes in appearance, and psychological distress. Coping strategies included sleep habit adjustments, multifaceted social support, and alleviating pregnancy discomforts. Informants expressed a normalization of insomnia as a common experience during pregnancy, a belief in self-regulation, and skepticism regarding the effectiveness of medical consultations.

Conclusions: This study provides insights into the multifaceted nature of insomnia experiences among Chinese pregnant women, emphasizing the need for tailored, evidence-based interventions that address misconceptions about insomnia and promote effective coping strategies for managing insomnia symptoms during pregnancy.

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Locus Coeruleus-Cingulate Cortex Hyperconnectivity during N2 Sleep: A Functional Pathway to Depression in Insomnia Disorder

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Introduction: Insomnia disorder (ID) frequently coexists with substantial psychiatric comorbidity, particularly anxiety and depression. The locus coeruleus (LC), a pontine nucleus within the ascending reticular activating system, plays a crucial role in sleep-wake regulation and emotional processing. However, the neurobiological mechanisms underlying the association between ID and emotional dysregulation remain incompletely understood. This study investigated LC-based whole-brain functional connectivity patterns across different sleep stages and their associations with subjective sleep quality and emotional symptoms in patients with ID.

Materials and methods: Simultaneous electroencephalography and functional magnetic resonance imaging (EEG-fMRI) data were acquired from 37 patients with ID and 30 well-matched healthy controls (HC) during their nocturnal sleep. Using a probabilistic template, the LC region was defined as the seed for whole-brain connectivity analyses. Group-by-stage interactions in LC-based functional connectivity were assessed using a linear mixed-effects model. Associations between functional connectivity patterns and Pittsburgh Sleep Quality Index (PSQI), Self-Rating Depression Scale (SDS), and Self-Rating Anxiety Scale (SAS) were evaluated using Spearman's rank correlations.

Results: Significant group-by-stage interactions were observed in multiple brain regions, including the cingulate cortex, right insular cortex, left temporal cortex and left insular cortex. Post-hoc analyses revealed that patients with ID exhibited significantly enhanced LC-cingulate cortex functional connectivity during N2 sleep compared to healthy controls ($p = 0.024$, Bonferroni-corrected). Within the total sample, N2-specific LC-cingulate cortex connectivity strength demonstrated significant positive correlations with both SDS scores ($r = 0.337$, $p = 0.018$, Bonferroni-corrected) and PSQI scores ($r = 0.401$, $p = 0.003$, Bonferroni-corrected).

Conclusions: The observed alterations in LC-cingulate cortex functional connectivity during N2 sleep suggest a distinct neural circuit that may underlie the dysregulation of emotional processing in ID,

providing a potential neurobiological substrate for the well-documented association between sleep disruption and emotional symptoms.

Longitudinal associations between couple relationship quality and insomnia symptoms among Chinese couples: A cross-lagged panel design

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Introduction: Insomnia is a highly prevalent sleep disorder linked to elevated risks of various physical and mental health conditions. Recent evidence from our team suggests that couple relationship quality plays a critical role in sleep health. Although substantial research supports the association between couple relationship quality and sleep quality, few studies have focused specifically on insomnia. To date, only three cross-sectional studies have indicated that higher couple relationship quality is associated with less severe insomnia symptoms. However, the longitudinal directionality of this association remains unclear. This study aimed to investigate the bidirectional relationship between couple relationship quality and insomnia over time among Chinese couples.

Materials and methods: A total of 247 Chinese adults (median age = 30 years [IQR = 7]; 72.1% women) in committed relationships were recruited via social media to participate in a two-wave longitudinal survey conducted over six months. Relationship quality was measured using the Locke-Wallace Marital Adjustment Test, and insomnia severity was assessed with the Insomnia Severity Index. Cross-lagged panel models were used to examine the temporal associations between overall relationship quality (and specific relational dimensions) and insomnia severity. Multiple regression analyses were performed to assess whether changes in relationship quality predicted changes in insomnia severity.

Results: Higher overall relationship quality at baseline significantly predicted lower insomnia severity at 6-month follow-up ($\beta = -0.141$, 95% CI = -0.231 to -0.052 , $p = 0.010$), with the effect being significant among females ($\beta = -0.139$, 95% CI = -0.244 to -0.035 , $p = 0.028$) but not males. Among specific relational dimensions, greater contentment and communication ($\beta = -0.132$, 95% CI = -0.208 to -0.055 , $p = 0.005$), as well as shared philosophy ($\beta = -0.167$, 95% CI = -0.253 to -0.082 , $p = 0.001$), at baseline predicted lower insomnia severity at follow-up. Baseline insomnia severity did not significantly predict subsequent changes in either overall couple relationship quality or its specific dimensions. Regression analyses further indicated that improvements in overall relationship quality ($\beta = -0.181$, SE = 0.013, $p = 0.004$), as well as in contentment and communication ($\beta = -0.177$, SE = 0.017, $p = 0.007$), significantly predicted alleviation of insomnia, independent of depression, anxiety, and age.

Conclusions: Couple relationship quality appears to be a significant longitudinal predictor of insomnia severity. Interventions that enhance overall relationship quality—particularly contentment and communication, and shared philosophy—may help mitigate future insomnia risk. These findings underscore the importance of integrating relational factors into the assessment and treatment of insomnia.

Long-term real-life experience with daridorexant in patients with chronic insomnia

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Introduction: Daridorexant is the new dual orexin-receptor antagonist approved in Europe, USA and Canada for the treatment of chronic insomnia. Its clinical efficacy and safety was showed in randomized controlled studies. However, the long-term real-world data including health-related quality of life is still not available. We performed an prospective observational study to investigate one-year outcome of daridorexant treatment and its influence on the health-related quality of life (HrQoL) in patients with chronic insomnia.

Materials and methods: Patients with chronic insomnia diagnosed according to DSM V criteria were participants of this study. The clinical and HrQoL evaluation was performed prior to begin the therapy

with daridorexant (baseline) in the standard dosis of 50qd and after 3, 6 and 12 months. The following sleep parameters were measured: wake after sleep onset (WASO), latency to persistent sleep (LPS), total sleep time (TST) and subjective total sleep time (sTST). HrQoL was assessed using EuroQoL5D (EQ5D Index and EQVAS: visual analogue scale).

Results: 102 patients aged 52.8 ± 9.4 years (56.9% females) participated in our study. The baseline values of sleep parameters showed a continuous and constant improvement during the study period: WASO at baseline 93.8 ± 10.3 min vs 62.1 ± 9.9 min after 12 months ($p < 0.01$), LPS at baseline 62.8 ± 9.3 min vs 33.5 ± 8.7 min after 12 months ($p < 0.01$), TST at baseline 321.0 ± 20.5 min vs 403.6 ± 21.4 min after 12 months ($p < 0.01$), sTST at baseline 310.1 ± 23.7 min vs 388.2 ± 24.0 min after 12 months ($p < 0.01$). The EQ5D Index and EQVAS were reduced by approximately 23% in comparison to general German population. The baseline EQ5D Index value (0.60 ± 0.13) improved by 22% (0.73 ± 0.17) after 12 months of daridorexant treatment baseline (0.61 ± 0.8). Similar increase of HrQoL was observed on EQVAS (61.3 ± 12.6 at baseline versus 74.5 ± 17.4 , $p < 0.01$).

Conclusions: We provide the real-world data showing sustained improvement of sleep parameters and HrQoL in patients treated with daridorexant for chronic insomnia.

Long-Term Risk of Dementia in middle-age and older adults with Sleep Disorders: Evidence from 20 Years of Nationwide Taiwanese Data

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Introduction: A growing body of research has identified an association between various sleep disorders and increased dementia risk; however, the extent to which specific types of sleep disorders differentially contribute to dementia onset remains unclear. This research aimed to utilize comprehensive population-representative data to understand the risk of dementia in patients with sleep disturbances, and to compare the effects and risk factors of different types of sleep disorders on the risk of dementia.

Materials and methods: A retrospective study contained adults ≥ 40 years of age who enrolled in National Health Insurance Research Database (NHIRD) from 2000 to 2020. The subjects are: 1) patients with sleep disorders encompassed insomnia, sleep-related breathing disorders (SBDs), and restless leg syndrome (RLS) as their primary or secondary diagnosis according to the International Classification of Diseases; 2) aged 40 years or older; 3) with at least ten years of observable data in the health database. The incidence rate of all-cause dementia, Alzheimer's disease (AD), vascular dementia (VD) per 1,000 person-years will be observed. Cox proportional hazards model will focus on risk factors associated with dementia.

Results: Among the 236,837 participants, the majority were classified as having insomnia ($n = 233,529$), followed by those with sleep-related breathing disorders (SBDs; $n = 2,367$) and restless legs syndrome (RLS; $n = 1,209$). The overall incidence of all-cause dementia among subjects with sleep disorders was 7.83 per 1,000 person-years (PYs), with incidences of AD and VD reported at 1.31 and 1.11, respectively. Kaplan–Meier survival analysis revealed significantly lower dementia-free survival among participants with RLS (log-rank $p < .0001$). Participants with RLS exhibited the highest incidence of dementia (15.55/1,000 PYs) and demonstrated significantly elevated risks of all-cause dementia (adjusted hazard ratio [aHR], 1.96; 95% confidence interval [CI], 1.73–2.21), AD (aHR, 4.73; 95% CI, 4.57–4.90), and VD (aHR, 4.73; 95% CI, 4.57–4.90) compared to those with insomnia. Additional risk factors included advanced age, female sex, depression, alcohol abuse, and a high comorbidity burden.

Conclusions: RLS confers the highest risk of all-cause and subtype-specific dementia compared with insomnia and SBDs. Advanced age, female sex, depression, alcohol abuse, and a high comorbidity burden further compound this risk, underscoring the need for targeted screening and management strategies in these vulnerable populations.

Acknowledgments: sleep disorders, insomnia, sleep-related breathing disorder (SBDs), restless leg syndrome (RLS), Alzheimer's disease (AD), vascular dementia (VD), National Health Insurance Research Database (NHIRD)

Managing Insomnia in an Adult Female with ADHD and Sedative Abuse: A Case Report on the Combined Use of Lemborexant, Agomelatine, and Methylphenidate

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Introduction: Insomnia is a frequent and impairing comorbidity in adults with Attention-Deficit/Hyperactivity Disorder (ADHD), often exacerbated by the core symptoms of hyperarousal, emotional dysregulation, and stimulant treatment. The situation becomes more challenging when insomnia coexists with past sedative misuse, such as benzodiazepine abuse, which limits therapeutic options.

Pharmacological management of insomnia in such patients must balance the need for ADHD symptom control with strategies that restore circadian stability and improve sleep quality—without inducing dependence or next-day sedation.

Materials and methods: A 38-year-old woman, an art performer and mother of two, presented with persistent insomnia and difficulty falling and staying asleep. She had a longstanding diagnosis of adult ADHD and a history of alprazolam abuse. There was also past cannabis use, although not active at the time of consultation.

The patient had previously tried lemborexant 5 mg (an orexin receptor antagonist) with minimal benefit. After structured discontinuation of alprazolam, a combined regimen was initiated: lemborexant was titrated to 10 mg, agomelatine 25 mg was added for circadian regulation, and methylphenidate was reintroduced for ADHD symptom control. Sleep hygiene education and routine stabilization were also implemented.

Results: After two month of therapy, the patient experienced substantial improvement in sleep quality under the combination therapy. The Pittsburgh Sleep Quality Index (PSQI) score improved significantly, with subjective reports of easier sleep initiation, fewer nocturnal awakenings, and more restorative sleep.

Importantly, ADHD symptoms—such as mental restlessness, distractibility, and emotional lability—were better controlled with methylphenidate, leading to improved daytime functioning. This, in turn, reduced bedtime hyperarousal and mental rumination, indirectly supporting improved sleep onset. The synergistic effects of agomelatine and lemborexant appeared to counterbalance stimulant-induced arousal without inducing sedative side effects or tolerance.

This case illustrates that effective treatment of insomnia in adult ADHD patients with a history of substance misuse may require a strategic pharmacologic combination. Rather than avoiding stimulants, judicious use alongside sleep-promoting agents may yield superior outcomes when carefully titrated and monitored.

Conclusions: Managing insomnia in adults with ADHD and prior sedative abuse is clinically challenging. However, this case demonstrates that a thoughtfully designed regimen—combining lemborexant, agomelatine, and methylphenidate—can lead to meaningful improvement in both sleep and daytime functioning. The key lies in targeting complementary neurobiological mechanisms: orexin inhibition for arousal, melatonergic support for circadian rhythm, and dopaminergic enhancement for executive dysfunction.

This case supports the idea that stimulant use could be considered in patient with insomnia and have ADHD comorbidity. Further exploration of such integrative approaches is warranted.

Mechanistic Insights into Cognitive Behavioral Therapy for Adolescents with Comorbid Insomnia and Anxiety: Mediation Analysis in a Randomized Controlled Trial

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Introduction: Insomnia and anxiety are highly prevalent and frequently co-occurring in adolescents. Their comorbidity can exacerbate each condition and lead to significant psychosocial and functional impairments. Cognitive behavioral therapy for insomnia (CBT-I) and cognitive behavioral therapy for anxiety (CBT-A) have demonstrated efficacy in reducing insomnia and anxiety symptoms, respectively. However, the mechanisms underlying their effects on comorbid anxiety symptoms and insomnia disorder remain unclear. This study aimed to explore whether improvement in insomnia / anxiety would mediate anxiety / insomnia reduction.

Materials and methods: This was a secondary analysis of a three-arm randomized controlled trial conducted in adolescents with comorbid insomnia and anxiety. Participants were aged 12-20 years had DSM-5 insomnia disorder with a score of ≥ 9 on the Insomnia Severity Index (ISI) and presented with increased anxiety symptoms (Spence Children's Anxiety Scale (SCAS) scores of > 37 for females and > 32 for males). A total of 135 participants (mean age: 18.31 ± 1.61 years; 76% female) were recruited randomly assigned to one of three groups: eight weekly sessions of group-based CBT-I ($n=47$), eight weekly sessions of group-based CBT-A ($n=45$), or a waitlist control group (WL, $n=43$). All participants were assessed at baseline and post-treatment for their insomnia severity (via ISI) and anxiety symptoms (via the Hospital Anxiety and Depression Scale—Anxiety subscale, HADS-A).

Results: There was a significant group $\times$ time interaction effect on insomnia severity ($F(2, 119.84) = 10.95, p < 0.001$) and anxiety symptom severity ($F(2, 108.93) = 3.59, p = 0.031$). Compared to the WL, both CBT-I and CBT-A led to significant reductions in insomnia (CBT-I: $d = -2.06$; CBT-A: $d = -1.14$; WL: $d = -0.55$) and anxiety symptoms (CBT-I: $d = -0.86$; CBT-A: $d = -0.33$; WL: $d = -0.3$). Mediation analysis showed that, within the CBT-I group, improvements in anxiety was fully mediated by reductions in insomnia severity, with an indirect effect of -1.9 ($SE = 0.8, 95\% CI: -3.6$ to -0.36). However, reductions in anxiety did not significantly mediate improvements in insomnia within the CBT-I group. No significant mediating effects were found for either improving insomnia through changing anxiety or reducing anxiety through improving insomnia within the CBT-A group.

Conclusions: The findings suggest that improvements in insomnia symptoms following CBT-I may mediate the improvement of anxiety in adolescents with comorbid insomnia and anxiety. This underscores the transdiagnostic implications of targeting insomnia to alleviate anxiety symptoms in young people. Future research should investigate the underlying neurobiological and behavioral mechanisms and explore sequencing CBT-I and CBT-A protocols to optimize treatment effects.

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Melatonin Prolonged-Release may improve insomnia and depression in epilepsy patients

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Introduction: Insomnia is one of the most common sleep problems in general population and is highly prevalent among patients with epilepsy. Despite the well-documented effects of melatonin on insomnia and potential anticonvulsive effect, there only limited information on the effect of melatonin in epilepsy patients with the comorbid insomnia. We performed this pilot study to evaluate the effect and safety of prolonged release (PR) formulation of melatonin in epilepsy patients with insomnia.

Materials and methods: We prospectively enrolled 34 adult patients with epilepsy from March 2024 to February 2025. We collected and compared the Insomnia Severity Index (ISI) and the Korean version of the Neurological Disorders of Depression Inventory for Epilepsy (K-NDDI-E) before and after melatonin PR intake, and analyzed the results using the Wilcoxon signed-rank test.

Results: A total of 34 patients (13 males, mean age 55.3 ± 11.1 years) were included in the analysis. 31 patients were classified as having focal-onset seizures and 3 patients were classified as having generalized-onset seizures. A significant improvement, as measured by the ISI, from 16.0 ± 4.4 to 12.2 ± 5.2 after 12 weeks of melatonin PR ($p = 0.041$). In addition, a significant improvement in depression,

as measured by the K-NDDI-E, from 11.3 ± 4.2 to 9.8 ± 3.2 after 12 weeks of melatonin PR ($p = 0.001$). None of the patients discontinued melatonin PR due to seizure aggravation during the study.

Conclusions: Our study shows that melatonin PR was effective in improving sleep quality in epilepsy patients with insomnia and was also effective in improving depression. This finding suggests that melatonin PR may be a potential treatment option for epilepsy patients with both insomnia and depression.

Mindfulness-imbued insomnia therapy enhances antidepressant outcomes for pregnant women with insomnia and depression: A comparative effectiveness randomized controlled trial of CBTI and PUMAS

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Introduction: Insomnia affects half of pregnant women and significantly heightens the risk for comorbid depression. Among pregnant women with insomnia, nearly half also experience depression, compounding challenges to quality of life, mother-infant bonding, and perinatal health outcomes. Identifying effective treatments for co-occurring insomnia and depression during pregnancy remains a critical priority. Cognitive-behavioral therapy for insomnia (CBTI) improves sleep quality but has limited impact on depressive symptoms—an effect attributed to persistent cognitive arousal (e.g., worry and rumination). Addressing cognitive arousal may enhance depression outcomes for pregnant women with insomnia. Emerging evidence suggests that mindfulness-based interventions substantially reduce cognitive arousal during pregnancy. This randomized controlled trial (RCT) evaluated the comparative effectiveness of CBTI versus Perinatal Understanding of Mindful Awareness for Sleep (PUMAS), which integrates mindfulness and behavioral sleep strategies, targeting insomnia, depression, and cognitive arousal.

Materials and methods: A single-site, two-arm RCT of N=100 pregnant women with DSM-5 insomnia disorder and comorbid depression were randomized to CBTI or PUMAS. All treatment was delivered via six weekly telemedicine video sessions. Clinical symptoms were assessed a week before treatment, weekly throughout therapy, then one week after treatment. Clinical outcomes included the insomnia severity index (ISI), Edinburgh postnatal depression scale (EPDS), and two nocturnal cognitive arousal measures: (1) general nocturnal cognitive arousal via the pre-sleep arousal scale's cognitive factor (PSASC) and (2) perinatal-focused nocturnal rumination via the perinatal rumination scale at night (PRS-Night). Linear mixed models (LMM) using an intent-to-treat (ITT) approach were used to test treatment effects across repeated measures by evaluating Treatment X Time interactions. Covariates included time, age, gestational week, race, and session attendance. Insomnia remission was operationalized as posttreatment ISI scores of ≤ 7 , and depression remission was operationalized as $EPDS < 10$.

Results: Over 90% of patients completed ≥ 4 sessions, indicating high engagement. LMM analyses revealed that both CBTI and PUMAS resulted in insomnia severity reductions but overall, did not differ from one another ($b = -.14$, $p = .142$). However, insomnia remission rates were significantly higher for PUMAS as compared to CBTI (78.0% vs 50.0% remission, $\chi^2 = 8.51$, $p = .004$). Regarding depression, LMM analyses showed that PUMAS produced greater reductions in EPDS scores as compared to CBTI ($b = -.31$, $p < .001$), which also corresponded to higher depression remission rates for the PUMAS group (82.0% vs 58.0% remission, $\chi^2 = 6.86$, $p = .009$). Regarding cognitive arousal, LMM analyses showed that, relative to CBTI, PUMAS produced greater reductions in PSASC ($b = -.34$, $p = .009$) and PRS-Night scores ($b = -.44$, $p = .007$). Mediation analysis using PRODCLIN revealed that PUMAS-linked reductions in perinatal depression were mediated by decreases in nocturnal cognitive arousal, highlighting its role as a key mechanism of therapeutic change.

Conclusions: CBTI and PUMAS are effective for prenatal insomnia, whereas PUMAS was superior to CBTI for alleviating depression. Mechanistic findings suggest that reducing general and perinatal-focused rumination at night enhances PUMAS antidepressant effects. Our findings support triaging pregnant women with insomnia and comorbid depression to PUMAS over CBTI, whereas prenatal insomnia patients without depression may benefit similarly from either cognitive-behavioral or mindfulness-based therapies.

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Multimodal assessment of sleep-wake perception in insomnia disorder

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Introduction: Insomnia disorder is a prevalent health problem. The primary diagnostic criterion is a subjective complaint about reduced quantity or quality of sleep, which is often not observed in objective sleep measurements.

Materials and methods: Thirty patients with insomnia disorder (20 female, 8 male, 2 divers, 39±15 years) and 30 healthy controls (21 female, 9 male, 36±13 years) reported on their sleep-wake perception from up to 12 awakenings performed from consolidated NREM sleep.

Results: We show that patients with insomnia disorder, characterized by substantial subjective sleep complaints, did not differ on objective measures of sleep continuity, sleep architecture, spectral power, spectral slope, and phase-amplitude coupling of slow oscillatory and spindle activity. Perception of wakefulness following 559 serial awakenings from NREM sleep was frequent in both patients (59.7±33.5%) and controls (47.9±32.5%), with no significant group difference ($p = 0.223$; Cohen's $d = 0.32$, small effect size). High frequency spectral power, as an index of cortical arousal prior to awakening, but not standard measures of sleep, predicted the perception of wakefulness across groups, possibly related to physiological wake-like activity during sleep.

Conclusions: Our results support the notion that sleep-wake regulatory systems and direct sleep-wake perception are often intact in patients with insomnia disorder. These results propose empirical support for cognitive behavioral therapy for insomnia as the first-line treatment.

Music Intervention for Insomnia: Does Liking the Music Matter?

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Introduction: Insomnia is highly prevalent in today's society and music interventions have been shown to be effective for individuals with this condition. However, there are considerable inconsistencies between studies regarding size and certainty of the effects, and the contributing mechanisms have not yet been tested empirically. In music interventions for other purposes, such as pain and relaxation, the extent to which participants like the music has been identified as an important influence. Therefore, we hypothesised that higher ratings of liking the intervention music would be associated with greater improvement in insomnia symptoms following the intervention period.

Materials and methods: We pooled data from three randomised controlled trials investigating music as a treatment for poor sleep. In all studies, participants in the music group listened to the intervention music at bedtime each night for at least three weeks and completed the Insomnia Severity Index (ISI) at baseline and post-treatment. Music liking was rated post-treatment on a 5-point scale. While Studies 1 and 2 only involved individuals fulfilling the criteria for insomnia disorder (DSM-V), Study 3 included pregnant women with a complaint of poor sleep. We used a linear mixed-effects model to predict ISI improvement based on Time (post-treatment vs. baseline), Liking, and Study, with random intercepts for participants.

Results: In the pooled sample ($n = 69$), we observed a trend for the interaction between Time and Liking ($p = .07$), suggesting that participants who liked the music more experienced greater

improvement in ISI scores. Study was identified as a meaningful control variable. Due to the differing sample in Study 3, we conducted a subsample analysis including only Studies 1 and 2 ($n = 40$). In this subsample analysis, the Time $\times$ Liking interaction was significant ($p = .016$).

Conclusions: Our findings suggest that the degree to which subjects liked the intervention music influenced its effectiveness in improving insomnia symptoms, especially in clinically diagnosed individuals. Limitations include low variance in the liking ratings, as well as one subject exerting a strong influence on the model fit. Excluding this individual weakened significance levels, but the effects remained directionally stable. Our results highlight the potential benefits of allowing participants to select their most-liked music in clinical interventions for sleep and contribute to the ongoing debate about subject- vs. experimenter-chosen intervention music.

Neural basis of emotion dysregulation in insomnia disorder: A task-based fMRI study

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Introduction: Insomnia disorder (ID) is one of the most prevalent sleep disorders, affecting approximately 10% of the adult population. Beyond its hallmark nighttime difficulties with initiating or maintaining sleep, insomnia is increasingly recognized for its adverse consequences on daytime functioning, particularly in cognitive and emotional domains. Among these, deficits in emotion regulation have been consistently reported, implicating alterations in both behavioral and neurobiological systems. However, the neural mechanisms underlying the emotional dysregulation in ID remain poorly understood. Functional neuroimaging approaches offer critical insights into the brain circuitry involved in emotional regulation in this population.

Materials and methods: To investigate the neural correlates of emotion regulation in ID, we employed task-based functional magnetic resonance imaging (fMRI) in a sample of 19 patients diagnosed with insomnia disorder and 28 age- and sex-matched normal sleepers (NS). All participants completed standardized self-report measures assessing insomnia severity, anxiety, and depressive symptoms. During fMRI acquisition, participants performed an explicit emotion regulation task comprising three conditions: passive viewing of neutral pictures, passive viewing of negative pictures, and cognitive reappraisal of negative pictures. For each trial, participants were instructed either to observe the picture naturally or to reinterpret its meaning in a way that reduced its emotional impact, followed by a self-report of their current negative feelings. Brain activation patterns were analyzed using whole-brain approaches, focusing on areas previously implicated in emotion regulation.

Results: Behavioral performance data confirmed that all participants reported higher negative affect in response to negative pictures compared to neutral ones. Individuals with ID reported significantly greater negative responses during the reappraisal condition than NS controls, suggesting the impaired capacity to downregulate negative affect. Neuroimaging findings revealed that, relative to passive viewing of negative stimuli, the ID group exhibited significantly reduced activation during reappraisal in the sub-gyral region of the temporal lobe, the inferior frontal gyrus (IFG), and the right para-hippocampal gyrus compared to NS. These areas are known to support top-down cognitive control and contextual modulation of emotional responses.

Conclusions: Our findings provide convergent behavioral and neurobiological evidence for impaired emotion regulation in individuals with insomnia disorder. Specifically, hypoactivation in prefrontal and temporal-limbic regions during cognitive reappraisal suggests disrupted neural mechanisms underlying emotional processing. These results highlight the importance of targeting emotion regulation processes in the treatment of insomnia and indicate potential neural targets for intervention.

Novel Approach for Biologically-Guided Therapeutics in Insomnia

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Introduction: Sleep is a fundamental biological process whose disruption is implicated in neurodegenerative and psychiatric disorders. Despite the global burden of insomnia—12.5% of the population worldwide—current pharmacological treatments remain limited by suboptimal efficacy and adverse effects such as dependence and cognitive impairment. This therapeutic gap stems partly from a lack of mechanistic understanding of how brain activity is regulated across sleep stages and neural organizational levels. Defining sleep-related neural signatures—from single-cell to population dynamics—is expected to support the development of more precise, biologically-guided treatments. Importantly, current hypnotics, including benzodiazepines (e.g., diazepam) and non-benzodiazepine Z-drugs (e.g., zolpidem), differentially modulate GABAergic circuits, offering an opportunity to understand sleep control at a mechanistic level.

Materials and methods: To investigate the pharmacology of diazepam (a benzodiazepine) and zolpidem (a Z-drug) on sleep-dependent brain dynamics, we used 1) in vivo whole-cell patch-clamp recordings to measure subthreshold membrane potentials of layer 2/3 pyramidal neurons in the prefrontal of head-restrained mice across wakefulness, NREM, and REM sleep; 2) longitudinal single-cell calcium imaging in freely behaving mice to track the activity of genetically-defined neuronal populations from the hypothalamus and neocortex. Pharmacological interventions included systemic administration of diazepam (a benzodiazepine) and zolpidem (a Z-drug), along with local NMDAR antagonists to probe excitatory and inhibitory mechanisms underlying sleep regulation.

Results: At the single-cell level, we found that Diazepam reduced the depolarization of cortical neurons in the prefrontal cortex, possibly by enhancing GABAergic inhibition via parvalbumin (PV+) interneurons during NREM sleep. In contrast, Zolpidem, selectively acting at $\alpha 1$ -containing GABA-A receptors, induced a similar decreased of neuronal excitability in the prefrontal cortex, although with less impact on interneuron-driven inhibition, reflecting distinct circuit-level mechanisms. Interestingly, subthreshold depolarization was reduced during REM sleep as compared to NREM sleep and wake states, while the opposite was found in retrosplenial neurons, suggesting a region-specific modulation of excitability across sleep states.

At the population level, hypothalamic neurons displayed overlapping, state-dependent activity patterns rather than strict state selectivity. These distributions were stable across time, with minimal disruption by sleep deprivation. However, both Diazepam and Zolpidem modulated activity biases—Diazepam shifted cellular activity toward NREM sleep, while Zolpidem promoted rapid NREM initiation associated with a distinct neuronal activity signature, suggesting different pharmacodynamic mechanisms.

Conclusions: Our study reveals that despite a common GABA-A receptor pathway, Diazepam and Zolpidem influence sleep through divergent receptor selectivity and network recruitment. These findings emphasize a novel biologically driven approach for pre-clinical drug development based on single cell and network biomarkers relevant to the underlying neural dynamics of EEG signatures of sleep. Long-term perspectives include the development of predictive tools to improve drug development and personalized treatment of insomnia and other sleep disorders.

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Nurse-Led, App-Based Sleep Behavioral Treatment for Insomnia Among Survivors of Traumatic Brain Injury: A Randomized Controlled Trial

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Introduction: Insomnia is a common issue among individuals with traumatic brain injury (TBI), yet effective treatment options remain limited for this population. This study evaluated the effects of a nurse-led, app-based **Sleep Behavioral Treatment for Insomnia (SBTi)** in individuals with TBI.

Materials and methods: A parallel, three-arm randomized controlled trial was conducted between August 2022 and January 2025. Patients diagnosed with TBI for at least three months and experiencing insomnia symptoms for more than one month were recruited and randomly assigned to one of three groups: a 4-week face-to-face SBTi, an app-based SBTi, or a sleep hygiene control group. Sleep outcomes were assessed using the Insomnia Severity Index (ISI), sleep diary, and actigraphy. Measurements were taken at baseline (T0) and weekly at T1 (week 1), T2 (week 2), T3 (week 3), and T4 (week 4) of the treatment. Generalized Estimating Equation (GEE) models were used for data analysis.

Results: A total of 80 patients (mean age: 45.9 years) were included and randomly assigned to the face-to-face SBTi (n = 27), app-based SBTi (n = 27), or sleep hygiene control group (n = 26). Compared to the sleep hygiene group, both the face-to-face and app-based SBTi groups showed significantly lower ISI scores at T3 and T4 ($p < 0.05$). The face-to-face SBTi group had significantly shorter subjective and objective wake after sleep onset (WASO) at T4, while the app-based SBTi group showed shorter WASO at T1, T2, and T3 ($p < 0.05$). For both subjective and objective sleep efficiency (SE), significant improvements were observed in the face-to-face and app-based SBTi groups at T3 and T4 compared to baseline in the sleep hygiene group ($p < 0.05$).

Conclusions: Both face-to-face and app-based SBTi demonstrated significant improvements in sleep outcomes, supporting their effectiveness in managing insomnia in individuals with TBI.

One-month follow-up results of Patient-Reported Outcomes for LEMborexant treatment in Chinese patients with insomnia (PROEM): a multicenter, prospective, real-world observational study

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Introduction: Lemborexant (LEM) is a novel dual orexin receptor antagonist approved to treat adults with insomnia in the United States, Canada, Japan and some other countries. This first prospective study to assess LEM treatment for patients with insomnia in routine clinical practice in China was conducted under the "Hong Kong and Macao Medicine and Equipment Connect" policy. Recently, LEM has been approved to treat adult with insomnia in China.

Materials and methods: This 12-week, multicenter, prospective, real-world observational study (NCT06225947) enrolled 205 adult patients with insomnia who visited 1 of the 5 participating hospitals in Guangzhou, China from February 2024. All patients were treated with LEM as per routine clinical practice. The purpose of this interim report is to describe the efficacy and safety after 4 weeks treatment of LEM. The primary endpoint was the remitter rate after 4 weeks of treatment (the percentage of patients with a post-treatment Insomnia Severity Index [ISI] score of < 8). The responder rate (the percentage of patients whose ISI score decreased ≥ 6 points from baseline), mean changes in the ISI, Patient Health Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) scores from baseline were also determined. Treatment-emergent adverse events (TEAEs) were recorded.

Results: Through April 14, 2025, 167 patients had been taking LEM for ≥ 4 weeks, and 38 patients had withdrawn from the study. The full analysis set (FAS) included 200 patients, and the safety set included 205 patients. The FAS population had a mean age of 46.08 ± 14.56 years and 124 (62.0%) patients were female. Their mean duration of insomnia was 7.55 ± 8.66 years and mean baseline ISI score was 17.44 ± 4.45 . Ninety-one (45.5%) patients had comorbid anxiety (GAD-7 score ≥ 5) and 132 (66.0%) patients had comorbid depression (PHQ-9 score ≥ 5). Seventy-five (37.5%) and 44 (22.0%) patients had been taking benzodiazepine or non-benzodiazepine hypnotics, respectively. Forty-two (21.0%), 33 (16.5%) and 125 (62.5%) patients received LEM as initial monotherapy, switched to LEM, or added LEM to their existing hypnotic therapy, respectively. The remitter rate after 4 weeks of treatment was 30.5% (61/200), and the responder rates after 1, 2 and 4 weeks of treatment were 36.0% (72/200), 56.5% (100/177) and 60.4% (96/159), respectively. Patients who took LEM as initial monotherapy had a higher remitter rate (50.0% [21/42]) than those who switched to LEM (27.3% [9/33]) and those who

took it as add-on therapy (24.8% [31/125]) after 4 weeks of treatment. The mean ISI, PHQ-9 and GAD-7 scores all decreased significantly from baseline after 4 weeks of treatment (-7.17 ± 5.83 , $P < 0.001$; -2.63 ± 4.04 , $P < 0.001$; and -1.77 ± 3.80 , $P < 0.001$, respectively). Thirty-three (16.1%) patients reported treatment-related TEAEs, all of which were mild or moderate. Eight (3.9%) patients withdrew from the study due to TEAEs. The most common TEAEs were somnolence (11 [5.4%]) and dizziness (10 [4.9%]).

Conclusions: This first prospective study of LEM treatment in China demonstrated that LEM treatment was effective, safe and tolerable in treating Chinese adult patients with insomnia. LEM treatment also improved the patients' mood.

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Pathophysiological subtypes of paediatric insomnia based on familiar and clinical features

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Introduction: Pediatric insomnia is a multifaceted combination of biological, circadian, neurodevelopmental, and environmental variables. Recent studies have underscored the significance of genetic factors in childhood insomnia, elucidating how not only familial predisposition to insomnia plays a pivotal role, but also predisposition to other medical conditions (e.g., atopy, anemia, iron deficiency, psychiatric disorders, etc.). Various pathophysiological subtypes have been proposed based on clinical presentations of insomnia, reflecting specific sleep issues, pediatric disorders, and familial history. This study aims to delineate distinct clusters of clinical and familial features to ascertain whether specific familial predispositions are more commonly associated with particular pediatric insomnia phenotypes.

Materials and methods: We conducted a retrospective review of 424 medical records of children with insomnia admitted to the Child Neuropsychiatry Unit, Sant'Andrea Hospital, Rome, from January 2015 to October 2022. Demographic data, clinical features of insomnia, and medical and familial sleep histories were collected. Hierarchical and non-hierarchical cluster analyses were performed to identify the most representative model and to assess the stability and reproducibility of the clusters.

Results: Three reproducible and stable groups were identified, demonstrating significant differences ($p < 0.001$) in the frequency of various clinical and familial features. The first cluster ($n=144$) comprised children with insomnia onset post-weaning (10.4%) and medical histories of atopy (17.4%) or gastroesophageal reflux (12.5%). The second cluster ($n=119$) included children experiencing prolonged awakenings (29.4%), night terrors (24.4%), or sleepwalking (3.4%). The third cluster ($n=161$) consisted of children exhibiting restless sleep characterized by hyperactivity (63.4%) or symptoms of restless leg syndrome (RLS) (11.2%), with 51.6% experiencing delayed sleep onset and nocturnal awakenings. Regarding familial history, the first cluster had a high prevalence of allergies (87.5%), while the third cluster showed a predisposition to RLS (30.4%) and iron deficiency (75.2%).

Conclusions: Our findings support the existence of distinct pathophysiological subtypes within pediatric insomnia. We hypothesize that these insomnia subtypes may involve dysregulation of neurotransmitter systems implicated in sleep regulation, such as histamine, serotonin, and dopamine. Identification of these distinct phenotypes through meticulous medical and familial history-taking may inform personalized treatment strategies for pediatric insomnia, potentially revolutionizing current approaches to managing children's sleep disorders.

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Patient and Clinician Perspectives on Treating Perimenopausal Sleep Problems

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Introduction: Up to 60% of females experience transient perimenopausal sleep difficulties, and an estimated 30% develop chronic insomnia around the time of menopause. Patients seeking treatment for vasomotor symptoms report that improving sleep is their top priority when selecting among treatment choices. From the clinician's perspective, insomnia is one of the leading reasons for initiating therapy for menopausal symptoms. To inform an upcoming randomized clinical trial (RCT) comparing treatments for menopause-associated insomnia, we surveyed clinicians who treat midlife patients and individuals with current or past menopausal sleep difficulties about their treatment experiences and preferences.

Materials and methods: In April-May 2024, we used e-mails to colleagues and public social media posts to circulate two IRB-approved Qualtrics survey initiations: one geared toward clinicians (20 items) and the other aimed at individuals who may have experienced perimenopausal insomnia (17 items). Participants were not compensated, but the investigators donated \$1US to one of three participant-selected charities for each completed survey.

Results: Of those who initiated a survey, completion rates were 77.2% for clinicians (n=61 of 79) and 70.2% for perimenopausal individuals (n=92 of 131). Most clinicians were physicians (75%), and 56% specialized in internal medicine or family medicine; 92% identified as women, and 25% identified as historically underrepresented in medicine. Most perimenopausal persons identified as women, and one identified as gender non-conforming; 16% reported a racial/ethnic minority identity; 48% were perimenopausal, and 42% were postmenopausal. Perimenopausal insomnia was rated as a "moderate-to-severe problem" by 88.7% of perimenopausal people and 98.3% of clinicians. *Sleep hygiene*, *melatonin*, and *hormone replacement therapy* were the most common treatments used by those with perimenopausal insomnia, but only 18.6% reported that their symptoms were treated "fairly well-to-very well." Perimenopausal people identified the most important treatment goals as *not waking up at night*, *falling back to sleep quickly*, *feeling refreshed upon waking*, and *clearer thinking*. At least half of clinicians reported using the following treatment modalities with their patients: *sleep hygiene* (95%), *trazodone* (68%), *melatonin* (63%), *cognitive-behavioral therapy for insomnia* (62%), and *antidepressants such as venlafaxine* (51%). In terms of efficacy, clinicians ranked *sleep hygiene*, *hormone replacement therapy*, and *cognitive-behavioral therapy for insomnia* as the "treatments that work the best." With respect to our upcoming RCT for perimenopausal insomnia treatment, 75.3% of perimenopausal people reported they would be "somewhat-to-very likely" to participate, and 98% of clinicians reported that they would be "somewhat-to-very likely" to refer their patients. Among potential participants and clinicians, opposition to pharmacologic treatment was the main reason for lack of interest in the RCT.

Conclusions: In this convenience sample, perimenopausal insomnia was rated as an important problem by patients and clinicians. Most perimenopausal people reported experiencing insufficient treatment of their insomnia symptoms and identified the need to address sleep maintenance and daytime functioning as the top treatment targets. Sleep hygiene was the most common therapy used in both groups. Although hormone replacement therapy was identified as one of the most effective treatments by clinicians and potential patients, clinicians were more likely to prescribe medications that were ranked as less effective.

Performance of an Asian-modified STOP-BANG for Obstructive Sleep Apnea Screening in Patients with Insomnia

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Introduction: Identifying obstructive sleep apnea (OSA) in patients presenting primarily with insomnia is challenging, as these individuals may not report classical OSA symptoms and often describe fatigue rather than excessive daytime sleepiness. OSA prevalence is higher in this population, and there is a bidirectional relationship between OSA and insomnia. The STOP-BANG questionnaire, a validated screening tool that assesses snoring, tiredness, observed apneas, high blood pressure, BMI, age, neck circumference, and gender, is widely used in general and Western OSA populations. In Asian populations, unique craniofacial features and lower BMI thresholds may increase OSA risk at lower BMI

than in Western cohorts, prompting modified STOP-BANG cut-offs. However, evaluation of the STOP-BANG in an Asian insomnia clinic population remains limited. This study assessed whether an Asian-modified BMI cut-off improves STOP-BANG performance for OSA screening in this context.

Materials and methods: We retrospectively reviewed all diagnostic polysomnograms (PSGs) ordered by the Department of Psychiatry from January 1, 2015 to December 31, 2019 for adults referred for insomnia. STOP-BANG scores were retrospectively determined using standardized intake questionnaires and clinical records, applying two BMI cut-offs: ≥ 35 kg/m² (original) and ≥ 30 kg/m² (Asian-modified); all other criteria were unchanged. A score of ≥ 3 indicated high risk. OSA severity was classified using AASM 2013 criteria (3% desaturation/arousal), with primary analysis focused on detecting moderate-to-severe OSA (AHI ≥ 15).

Results: A total of 116 patients were included, with 84% Chinese, 4% Malay, 3% Indian, and 7% of other ethnicities; 59% were male. Of these, 39 (34%) had moderate-to-severe OSA. With a STOP-BANG score ≥ 3 , the original model (BMI ≥ 35) achieved a sensitivity of 89.7% (95% CI: 77.8-96.7), NPV 91.1% (CI: 80.5-97.2) and specificity of 53.2% (95% CI: 42.1-64.1) for moderate-to-severe OSA. The Asian-modified model (BMI ≥ 30) increased sensitivity to 94.9% (95% CI: 85.0-99.1) and NPV to 95.1% (95% CI: 85.7-99.2), while specificity was slightly lower at 50.6% (95% CI: 39.6-61.7). AUC was 0.741 (original) and 0.755 (Asian-modified).

Conclusions: STOP-BANG performed moderately well as a screening tool for moderate-to-severe OSA in Asian insomnia clinic patients. Adopting an Asian-specific BMI cut-off (≥ 30 kg/m²) increased sensitivity and NPV but at the cost of lower specificity, resulting in more false positives and potentially unnecessary PSG referrals. Given the relatively high prevalence of moderate/severe OSA in this population, routine use of STOP-BANG may facilitate case detection, but a negative result does not fully exclude OSA, especially in patients with atypical presentations. Limitations include the retrospective design, modest sample size, and predominantly Chinese cohort. STOP-BANG with an Asian-specific BMI cut-off may serve as a practical first-line screening tool for case-finding in insomnia clinics, although confirmatory testing remains warranted for high-risk patients. Future studies should validate these findings in broader Asian populations.

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Predicting Insomnia Symptoms Among Youth Using Multimodal Ecological Momentary Assessment

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Introduction: Insomnia is common among youth and often co-occurs with depression. Ecological momentary assessment (EMA), widely used for depression monitoring, may also offer a scalable, real-time method for identifying insomnia symptoms. This study explores the feasibility of using linguistic and acoustic features from a speech-based EMA to predict insomnia symptoms in youth.

Materials and methods: This is part of an ongoing study on depression detection using EMA, which recruited 328 Chinese youth aged 18-24 years from the community in Hong Kong. Structured Clinical Interview for DSM-5 (SCID-CV) was administered to assess lifetime diagnoses based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Results indicated that 23% of participants met criteria for a history of depression, while 17% of anxiety disorder(s). Of these, 300 participants completed a 7-day EMA, which included twice-daily voice recordings via Telegram, with a minimum compliance rate of 70% required for inclusion in the analysis. Acoustic features were extracted using Praat and openSMILE while transcripts were analysed by using the Linguistic Inquiry and Word Count (LIWC) tool. Insomnia symptoms were assessed by the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement, with scoring ≥ 1 classified as having insomnia symptoms. Machine learning models were developed using linguistic, acoustic, and combined feature sets.

Results: Among the 300 participants, 203 (mean age=20.66, SD=2.00, 74% female, 17% with lifetime history of depression) did not have insomnia symptoms while 97 (mean age=20.74, SD=2.09, 79% female, 38% with lifetime depression) had insomnia symptoms in the past week. No significant differences in age or gender were observed, but lifetime history of depression was significantly associated with having insomnia symptoms ($p<.01$). Logistic regression adjusting for sex, age, and lifetime depression diagnosis revealed significant associations between insomnia symptoms and both linguistic and acoustic features. Increased use of impersonal pronouns (OR=1.83, 95% CI: 1.22-2.75, $p<.01$), and sad-related words (OR=1.72, 95% CI: 1.13-2.61, $p=.01$) were significantly associated with having insomnia symptoms. Shorter and more uniform speech pauses are associated with a higher likelihood of having insomnia symptoms (mean pause duration: OR=0.19, 95% CI: 0.05-0.76, $p=.02$; mean pause variability OR=0.09, 95% CI: 0.01-0.69, $p=.02$). Among eight common machine learning algorithms tested, random forest using LIWC features performed the best (AUC=0.61, F1=0.61).

Conclusions: This study demonstrates that linguistic and acoustic features captured through an EMA can reveal potential markers of insomnia symptoms in youth. Linguistic features such as impersonal pronouns and sad-related words, along with acoustic markers like shorter and less varied speech pauses, were significantly associated with having insomnia symptoms. These findings suggest that subtle changes in language and speech patterns may reflect underlying sleep disturbances, potentially linked to emotional dysregulation, cognitive dysfunction and fatigue. Extracting insomnia-related signals from non-sleep-targeted voice data highlights the potential of EMA for broader symptom detection. Future studies should incorporate sleep-specific EMA items, longitudinal follow-ups, and subgroup analyses to enhance prediction.

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Prediction of treatment outcome on digital cognitive behavioural therapy for insomnia using machine learning and usage data

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Introduction: Digital cognitive behavioural therapy for insomnia (dCBT-I) is recognized as an accessible and scalable intervention for treating insomnia. However, its effectiveness depends on patient adherence. Machine learning (ML) holds potential for outcome prediction, as it is designed to optimize predictive accuracy. Unlike classical statistical methods, which aim to describe relationships between variables based on predefined assumptions, ML can capture complex, nonlinear, and individualized patterns in data. This study employs ML techniques to evaluate the accuracy of ML models in predicting remission after intervention.

Materials and methods: The study recruited 35 participants aged 18-25 years (Mean ISI Score $\pm$ SD:19.3 $\pm$ 2.97;60% Female) to use a 28-day dCBT-I app. They met the DSM-IV-TR criteria for insomnia disorder, with an Insomnia Severity Index (ISI) score of 15 or higher. Those were excluded if they had a history of sleep disorders (other than insomnia), mental disorders (other than depression and anxiety), intellectual disabilities, severe suicidality, current pharmacological treatment or structured psychotherapy, or had recently engaged in shift work or trans-meridian travel.

During the intervention, participants provided daily sleep diaries, and their usage data was automatically tracked. App usage features, including daily usage durations (e.g., time spent on an app page), usage patterns (e.g., mean and maximum daily usage), time spent on each page (e.g., latest review time on a given day), and noncontinuous use of the app (e.g., number of days between two discrete usage) were recorded.

The state-of-the-art ML algorithms were used to predict whether participants achieved a post-intervention ISI score below 8, indicating remission of insomnia. We applied five-fold cross-validation and grid search for hyperparameter tuning, used the Synthetic Minority Over-sampling Technique

(SMOTE) to address class imbalance, and evaluated model performance using the Receiver Operating Characteristic–Area Under the Curve (AUC). Statistical significance between models was assessed using the DeLong test. SHapley Additive exPlanations (SHAP) was used to identify the important factors contributing to the models' predictions.

Results: In the study, 9% of participants (n=3) dropped out, while 91% (n=32) completed the 28-day dCBT-I app. In the completer analysis, 81% of participants experienced reduced ISI score (Mean Pre ISI Score $\pm$ SD:19.41 $\pm$ 3.15, Mean Post ISI Score $\pm$ SD:11.94 $\pm$ 5.65, Cohen's d=1.69, p<.001). Across all predictive models, XGBoost achieved the highest performance to predict remission (AUC=0.88, F1=0.86; p<.001), significantly outperforming other models (p<.05). Furthermore, Feature Importance analysis revealed that noncontinuous use of the app was the most predictive factors for remission after intervention across all models. Those remitted from insomnia (<8) (Mean days $\pm$ SD:4.75 $\pm$ 6.85) had a shorter gap in noncontinuous use of the app compared with other participants (Mean days $\pm$ SD:7.08 $\pm$ 3.80, p=.02).

Conclusions: Our findings indicate that ML models with users' engagement and adherence data of dCBT-I can accurately predict treatment outcome. In addition, noncontinuous use of the app emerged as the most important factor influencing model performance in predicting remission of insomnia, highlighting the importance of fostering sustained participation and adherence in digital interventions.

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Predictors of Adherence to Digital CBT for Insomnia (dCBT-I) and Its Impact on Treatment Efficacy: A Large-Scale Real-World Analysis

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Introduction: While digital Cognitive Behavioral Therapy for Insomnia (dCBT-I) is a first-line treatment, variable adherence limits its real-world effectiveness. This study aimed to identify key determinants of dCBT-I adherence and quantify its prognostic value on clinical outcomes in a large patient cohort.

Materials and methods: We conducted a retrospective analysis of 3420 adults with DSM-5 insomnia treated with a dCBT-I mobile application between January 2017 and June 2024. Adherence was quantified using a novel, weighted scoring system based on engagement with core modules (sleep restriction, stimulus control, cognitive restructuring). Baseline demographic and clinical data, including the Pittsburgh Sleep Quality Index (PSQI), GAD-7, and PHQ-9, were collected. Multivariate logistic regression was used to identify independent predictors of high versus low adherence. Treatment response was defined as a $\geq 50\%$ reduction in the total PSQI score at an 8-week follow-up. Receiver Operating Characteristic (ROC) analysis was performed to evaluate the predictive power of the adherence score for achieving a positive treatment response.

Results: Multivariate logistic regression revealed that higher adherence was independently predicted by **older age** (≥ 40 vs. < 40 years; OR=2.85, 95% CI: 1.52-5.34, p=0.001), **higher education level** (College vs. Primary; OR=3.10, 95% CI: 1.61-5.96, p<0.001), **lower baseline anxiety** (per point on GAD-7; OR=0.88, 95% CI: 0.81-0.95, p=0.002), and **greater baseline insomnia severity** (per point on PSQI; OR=1.21, 95% CI: 1.05-1.40, p=0.008). The high-adherence group demonstrated a significantly greater mean reduction in PSQI scores at 8 weeks compared to the low-adherence group (**-8.5 $\pm$ 2.1 vs. -3.2 $\pm$ 1.8; p < .001**). The adherence score robustly predicted treatment response, with an Area Under the Curve (AUC) of **0.81** (95% CI: 0.75-0.87), a sensitivity of 78%, and a specificity of 75% at an optimal cut-off.

Conclusions: Adherence to dCBT-I is a powerful mediator of treatment success and is influenced by a distinct profile of demographic and clinical factors. Our findings suggest that an engagement-based adherence score can serve as a strong prognostic tool. This underscores the necessity of developing personalized, adaptive dCBT-I interventions that provide targeted support to at-risk populations (e.g., younger, less educated, highly anxious patients) to maximize engagement and improve clinical outcomes in real-world settings.

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Preliminary observations on insomnia phenotypes based on daily electroencephalography sleep monitoring in the natural sleeping environment

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Introduction: The most commonly used classification of insomnia phenotypes focuses on the distinction between objectively defined short (<6h) and normal/near-normal (≥6h) sleep duration in the presence of subjective sleep complaints. Despite the common night-to-night variability in insomnia symptoms, objective sleep measurement is often restricted to a single recording in artificial laboratory environments. Using one week of EEG monitoring in the natural sleeping environment, this study assessed: i) the temporal stability of insomnia phenotypes, ii) the relation between EEG and sleep diary estimates of sleep duration; and iii) factors linked to larger gaps between EEG-based and subjective estimates.

Materials and methods: Thirty-three adults (36.1±11.6 y.o.; 81.8% female) with insomnia disorder and depression symptoms underwent up to 7 days of home-based sleep monitoring with a portable EEG monitor (Muse-S, InteraXon) for objective measurement and the consensus sleep diary to document subjective perceptions. Sleep EEG was scored with a validated automated algorithm. To track intra- and inter-individual variability in phenotypes, each individual EEG recording was classified in short (<6h) versus normal/near-normal (≥6h) sleep duration.

Results: Preliminary results suggest that 29% of participants had unstable insomnia phenotypes across the week of EEG monitoring, having at least a quarter of the nights with sleep duration above 6 hours and at least a quarter of the nights below 6 hours. Conversely, 18% had more stable short sleep phenotype and 53% had more stable normal/near-normal phenotypes. Subjective sleep durations based on diaries ranged between values that were 6 hours shorter than objective EEG-based measures to 12 hours longer than EEG-based measures, with a distribution that was moderately positively skewed. Over one third of participants had a mixed profile, with some nights for which diary-based sleep duration was shorter than EEG-based sleep duration and other nights where diary-based sleep durations were longer than EEG-based values. Lower estimation of subjective sleep duration relative to EEG-based measures was associated with more frequent EEG-based awakenings ($r=-.27$, $p=.044$), higher amounts of N2 sleep ($r=-.30$, $p=.024$), and lower percentage of N3 sleep ($r=.29$, $p=.028$).

Conclusions: These preliminary observations highlight the potential fluidity of insomnia phenotypes for a considerable proportion of individuals with insomnia. This raises questions about defining phenotypes based on a single night or averages that may obscure intra-individual variability. Objective measures are needed to identify this phenotype and this study confirms that subjective estimates are not helpful in predicting this phenotype as they differ from objective estimations in either direction, i.e., underestimation, overestimation, or both, and are unstable across time. However, in individuals with shallower sleep, there is a tendency towards lower subjective sleep duration estimations relative to EEG-based measures. Further work in larger insomnia samples and quantified EEG analyses is required to assess the daily sleep EEG signature of insomnia phenotypes. These preliminary observations raise concerns about relying on a single night of EEG recording to characterise insomnia phenotypes and call for more research to determine the minimal number of recordings for reliable phenotyping.

Psychological Aspects of Sleep Disorders – Insomnia and Maladaptive Cognitions: Results of the Multicenter Study “How Does Russia Sleep? (SleepStudyRu)”

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Introduction: Insomnia is a prevalent sleep disorder with significant impacts on quality of life and mental health ([Porcheret K. et al., 2024](#)). Recent studies highlight the role of cognitive factors, such as rumination, reflection, and perfectionism, in the development and maintenance of insomnia ([N.K. Tang et al., 2023](#)). Additionally, anxiety and depression often accompany insomnia and may impact cognitive factors.

Materials and methods: A cross-sectional study was conducted within the multicenter project "How Russia Sleeps," involving 723 volunteers aged 18 to 65. Validated Russian-language scales were used: Insomnia Severity Index (ISI), Ruminative Responses Scale (RRS), Multidimensional Perfectionism Scale (MPS), Beck's Anxiety Inventory (BAI), Beck's Depression Inventory (BDI).

Results: Psychological Profile Characteristics of Individuals with Sleep Disorders

Findings:

- The Insomnia Severity Index (ISI) showed a significant positive correlation with level of depressive rumination ($p \leq 0.01$). A tendency toward repetitive, negatively toned thoughts focused on depressive symptoms was associated with more pronounced sleep disturbances. This aligns with the understanding of rumination as a potential risk factor for the chronicity of insomnia.
- A similarly strong positive correlation was identified between ISI scores and distressing thoughts ($p \leq 0.01$). The presence of cyclical, passive reflections on failures was linked to greater severity of insomnia symptoms.
- A significant positive correlation was also found between ISI scores and levels of reflection ($p \leq 0.01$). This suggests that even relatively constructive, goal-directed thinking related to problem-solving may be associated with difficulties in initiating and maintaining sleep.
- A significant positive correlation was observed between ISI scores and anxiety levels as measured by the Beck Anxiety Inventory ($p \leq 0.01$). Higher anxiety scores were associated with more severe sleep disturbances. This supports the contemporary psychophysiological model of insomnia, which considers anxious experiences as contributing factors to insomnia.
- ISI scores also demonstrated statistically significant positive correlations with various forms of perfectionism:
 - Self-oriented perfectionism ($p \leq 0.01$)
 - Other-oriented perfectionism ($p \leq 0.01$)
 - Socially prescribed perfectionism ($p \leq 0.01$)

Conclusions: Insomnia is significantly associated with cognitive and emotional factors, particularly rumination, distressing thoughts, reflection, anxiety, and depression.

Various forms of perfectionism (self-oriented, other-oriented, socially prescribed) showed significant positive correlations with the severity of insomnia symptoms, indicating a potential role of perfectionistic attitudes in the development and maintenance of sleep disturbances.

These findings underscore the importance of considering cognitive processes in the development of therapeutic interventions for individuals with insomnia, particularly within the framework of cognitive-behavioral therapy (CBT), including addressing rumination, anxious thoughts, and perfectionistic attitudes.

Real-world data on the abuse potential of medications for the treatment of insomnia

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Introduction: Insomnia disorder is a chronic medical condition that is estimated to affect 12% of adults. Although CBTi is recognized as an important first line therapy it can be challenging to access and implement, resulting in problems with compliance. As a result many individuals with insomnia disorder receive medication treatment, often for prolonged periods of time. The potential for abuse of hypnotics can prevent patients from accessing necessary medications to effectively treat insomnia as a chronic condition. This study examined the real-world abuse potential of approved and off-label medications used for the treatment of insomnia, employing data from the FDA Adverse Event Reporting System (FAERS) database.

Materials and methods: Data from 1 January 2014 to 31 March 2024 were retrieved from the FAERS database. We compared the occurrence of unsolicited reported drug abuse events defined via Standardized Medical Dictionary for Regulatory Activities (MedDRA) Queries SMQ). Drugs of interest included Schedule IV drugs (benzodiazepines, Z-drugs, dual orexin receptor antagonists [DORAs]) and non-scheduled drugs (trazodone, doxepin, ramelteon). Trazodone was selected for comparison as it is one of the most widely prescribed medications for insomnia in the US, despite it not being approved for this condition. Relevant reported adverse events denoting drug abuse were identified if they contained an event with any preferred terms (PTs) from the SMQ categories: drug abuse, dependence, and withdrawal (MedDRA v26.1), with a modified SMQ applied to exclude cases with PTs associated with overdose or suicidal behaviors. Only PT's with a frequency threshold > 1% in any drug group are reported. Trazodone and zolpidem were used as reference drugs for disproportionality as they are the most widely prescribed drugs for insomnia in the US. Reporting odds ratios (ROR) and proportional reporting ratios (PRR) were used as disproportionality measures.

Results: Rates of adverse event cases of abuse, dependence, and withdrawal retrieved were highest for benzodiazepines approved for any indication (27.7%), followed by benzodiazepines approved for insomnia (23.0%), trazodone (22.7%), doxepin (22.3%), Z-drugs (15.3%), ramelteon (8.0%), and DORAs (2.6%). DORAs were associated with a low ROR value relative to Z-drugs (ROR = 0.150; 95% CI [0.131, 0.171]), and to trazodone (ROR = 0.092; 95% CI [0.081, 0.105]). Similar results were obtained using the PRR to measure disproportionality.

Conclusions: This study identified significantly fewer reported cases of abuse, misuse, overdose, dependence and withdrawal for DORAs compared with drugs typically prescribed long term for insomnia treatment. This included benzodiazepines (both indicated for and used off label) as well as z-drugs. The DORA class had significantly lower odds of reporting for adverse events denoting drug abuse when compared with both the scheduled drug zolpidem and the non-scheduled drug trazodone. This suggests that categorization of DORAs as Schedule IV drugs may overstate their abuse potential.

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Real-World Treatment Patterns of Sleep Medications in the United States Veterans Affairs Health System

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Introduction: This study evaluated treatment patterns for select sleep medications in the Veterans Affairs Health System (VAHS) and the Centers for Medicare and Medicaid Services (CMS).

Materials and methods: We identified all patients aged ≥50 years with select sleep medication prescriptions in the merged VAHS and CMS databases (2020–2022). This age threshold was chosen to capture older adults who are more likely to experience chronic insomnia and may have greater exposure to polypharmacy. Clinical Practice Guidelines for pharmacological treatment of insomnia

define nonbenzodiazepines such as z-drugs as first-line. Other treatments may include the melatonin receptor agonist (ramelteon) or sedating antidepressants (trazodone, off label). The FDA has also approved three dual orexin receptor antagonists (DORAs), suvorexant, lemborexant, and daridorexant. These newer agents target the sleep-wake cycle differently by inhibiting the binding of orexin neuropeptides to their receptors, thereby reducing wakefulness. Frequency distributions of the select sleep drugs were examined. Data were descriptively analyzed to characterize prescription frequency, concurrent medication use, and changes over time. Patients were followed longitudinally within the 3-year window to assess treatment continuity and medication switches.

Results: Among Veterans using VA outpatient services (N=6,761,233), we identified 906,519 patients with ≥ 1 sleep drug prescribed during the 2020-2022 study period. Patients had a mean (SD) age of 65.2 (13.1) years at first prescription; 9.4% were women, 17.8% were Black/African American vs 71.1% White, and 6.7% were Hispanic vs 87.5% non-Hispanic. Overall, an estimated 2.6% were prescribed zolpidem, 0.7% temazepam, 0.28% eszopiclone, 0.12% ramelteon, 0.6% zaleplon, 0.5% suvorexant, 0.4% triazolam, 0.006 lemborexant, 0.005% estazolam, and 0.0001% daridorexant. Use of sedative antidepressants was prevalent (trazodone 10.4%; doxepin 0.9%). Over the 3-year period, most patients (89%) used a single sleep medication and 9.6% used 2 drugs. Melatonin supplements were prescribed in 46.2% of patients in conjunction with the other sleep medications.

Conclusions: The Z-drug zolpidem was the most commonly prescribed medication indicated for insomnia. Sedative antidepressants were also frequently utilized, likely due to their affordability and the lack of widely accepted, cost-effective alternatives for managing insomnia. This reliance on off-label agents such as trazodone suggests a potential gap between clinical guidelines and real-world practice, possibly reflecting formulary constraints, prescriber familiarity, or patient comorbidities. Lemborexant and daridorexant, more recently approved for insomnia, were prescribed less frequently and have not yet become mainstream frontline treatments. However, their novel dual orexin receptor antagonist mechanism provides a viable alternative therapeutic option for new users seeking effective insomnia management. Future research should examine whether newer agents gain broader adoption over time as prescribing trends respond to effectiveness, cost, and evolving treatment guidelines.

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Relation Between Individual and Neighborhood-Level Lifetime Stressor Exposure and Insomnia Symptoms

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Introduction: Introduction:

Insomnia is a prevalent disorder, impacting around 10% of adults worldwide. The link between insomnia and acute stressor exposure has been well-documented. However, less is known about the role that lifetime stressor exposure plays in the development and course of insomnia. Lifetime stressor exposure has been shown to contribute to the dysregulation of neuroendocrine, physiological, and psychological processes that directly impact sleep. Evidence on the impact of lifetime stressor exposure has focused primarily on individual-level stressors such as stressful life events. Less is known about the role that neighborhood-level stressors play in stress-related pathology, including insomnia. The current study aimed to investigate the association between both individual (self-reported life events) and neighborhood-level (objective markers of neighborhood deprivation) lifetime stressor exposure and insomnia symptoms.

Materials and methods: Data was collected from 143 participants (57% women, 38% White, 34% Latinx/Hispanic, 27% Black/African American, mean age = 19.83) from a university and surrounding community in the Mid-Southern region of the United States. Participants were asked to rate their insomnia symptoms using the Insomnia Severity Index (ISI) and individual-level stressor exposure using the Stress and Adversity Inventory (STRAIN). Total scores for ISI and total stressor count from the

STRAIN were used. Participants were also asked to provide a lifetime residential history which was linked the Area Deprivation Index (ADI) to create a composite score of neighborhood-level stressor exposure. A multiple linear regression was conducted with race, gender, and household income entered as covariates.

Results: Unadjusted analyses revealed a small, but significant effect of individual-level lifetime stressor exposure (total stressor count via STRAIN) on ISI scores ($b = 0.16$, $t(5,128) = -2.77$, $p < .05$). No significant effect of lifetime neighborhood-level stressor exposure on ISI was found. The main effect of individual-level stressor exposure remained significant in the adjusted analyses ($b = 0.16$, $t(5,120) = 3.06$, $p < .05$), even after controlling for race, gender, and household income.

Conclusions: Findings from the current study suggest that individual-level lifetime stressor exposure (e.g. stressful life events), but not neighborhood-level stressor exposure, is associated with the development and maintenance of insomnia. Future work would benefit from employing longitudinal designs to disentangle the mechanisms (e.g. stress-induced hyperarousal) by which this occurs to identify potential targets for prevention or early intervention.

Research Progress on the Role of Ferroptosis in Insomnia with Depression

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Introduction: Insomnia is a prevalent sleep disorder that not only impairs daily functioning but also significantly increases the risk of developing depression. Depression is a common chronic mental illness. Insomnia and depression often coexist as comorbidities. The commonly used antidepressant drugs have slow onset and are prone to relapse, so exploring new antidepressant targets and methods is a necessary process to address the current status of depression treatment. Iron death is a novel form of cell death discovered in recent years, and numerous studies have shown that iron death plays an important role in neurological and psychiatric disorders. Recent studies have also shown that ferroptosis may play an important role in the pathogenesis and treatment of insomnia with depression. This review analyzes and summarizes the role of ferroptosis in the pathogenesis and treatment of insomnia with depression, aiming to provide new ideas and possible targets for the treatment of insomnia with depression.

Materials and methods: This is a review article. The materials mainly come from numerous existing research studies on ferroptosis, insomnia, and depression. The methods involve a comprehensive analysis and summary of relevant literature to explore the role of ferroptosis in insomnia with depression.

Results: Inhibiting tsRNA - 3029b reduces neuronal ferroptosis in CUMS - model mice, improving depressive - like behaviors, indicating epigenetics' role in depression. Ferroptosis is involved in the antidepressant effects of resveratrol, melatonin, and ECT with etomidate. Resveratrol and melatonin improve depression by inhibiting ferroptosis, and etomidate may enhance ECT's effect by protecting neurons from ferroptosis.

Conclusions: Ferroptosis plays an important role in many neurological and psychiatric disorders, including schizophrenia, insomnia, Alzheimer's disease, Parkinson's disease, autism, epilepsy, and cerebral infarction. The impact of ferroptosis on neural plasticity and inflammation is crucial in the pathogenesis and treatment of insomnia with depression. Ferroptosis - related genes and pathways may serve as new therapeutic targets for depression.

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Resolving subjective emotional distress overnight: sleep diary data from a randomized controlled trial on Cognitive Behavioral Therapy for insomnia

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Introduction: The phrase "sleep on it" reflects a common experience: distress often feels less intense after a good night's sleep. Unfortunately, many people—especially those with mental disorders—struggle with poor sleep. 70% of individuals with mental disorders experience sleep complaints, which worsen symptoms and hinder treatment outcomes. REM sleep is believed to facilitate the overnight resolution of daily distress—but only if it is uninterrupted. Insomnia, characterized by fragmented REM sleep, may impair this process, preventing the natural overnight reduction of negative emotions. Cognitive Behavioral Therapy for Insomnia (CBT-I) is the first-line treatment for insomnia and has shown to improve both sleep and comorbid mental complaints such as depression and posttraumatic stress disorder. This Randomized Controlled Trial examines the effect of online guided iCBT-I (iSleep) on the overnight resolution of emotional distress in people with clinically relevant insomnia and anxiety complaints. By improving sleep, we expect participants that have received iCBT-I to: 1) experience less negative feelings in general; 2) experience more decrease in negative feelings overnight.

Materials and methods: Participants ($n = 149$, 106 females, $M_{age} = 54$) were randomized in either CBT-I group ($n = 76$) or active control (sleep diary only). At baseline, post-treatment, and 6-months follow-up, participants completed the Consensus Sleep Diary for one week, from which several sleep metrics were derived. In addition, to monitor overnight changes in mood, they filled out their level of depressed, anxious, and tense mood every evening and morning, on a 5-point Likert scale. Sleep quality rating (Likert 1-5) and WASO was used as a proxy for uninterrupted REM sleep. Data was analyzed using random intercept mixed linear models, with morning mood ratings as outcomes, and evening mood ratings as predictors to model the overnight mood change.

Results: In general, iCBT-I improved depressive and tense feelings at 6-months follow-up. Moreover, at 6-months follow-up, we found a significant effect of iCBT-I on the overnight resolution of depressive feelings (interaction effects of iCBT-I x timepoint: $b = -0.26$, $p = 0.046$), but not for anxiety and tenseness. Interestingly, this iCBT-I effect was stronger after more depressed evenings (significant interaction of evening depressive feelings x iCBT-I x timepoint T2: $b = 0.32$, $p = 0.005$). Analyses separating within- vs. between subject effects showed that this is solely a within-subject effect, indicating that iCBT-I has a stronger effect on the more depressed evenings within a person. Across groups, the overnight resolution of all negative feelings was highly dependent on sleep quality ($b = -0.22$ to -0.12 , all $p < 0.001$) and WASO ($b = 0.001$ to 0.002 , all $p < 0.012$).

Conclusions: This suggests that iCBT-I improves the overnight resolution of depressive feelings in individuals with insomnia and anxiety complaints, especially after evenings when they felt most depressed. Moreover, only during nights of experienced good sleep quality, negative emotions can dissolve. Both findings highlight the fundamental role of sleep on emotional processing, and the importance of treating insomnia for good mental wellbeing.

Trial registration: International Clinical Trial Registry Platform (NL9776). Registered on 2021-10-07.

Restless Minds in Restless Nights: Insomnia and Mental Health in Medical Residents with ADHD

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Introduction: Insomnia is a prevalent and impairing symptom among medical professionals, particularly during specialty training. Its potential impact on functioning and well-being may be particularly high in individuals with comorbid ADHD. This study aims to explore the prevalence of insomnia in this population and its association with psychiatric comorbidities, ADHD symptoms, stimulant use, and training-related variables.

Materials and methods: We conducted a cross-sectional, anonymous online survey targeting medical residents in Portugal. The survey assessed sociodemographic data, presence of insomnia, psychiatric comorbidities, ADHD symptoms (6-item frequency-based scale), and stimulant use. Statistical analyses

included chi-square and Mann-Whitney U tests to examine associations between insomnia and key clinical and training variables.

Results: Out of 191 complete responses, 20 participants (10.5%) reported a diagnosis of insomnia. Insomnia was significantly associated with the presence of other psychiatric comorbidities ($p < 0.0001$), particularly anxiety ($p = 0.0016$) and depression ($p = 0.0022$). Although no specific rare comorbidity (e.g., bipolar disorder, OCD, autism spectrum disorder) showed significant associations individually, participants with insomnia had a markedly higher total burden of psychiatric diagnoses (median = 3 vs. 0; $p < 0.000000001$). No association was found between insomnia and total ADHD symptom scores or stimulant use. However, stimulant use was significantly associated with increased nocturnal restlessness ($p < 0.001$), a possible subclinical sleep-related manifestation. A non-significant trend was observed between insomnia and more advanced years of residency ($p = 0.090$).

Conclusions: Insomnia in medical residents is strongly associated with psychiatric comorbidity burden, particularly anxiety and depression. While not directly related to ADHD symptoms or stimulant use, restlessness in stimulant users may reflect subtle sleep disruption. These findings suggest insomnia as a clinical marker of psychological vulnerability in this population, with potential implications for mental health screening and support strategies during specialty training.

Rumination and Pre-sleep Arousal: The mediation role of attentional styles in adults with insomnia disorders

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Introduction: Rumination, as a cognitive activity, is a well-recognised risk factor of insomnia by triggering arousal and attention bias towards sleep-related threats. Previous studies suggested that individuals who ruminate at a higher level tend to have higher level of arousal before sleep and longer sleep-onset latency. Besides, both negative and positive information can induce arousal state and may impact sleep. However, there is limited evidence exploring how attentional styles for positive or negative information influence the association between rumination and arousal. The current study aims to investigate the potential mediating role of cognitive tendency focusing on positive or negative information between rumination and pre-sleep arousal.

Materials and methods: This was a cross-sectional study of the Hong Kong community-based sleep project. A total of 218 adults (mean age: 45.72 yrs $\pm$ 14.93; females: 76.6%) who met the DSM-V diagnostic criteria for insomnia disorder completed a battery of questionnaires including Pre-Sleep Arousal Scale (PSAS), Ruminative Response Scale (RRS) and Attention to Positive and Negative Information Scale (APNIS) for assessing hyperarousal before sleep, tendency to ruminate and cognitive tendency of focusing on positive (API) or negative information (ANI), respectively. Linear regression analysis was used to evaluate the association between rumination, attentional bias and pre-sleep arousal. Mediation analysis was performed to evaluate the influence of API/ANI on the association between rumination and pre-sleep arousal. Potential confounders included age, gender, education level and mental disorders were included as covariates in the analyses.

Results: The results indicated that women ($M=22.51$, $SD=6.11$) had a higher level of pre-sleep cognitive arousal than men ($M=20.47$, $SD=5.36$), $t(216)=2.13$, $p=0.03$. Regression analysis indicated that a greater tendency to engage in rumination and ANI was associated with both pre-sleep cognitive arousal (rumination: $B=0.27$, $SE=0.03$, 95% $CI=0.21-0.33$, $p<0.001$; ANI: $B=0.42$, $SE=0.07$, 95% $CI=0.29-0.55$, $p<0.001$) and somatic arousal (rumination: $B=0.23$, $SE=0.03$, 95% $CI=0.18-0.29$, $p<0.001$; ANI: $B=0.27$, $SE=0.06$, 95% $CI=0.15-0.38$, $p<0.001$). Rumination was positively associated with ANI ($B=0.25$, $SE=0.03$, 95% $CI=0.19-0.31$, $p<0.001$). Mediation analysis indicated that ANI partially mediated the association between rumination and pre-sleep cognitive arousal. The indirect effect from rumination to pre-sleep cognitive arousal through ANI was significant ($B=0.05$, $SE=0.02$, 95% $CI=0.02-0.10$), as well as the direct effect of rumination on pre-sleep cognitive arousal ($B=0.22$, $SE=0.04$, 95% $CI=0.14-0.29$, $p<0.001$), indicating that the relationship between rumination and pre-sleep cognitive arousal is

partially mediated by ANI. However, the indirect effect from rumination to pre-sleep somatic arousal through ANI was not significant. While for API, it did not play a role in the association between rumination and pre-sleep cognitive/somatic arousal.

Conclusions: The current findings revealed that a greater tendency to engage in rumination and predisposition to negative information could be risk factors that trigger cognitive arousal before sleep among people with insomnia. This suggests that interventions targeting reducing rumination and biased attention towards negative information could potentially help to reduce cognitive arousal and improve overall sleep quality.

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Safety and Efficacy of Lemborexant in Indian Adult Patients with Insomnia: A Phase 4, Prospective, Multicenter, Real-World Study

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Introduction: Insomnia is characterized by difficulties with onset, and/or maintenance of sleep, and early morning awakening, causing impairment of daily activities. Lemborexant (LEM), a dual orexin receptor antagonist, is approved in several countries, including the US and India, for the treatment of adult patients with insomnia. This post-marketing surveillance study evaluated the safety, tolerability, and efficacy of LEM in Indian patients.

Materials and methods: Adults aged between 18-65 years with a clinical diagnosis of insomnia were enrolled in the study and treated with LEM 5 or 10 mg as per the investigator's discretion. The study consisted of a screening period and a 6-month treatment period. The primary endpoint included assessment of safety in terms of the incidence of treatment-emergent adverse events (TEAEs) and discontinuations due to TEAEs. Efficacy was assessed using the Patient Global Impression – Insomnia (PGI-I) questionnaire. The data were summarized descriptively using SAS® Enterprise Guide® 7.1.

Results: In total, 110 patients were enrolled in this study. The mean ($\pm$ SD) age of patients was 45.27 $\pm$ 11.04 years, and most patients (56.3%) were males. The patients were treated with a dose of LEM 5 mg (n=106) or LEM 10 mg (n=4), and 103 patients received ≥ 1 dose of study drug. Overall, 39 (37.86%) patients experienced ≥ 1 TEAE, including 38 patients in the LEM 5 mg cohort and 1 patient in the LEM 10 mg cohort without any serious TEAEs. Among these, 13 (12.62%) patients reported TEAEs related to the study drug, including 12 patients in the LEM 5 mg and 1 patient in the LEM 10 mg cohort. The most frequently occurring TEAEs were headache (9 [8.74%]), somnolence (8 [7.77%]), pyrexia (6 [5.83%]), dizziness (5 [4.85%]), head discomfort, and cough (4 [3.88%], for each). Most TEAEs were of mild (27 [26.21%]) intensity, followed by moderate (10 [9.71%]) intensity, and only 2 (1.94%) patients reported severe TEAEs. A dose-dependent increase in the percentage of patients was observed, reporting "positive medication effect" at the end of 1 month (56.31%, 58/103 patients; LEM 5 mg group: 55/99 patients and LEM 10 mg group: 3/4 patients), 3 months (68.93%, 71/103 patients; LEM 5 mg group: 67/99 patients and LEM 10 mg group: 4/4 patients) and 6 months (72.82%, 75/103 patients; LEM 5 mg group: 71/99 patients and LEM 10 mg group: 3/4 patients) of treatment. A similar trend was observed for patients who reported that the study medication decreased time to fall asleep at the end of 1 month (59.22%, 61/103), 3 months (73.79%, 76/103), and 6 months (77.67%, 80/103) of the treatment. LEM increased total sleep time in 66.02% (68/103), 72.82% (75/103), and 79.1% (82/103) of patients at the end of 1 month, 3 months, and 6 months of treatment, respectively. Around 84.5% of patients mentioned that the strength of LEM prescribed was appropriate.

Conclusions: The current study provides real-world safety, tolerability, and efficacy data, showing that LEM treatment effectively addresses both sleep onset and sleep maintenance difficulties.

Sleep and cardiovascular parameters in women with different insomnia phenotypes: a cross-sectional study from EPISONO

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Introduction: Insomnia is twice as prevalent in women as in men. The repercussions of insomnia in women might be intensified by menopause, when female sexual hormones are low. It is well known that the cardiovascular risk in women is increased after menopause becoming similar to that observed in men; however, few studies have comprised the different phenotypes of insomnia in women before and after menopause. **Aims:** Investigate the sleep parameters of the polysomnography and cardiovascular factors in women with different phenotypes of insomnia in a Brazilian cohort.

Materials and methods: A total of 236 women (44.4±14.3 years, 37% on menopause) of the São Paulo Epidemiologic Sleep Study (EPISONO) 4th edition conducted in 2018 from São Paulo city, Brazil, were included in this study. They responded to an institutional women questionnaire to acquire information about menstrual cycle and menopause symptoms. The DSM-V was used to distribute participants with insomnia, according to the criteria of difficulty to initiate or maintain sleep, or wake up too early, accompanied by repercussions in daily routine. Full night polysomnography was used to obtain the total sleep duration (TSD) and other sleep parameters of the participants. Participants with insomnia were then distributed in 2 groups: insomnia with short sleep duration (when TSD was <6 hours - ISSD) and insomnia with normal sleep duration (when TSD was >6 hours - INSD). Women without insomnia were distributed in 2 groups: with TSD >6 hours (control) and with TSD <6 hours (sleep restricted). Sleep and cardiovascular parameters (total cholesterol and fractions, homocysteine, blood pressure) were evaluated for each group, controlling for age, body mass index and menopausal status.

Results: Our findings demonstrated that sleep efficiency was significantly lower in ISSD group compared to all the other groups. Sleep latency was significantly increased in ISSD compared to INSD and the control with TSD>6h groups. REM sleep was statistically decreased in ISSD and sleep restricted groups compared to control. Systolic and diastolic blood pressures were higher in ISSD and sleep restricted groups compared to INSD. Participants on menopause presented worse results compared to premenopausal condition in wake after sleep onset, sleep efficiency, wake duration, homocysteine levels, and total cholesterol and fractions.

Conclusions: Alterations in sleep efficiency were associated with insomnia, whereas sleep restriction with or without insomnia was related to REM sleep and higher blood pressure. Cardiovascular parameters were negatively associated with menopause, confirming the protective effect of female sexual hormones on cardiovascular risk.

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Sleep and Subsequent Mental Disorders in Young Adults: A National Prospective Diagnostic Study

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Introduction: Sleep disturbances are common among young adults and may represent a key risk factor for developing mental disorders. While prior research has established links between insomnia and depression, most studies have relied on screening tools, lacked diagnostic precision, or failed to distinguish among types of anxiety disorders. This study prospectively examined the associations between insomnia, sleep characteristics, and DSM-5 mental disorders over one year in a large national student cohort.

Materials and methods: This prospective cohort study linked data from the 2022 wave of the Students' Health and Wellbeing Study (SHoT) with follow-up diagnostic assessments using the Composite

International Diagnostic Interview (CIDI 5.0) in 2023. Participants were full-time Norwegian students aged 18–35 ($N = 53,362$), of whom 10,460 completed at least one CIDI diagnostic module. Sleep parameters in 2022 included insomnia (operationalized using DSM-5 criteria), sleep duration, sleep onset latency (SOL), and wake after sleep onset (WASO). Mental disorders assessed in 2023 included major depressive episode (MDE), generalized anxiety disorder (GAD), panic disorder, agoraphobia, specific phobia, and social anxiety disorder. Multivariable log-binomial regression models estimated relative risks (RR), adjusting for age, sex, baseline mental health (HSCL-25), delayed sleep-wake phase disorder (DSWPD), hypnotic medication use, and somatic illness.

Results:

Students with insomnia in 2022 had significantly increased risk of MDE ($RR = 3.50$; 95% CI: 3.18–3.84) and GAD ($RR = 2.82$; 95% CI: 2.55–3.12) in 2023. Elevated risks were also observed for panic disorder ($RR = 2.66$), agoraphobia ($RR = 2.61$), social anxiety disorder ($RR = 2.23$), and specific phobia ($RR = 1.88$). Short sleep duration showed a reversed J-shaped association with mental health: students sleeping <5 hours had the highest risk for MDE ($RR = 3.28$) and GAD ($RR = 2.85$), with elevated risks also observed for 5–6 and 6–7 hour sleepers. Long sleep duration (>9 hours) was also linked to increased risk, though to a lesser extent. Longer sleep onset latency and greater WASO showed robust, graded associations with subsequent mental disorders. For example, students with $SOL \geq 120$ minutes had a 5.66-fold increased risk of MDE compared to those with $SOL < 15$ minutes. Similar dose-response patterns were seen for GAD, panic disorder, and social anxiety disorder. After adjusting for baseline symptoms and covariates, these associations remained significant, though attenuated, indicating the independent predictive value of poor sleep on future mental health.

Conclusions: This study provides strong prospective evidence that sleep disturbances—including insomnia, short or long sleep duration, long SOL, and increased WASO—predict a range of DSM-5 mental disorders in young adults. The findings underscore the importance of early detection and intervention for sleep problems to prevent the development of depression and anxiety. Sleep should be prioritized in student mental health strategies as both a transdiagnostic risk factor and a potential intervention target.

Sleep Architecture and Neurocognitive Performance in Insomnia Comorbid Obstructive Sleep Apnea Patients

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Introduction: Insomnia and obstructive sleep apnea (OSA) are the two most prevalent sleep disorders. Approximately 30% of individuals with insomnia also meet the diagnostic criteria for OSA, forming a comorbid condition known as Comorbid Insomnia and Sleep Apnea (COMISA). This co-occurrence could lead to elevated risk of disrupted nocturnal sleep, impaired daytime and cognitive function compared to the individual condition. However, few have examined the negative consequences of COMISA using objective cognitive measures. This study aimed to examine the differences in sleep architecture and neurocognitive functions between COMISA and insomnia-only patients, and to investigate whether COMISA is associated with greater sleep and cognitive impairment.

Materials and methods: Participants who met DSM-V criteria for chronic insomnia were included in this study. All participants underwent one night of home-based polysomnography (PSG) and performed a battery of neurocognitive tests including Psychomotor Vigilance Task (PVT), Balloon Analogue Risk Task (BART), Go/No-Go, and N-back tasks (0-, 1-, and 2-back) to assess vigilance, impulse control, and working memory, respectively. OSA was defined as an apnea-hypopnea index (AHI) ≥ 15 events/hour. Daytime sleepiness and fatigue were assessed using the Epworth Sleepiness Scale and the Multidimensional Fatigue Inventory. Group comparisons between COMISA and insomnia-only participants were conducted using independent t-tests or Mann-Whitney U tests, wherever appropriate. Mean reaction time for the PVT, Go/No-Go, and N-back were further analyzed using generalized linear models with a gamma distribution and log link, adjusting for age, gender, and BMI.

Results: A total of 147 adults (mean age: 46.2 ± 14.81 years, males: 21.77%) were recruited in Hong Kong. Thirty participants were classified as COMISA and 117 as Insomnia-only. Compared to the insomnia-only group, COMISA participants were older, had higher BMI, were more likely to be male, and reported significantly greater daytime sleepiness (12.30 ± 3.99 vs. 10.15 ± 4.49 ; $P = 0.018$) but not daytime fatigue. PSG-derived data revealed that the COMISA group had significantly higher oxygen desaturation index, total arousal count, and REM arousal index ($P < 0.005$), but no differences in total sleep time, sleep onset latency, sleep efficiency, or wake after sleep onset. For the neurocognitive performance, COMISA participants exhibited slower reaction time on the PVT (459.02 ± 163.95 vs. 397.64 ± 95.32 ms; $P = 0.047$), Go/No-Go (522.52 ± 74.67 vs. 473.35 ± 71.56 ms; $P = 0.001$), and N-back (570.84 ± 65.46 vs. 528.56 ± 83.85 ms; $P = 0.004$) tasks, with no group differences in error rates. After adjusting for age, gender, and BMI, COMISA participants showed longer mean reaction time on both the 1-back ($B = 0.077$, 95% CI: 0.015–0.139; $P = 0.016$) and 2-back ($B = 0.083$, 95% CI: 0.016–0.150; $P = 0.015$) conditions.

Conclusions: Individuals with COMISA reported greater daytime sleepiness but not higher levels of fatigue compared to those with insomnia alone. Although there was no difference in sleep architecture, COMISA exhibited impairments in vigilance and attention, particularly under higher cognitive load. These findings highlight the need for targeted screening and cognitive monitoring in this high-risk subgroup.

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Sleep Architecture and REM Sleep Without Atonia in Post-COVID-19 Insomnia

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Introduction: Insomnia associated with COVID-19 infection is a common complaint in long-COVID. Studies to date have predominantly examined post-COVID-19 sleep disturbances with questionnaires. We aimed to investigate whether there are distinctive polysomnographic findings in post-COVID-19 insomnia compared to non-COVID-related chronic insomnia.

Materials and methods: We included 150 patients with chronic insomnia, stratified into three groups: post-COVID-19 insomnia, chronic insomnia during the pandemic without a history of COVID-19 infection, and pre-pandemic chronic insomnia. All patients underwent one-night video polysomnography (v-PSG). The sleep architecture, respiratory variables and REM sleep without atonia (RWA) were compared across the groups.

Results: Classical polysomnographic variables showed no significant differences across groups with regard to total sleep time, sleep efficiency, sleep stage percentages, and the apnea-hypopnea index. Post-COVID-19 insomnia patients had significantly increased RWA at both the chin and the flexor digitorum superficialis (FDS) ($p = 0.020$ for both), and higher nocturnal heart rates ($p = 0.046$). Sleep-bout analysis indicated shorter sustained N3-sleep periods ($p = 0.001$) and longer onset to stable REM-sleep ($p = 0.016$) in the post-COVID-19 insomnia group. Although sleep transitions did not withstand multiple comparison corrections, they revealed a trend towards decreased N3-sleep continuity and increased probabilities of transitioning to lighter stages (N3→N3: unadjusted- $p = 0.012$; REM→N1: unadjusted- $p = 0.027$) in the post-COVID-19 insomnia.

Conclusions: Classical PSG profile of post-COVID-19 insomnia does not differ from non-COVID-related chronic insomnia. However, subtle differences in RWA and sleep integrity suggest that post-COVID-19 insomnia is driven not merely by pandemic-related stress factors but by additional physiological alterations linked to viral CNS involvement.

Sleep Diary Entry Time can be a Predictive Marker for Digital CBT-I outcome: Post-hoc Analysis from Two Digital CBT-I Trials

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Introduction: Digital Cognitive Behavioral Therapy for Insomnia (dCBT-I) have the potential for personalized and tailored therapy. WELT-IP is an dCBT-I designed to improve insomnia symptoms remotely through mobile application. Data such as sleep diary entry time, recommended time-in-bed (r-TIB) compliance, and lesson compliance are collected to create database for future algorithms. These data could be predictive markers used to tailor personalized user experience (UX), especially on the first week of usage.

Materials and methods: Eligible participants were adults (19-65) with a primary diagnosis of chronic insomnia (DSM-5). Major assessments such as Insomnia Severity Index (ISI) were performed at baseline and post-treatment (7-weeks). Daily sleep diary was collected using a participant-recorded electronic diary via WELT-IP for at least 7 weeks. The post-hoc analysis of two pivotal trials (n=120) was performed using the initial seven sleep diaries. Sleep diary entry time was recorded at the minute level, and the average time of [entry time - time out of bed] was calculated for the initial seven sleep diaries.

Results: A total of 55 (full analysis data set of WELT-IP group) participant data was included in the analysis. Multivariate regression was used to analyze the strength of the relationship between the predictor and response. The improvement of ISI was used as response. Diary entry time had correlation of 0.41 (R² value) with $p < 0.0001$. As the patient enters the sleep diary 0.08 seconds earlier, endpoint ISI decreased by 1 unit ($p < 0.0001$).

Conclusions: This analysis shows some new insights into potential predictive markers of dCBT-I based on user's data input patterns and compliance. First week's sleep diary entry time can be a predictive marker for dCBT-I outcome. Specifically, the more the participant showed willingness in completing sleep diary right after awakening, the higher the correlation for increase in ISI. This can be utilized in designing patient experience in the first few weeks of app which could induce increased patient outcome.

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Sleep features and cognitive arousal in relation to insomnia and depression among adolescents – A case-control study

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Introduction: Insomnia and depression often coexist and are both common in adolescents. Previous studies have primarily examined sleep characteristics and pathophysiology separately for insomnia and depression in the adult population. Evidence has shown an association of cognitive hyperarousal with insomnia and depression, respectively. However, little is known about sleep alterations and underlying mechanisms in insomnia and depression, as well as their comorbidity among adolescents. The current study examined sleep characteristics and cognitive arousal in relation to insomnia and depression in adolescents.

Materials and methods: A total of 117 adolescents (mean age: 17.3 years, SD = 2.0, 55.0% female), including 29 adolescents with comorbid insomnia and depression (CO), 28 with insomnia alone (ID), 28 with depression alone (DD), and 32 healthy controls (HC) were recruited. DSM-5 criteria were used to determine depression and insomnia. All participants underwent a clinical interview to ascertain their eligibility and completed self-report questionnaires to assess insomnia, depression, depressive rumination as measured by the Ruminative Response Scale (RRS), sleep-focused rumination as measured by the Daytime Insomnia Symptom Response Scale (DISRS), pre-sleep somatic and cognitive arousal, as measured by the Pre-sleep Arousal Scale, 7-day wrist actigraphy and Sleep Diary, and a two-night laboratory-based polysomnographic assessment, with the first night serving as the adaptation night.

Results: Compared to HC, CO and DD showed higher levels of depressive rumination, sleep-focused rumination, and pre-sleep somatic and cognitive arousal, and ID only showed higher levels of sleep-focused rumination, and pre-sleep somatic and cognitive arousal. Compared to the ID group, those in the CO group showed elevated levels of depressive and sleep-focused rumination and pre-sleep

cognitive and somatic arousal. Additionally, DD group showed a higher level of depressive rumination than ID group, and a lower level of pre-sleep cognitive arousal than the CO group. In terms of subjective sleep parameters as measured by sleep diary, DD group reported shorter total sleep time (TST) than HC group, while ID group reported longer sleep onset latency (SOL) than HC and those with DD. Similarly, CO group reported longer SOL than HC and DD. In terms of objective sleep parameters measured by actigraphy, adolescents with ID exhibited longer SOL than those with DD. For objective sleep parameters measured by polysomnography, participants with DD exhibited shorter SOL than healthy controls. There were no significant differences in other macro-sleep features and REM-related variables across groups.

Conclusions: Insomnia is manifested with prolonged subjective and objective SOL and elevated sleep-focused rumination, while depression is associated with shorter subjective TST with elevated depressive rumination, and the comorbidity of insomnia and depression is linked to prolonged subjective SOL with elevated pre-sleep arousal and rumination. Tailored intervention strategies that address these factors may improve treatment outcomes for the respective groups.

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Sleep psychoeducation strategies for patients with chronic migraine and sleep quality complaints

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Introduction: Chronic migraine is a prevalent and debilitating condition, significantly associated with sleep disorders, particularly insomnia. Given the importance of the topic and the increasing use of non-pharmacological approaches in treating insomnia, this study aimed to evaluate the impact of sleep psychoeducation measures on the clinical aspects of migraine in chronic migraine sufferers with sleep quality complaints.

Materials and methods: Patients from the headache outpatient clinic of the Neurology Service at CHC-UFPR were screened using a standardized questionnaire developed by the service. The intervention group included 68 chronic migraine sufferers with sleep disturbance complaints, who answered the following questionnaires: Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Insomnia Severity Index (ISI). A detailed history of sleep-related habits was taken, and sleep psychoeducation guidelines were provided, supported by an informative booklet with key recommendations, where specific guidelines for each patient were noted. The control group consisted of 32 chronic migraine patients with no complaints of sleep disorders. In a third phase, two to three months after the intervention, the scales and questionnaires were reapplied, and data from medical records were collected to assess changes in the intensity and frequency of migraine and sleep quality.

Results: showed that in the control group, there was no statistically significant variation in the frequency and intensity of headaches. However, in the intervention group, there was a statistically significant reduction in both the intensity and frequency of pain. Regarding clinical characteristics of sleep disturbance, the intervention group showed a statistically significant reduction in the PSQI (from an average of 13.7 to 11.7) and the ISI (from 18.5 to 13.4), but there was no statistically significant variation in the ESS.

Conclusions: Sleep psychoeducation, supported by an informative booklet, led to positive results not only in sleep but also in the reduction of the intensity and frequency of headaches in chronic migraine sufferers.

Sleep-Related Symptoms and Fatigue in Children with Long-Covid: Analyses of the RECOVER Longitudinal Cohort Study

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Introduction: Sleep disturbance is highly prevalent in individuals diagnosed with post acute sequelae after SARS-CoV-2 COVID19 (PASC) or long COVID (LC). The NIH-funded RECOVER-pediatric cohort longitudinally follows children and adolescents who have and have not been infected with SARS-CoV-2 including identifying those with probable LC. Participants ages 0-25 years have been enrolled from >100 sites across the country. In this sub-analysis, we seek to answer the following research questions: What is the precise phenotype of sleep disturbance in children with LC? and what individual characteristics predict LC-related sleep disturbance?

Materials and methods: In RECOVER, parents reported sleep-related symptoms among children and adolescents at enrollment. Measures included: composite sleep duration, trouble sleeping, nightmares, feeling sleepy and feeling tired. Logistic regression models were conducted to examine insomnia (e.g. trouble falling or staying asleep), hypersomnia (e.g. daytime tiredness), mixed type (insomnia and hypersomnia) and sleep duration based on status (uninfected, LC probable, LC unspecified). Analyses were stratified by age group (middle childhood, adolescent). Models were adjusted for sex, race, rural, and medically underserved. Healthy vs. unhealthy sleep was defined based on children who met the recommended hours of sleep by age.

Results: The study sample was nearly evenly split in gender across all age groups, and about half of the sample was white. Approximately one-third of the sample was medically underserved. Compared to uninfected, participants with probable LC had higher odds of insomnia and hypersomnia across both age groups compared to the uninfected groups, with significant differences in mixed sleep among adolescents only. Fully adjusted logistic regression models demonstrate higher odds of insomnia in middle childhood (aOR 31.4 (95%CI 9.49- 125) and adolescents (aOR 28.6 (95%CI 18.8- 44.1) among LC-probable compared to the uninfected reference group; and hypersomnia 31.5 aOR (8.09 to 172) in middle childhood and 33.5 aOR (21.9 to 51.6) adolescence among PASC probable compared to the uninfected reference group, respectively. Mixed sleep type reported 32.6 aOR (20.3 to 53.1) among PASC probable compared to the uninfected reference group. An interaction of sex with PASC on insomnia, and an interaction of race on sleep duration with PASC in adolescents only, were also reported. An interaction with sex trended with mixed sleep disorder in adolescents as well (p=0.07).

Conclusions: We have identified important sleep phenotypes for children and adolescence demonstrating clear sleep disturbance in those with probable LC. Future research will examine sleep phenotypes among infancy and early childhood, as well as socio-demographic predictors of sleep problems and PASC across the life course.

Sleep-wake state discrepancy is more pronounced in individuals with insomnia than those with obstructive sleep apnoea (OSA)

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Introduction: Sleep-wake state discrepancy (SWSD) is the difference between self-reported and polysomnography-derived sleep parameter values. Individuals experiencing insomnia often report less total sleep time (TST) and greater sleep onset latency (SOL) than what is measured by polysomnography, which can contribute to greater SWSD. To better understand the clinical presentation and management of this phenomenon, it would be beneficial to understand sleep disorder specific presentations of SWSD. This study examines whether sleep-wake state discrepancy presents differently between individuals with insomnia versus obstructive sleep apnoea (OSA).

Materials and methods: Data presented is from an ongoing study in a clinical setting. All participants (N = 79) completed diagnostic in-laboratory (Level 1) or ambulatory polysomnography (Level 2) sleep studies and next-morning self-report sleep diaries. SWSD was calculated for SOL, wake after sleep onset (WASO), and TST by subtracting polysomnography-derived values from sleep diary-derived

values. We had two groups: insomnia-alone with no significant OSA (determined by Apnoea-Hypopnoea Index (AHI) <15h/h, and Insomnia Severity Index (ISI) >15), and OSA-alone (determined by AHI > 15h/h, and ISI <15). Forty-eight participants (age M = 49, SD = 18, 56.3% female, 43.7% male) had insomnia, and thirty-one had moderate to severe sleep apnoea without insomnia (age M = 53, SD = 13, 29% female, 71% male). SWSD scores are presented as: (Median minutes (Inter Quartile Range)). Kruskal-Wallis H-test assessed between group differences.

Results: For SOL, the group with insomnia-alone (13mins(44)) reported greater SWSD compared to the group with OSA-alone (-1.5mins(38)); ($X^2(1) = 6.712$, $p .01$), mean rank scores: 45.38 (insomnia-alone), 31.68 (OSA-alone). For WASO, the group with OSA-alone (-49mins(79)) reported greater SWSD compared to the group with insomnia-alone (-5mins(49)); ($X^2(1) = 10.28$, $p .001$), mean rank scores: 46.65 (insomnia-alone), 29.71 (OSA-alone). For TST, there was a significant difference in SWSD between the groups, though in opposite directions: insomnia-alone (-21mins(78)), OSA-alone (51mins(94)); ($X^2(1) = 15.256$, $p <.001$), mean rank scores: 31.9 (Insomnia-group), 52.55 (OSA-group).

Conclusions: Individuals with insomnia self-reported worse SWSD for SOL and TST compared to polysomnography, whereas individuals with OSA self-reported better sleep for WASO and TST than polysomnography. This suggests that SWSD profiles are likely to differ across sleep disorders. Therefore, it is recommended that focusing on SWSD in individuals with insomnia may be more fruitful than when working with individuals with OSA-alone. Future investigations should explore specific treatment considerations regarding SWSD in co-occurring insomnia and significant OSA, and sex differences should be considered.

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Sober sleep? Cognitive behavioral therapy for insomnia across the spectrum of alcohol use disorder

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Introduction: Comorbid insomnia is a common challenge among individuals with alcohol use disorder (AUD), increasing the risk of relapse and undermining treatment success. While cognitive behavioral therapy for insomnia (CBT-I) is the first-line treatment for chronic insomnia, its effectiveness within the context of AUD has not been well characterized. The aim of this meta-analysis was to quantify the effects of CBT-I on insomnia severity and alcohol-related outcomes in samples ranging from heavy-drinking individuals to those with severe AUD.

Materials and methods: A systematic search was conducted in MEDLINE, Cochrane Library, PsycINFO, and ClinicalTrials.gov for randomized controlled trials (RCTs) published from 1980 through February 2024. RCTs comparing CBT-I to control conditions among adults (≥ 18 years) with heavy drinking or AUD and comorbid insomnia were included. Two reviewers independently extracted data and assessed risk of bias using the Risk of Bias 2 tool. The primary outcome was insomnia severity, measured using the Insomnia Severity Index (ISI). Secondary outcomes included alcohol craving, alcohol-related psychosocial problems, and the number of heavy-drinking and abstinent days. All outcomes were evaluated at post-treatment and follow-ups. Multilevel meta-analyses were conducted to estimate mean differences for all outcomes, except for heavy-drinking and abstinent days, which were analyzed using incidence rate ratios.

Results: Eight RCTs involving 426 adults (68.78 % men) were included. Compared with control conditions, CBT-I resulted in a significant reduction in insomnia severity post-treatment [estimated ISI reduction = -5.51, 95% CI (-7.13 to -3.90)], with improvements maintained at 1-to-3-month [7 studies; estimate = -4.39, 95% CI (-6.08 to -2.70)] and 6-month follow-up [4 studies; estimate = -4.55, 95% CI (-6.77 to -2.33)]. No significant differences emerged for alcohol-related outcomes, which were inconsistently reported across studies. The included trials were judged as having low or moderate overall risk of bias for all outcomes.

Conclusions: CBT-I is effective in reducing insomnia severity in heavy-drinking and AUD samples, with sustained beneficial effects following treatment. These findings support its wide implementation in AUD prevention and treatment settings.

Social isolation and risk of insomnia: A cohort and Mendelian randomization study

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Introduction: Social isolation (SI) has been linked to various mental and behavioral disorders, including depression, anxiety, and schizophrenia. However, the causal relationship between SI and insomnia remains unclear. This study aimed to examine both the observational and genetic causal associations between SI and the risk of insomnia.

Materials and methods: This study utilized data from the UK Biobank, a large prospective cohort comprising over 500,000 participants aged 40–70 years, recruited between 2006 and 2010. SI was defined based on three components: number of household members, frequency of contact with others, and engagement in social activities. The primary outcome was incident insomnia, identified through hospitalization records and death registries in the UK Biobank. Cox proportional hazards models were used to assess associations between SI and incident insomnia. Additionally, bidirectional causal associations between genetic liability to SI and insomnia were examined using two-sample Mendelian randomization (MR). Genetic instruments were derived from the UK Biobank, and insomnia GWAS summary statistics were obtained from the European Bioinformatics Institute (EBI) and the FinnGen consortium (Round 12). Meta-analyses and sensitivity tests (MR-Egger, MR-PRESSO, and Cochran's Q) were conducted to validate causal estimates.

Results: Among the 489,741 participants (mean age 56.5±8.1 years; 54.5% female), 559 incident cases of insomnia were documented during a median follow-up of 12.7 years. SI was significantly associated with an increased risk of insomnia (HR = 1.56, 95% CI: 1.27-1.91). Each component of SI was also significantly associated with insomnia: living alone (HR = 1.36, 95% CI: 1.12-1.64), little contact with family/friends (HR = 1.25, 95% CI: 1.02-1.51), and fewer leisure/social activities (HR = 1.21, 95% CI: 1.01-1.44). These associations remained significant after adjusting for demographic, socioeconomic, and lifestyle factors. MR meta-analyses revealed no causal effect of overall SI on insomnia (OR = 0.73, 95% CI: 0.21-2.58), but identified potential causal effects of little contact with family/friends (OR = 1.14, 95% CI: 1.01-1.28) and fewer leisure/social activities (OR = 1.38, 95% CI: 1.03-1.85). Living alone showed no evidence of a causal association (OR = 1.00, 95% CI: 0.71-1.40). Bidirectional MR analyses found no evidence of a causal effect of insomnia on SI or its components. All sensitivity analyses supported the robustness of these findings.

Conclusions: Social isolation is a significant risk factor for insomnia. Among its components, little contact with family or friends and limited participation in leisure or social activities may be causal risk factors. These findings highlight the importance of promoting social engagement—particularly maintaining interpersonal connections and active participation in social life—as a potential strategy to prevent insomnia and improve sleep health.

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Student Sleep Across the Pandemic: Longitudinal Trends in Sleep Behavior and Sleep Problems Before, During, and After COVID-19 (2010–2023)

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Introduction: Sleep problems—including insomnia and difficulties initiating and maintaining sleep (DIMS)—are increasingly reported among university students. While the short-term sleep effects of the COVID-19 pandemic are well described, long-term trends in sleep problems and behaviors across the pre-, peri-, and post-pandemic periods remain insufficiently studied in this vulnerable population.

Materials and methods:

We used data from the Students' Health and Wellbeing Study (SHoT), a national survey conducted in 2010, 2014, 2018, 2021, 2022, and 2023 among full-time Norwegian students (N ≈ 200,000). DIMS was assessed in all waves using one item from the Hopkins Symptom Checklist-25 (HSCL-25) asking about difficulty falling or staying asleep over the past two weeks. Responses ranged from "Not at all" to "Extremely," with DIMS defined as reporting "Quite a bit" or "Extremely." In 2018, 2021, and 2022, additional self-reported sleep measures were collected: weekday bedtime, risetime, sleep onset latency (SOL), wake after sleep onset (WASO), and time in bed (TIB). Sleep duration was defined as TIB minus SOL and WASO. Sleep efficiency was calculated as (sleep duration ÷ TIB) × 100. DSM-5 insomnia disorder was operationalized using three criteria: (1) difficulties initiating, maintaining, or early morning awakening ≥3 nights/week; (2) daytime fatigue ≥3 days/week; and (3) sleep problems lasting ≥3 months. Analyses were stratified by sex and year, with 95% confidence intervals.

Results:

DIMS prevalence increased consistently from 2010 through 2023, with the highest levels observed in the most recent wave. Among women, it increased from 23.8% in 2010 to 32.4% in 2018, reached 34.1% in 2021, remained elevated at 32.8% in 2022, and climbed further to 38.3% in 2023—the highest level recorded. Among men, prevalence rose from 20.3% in 2010 to 26.2% in 2018, peaked at 32.4% in 2021, declined slightly to 28.4% in 2022, and increased again to 32.2% in 2023. DSM-5 insomnia symptoms followed a similar trend, rising from 2018 to 2021, with only partial improvement observed in 2022. From 2018 to 2021, sleep onset latency (SOL) increased from 50 to 59 minutes in women and from 43 to 54 minutes in men, followed by a modest decline in 2022 (51 and 46 minutes, respectively). WASO also rose across the period. Sleep efficiency decreased from 86.9% (2018) to 85.4% (2021) in women and from 88.6% to 86.7% in men, with slight improvement in 2022 (86.2% in women; 87.5% in men). Despite an increase in time in bed during the pandemic, mean sleep duration remained stable: 7h25 (2018), 7h32 (2021), and 7h27 (2022) in women; 7h24 across all years in men. Bedtime and risetime were delayed in 2021 and partially reverted toward pre-pandemic patterns in 2022.

Conclusions: Sleep problems and insomnia symptoms have increased markedly among university students since 2010, with pronounced peaks during the COVID-19 pandemic. While some indicators improved post-pandemic, 2023 DIMS levels were the highest recorded. These trends highlight the ongoing need for longitudinal sleep monitoring and targeted interventions to address persistent sleep challenges in student populations.

Study on the change of autonomic nerve function and insomnia disorder comorbid with diabetes mellitus

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Introduction: This study aimed to assess changes in autonomic nervous function in patients with insomnia disorder comorbid with diabetes mellitus, explore its underlying pathological mechanisms, and provide a basis for the clinical diagnosis and treatment of these patients.

Materials and methods: A total of 120 participants were enrolled in this study and assigned to four groups: a comorbid insomnia and diabetes mellitus group, an insomnia disorder group, a diabetes mellitus group, and a healthy control group, with 30 participants in each group. Autonomic nervous function was assessed using heart rate variability (HRV) and the SCOPA-AUT scale, while sleep status was evaluated using the Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), and sleep diaries. Additionally, postprandial blood glucose, glycated hemoglobin (HbA1c), and both fasting and postprandial islet function indicators were recorded. These metabolic parameters were subsequently included in the comprehensive analysis of intergroup differences in autonomic nervous function.

Results: The SCOPA-AUT scores for gastrointestinal, urinary, cardiovascular, and pupil regulation systems were significantly higher in the insomnia and diabetes comorbidity group compared to the insomnia disorder group, the diabetes group, and the normal control group ($P < 0.05$). However, no significant differences were found in the thermoregulatory and sexual functioning systems ($p > 0.05$). Analysis of HRV time-domain indices revealed that the mean heart rate (MeanHR) was significantly higher in the insomnia and diabetes comorbidity group compared to the insomnia group ($p < 0.05$). Analysis of HRV frequency-domain indices showed that the insomnia and diabetes comorbidity group had significantly increased low-frequency (LF) power and LF/HF ratio, along with decreased high-frequency (HF) power, compared to the other groups (all $p < 0.05$). Univariate linear regression analysis revealed that sex, duration of insomnia, fasting blood glucose, HbA1c, SCOPA-AUT score, and PSQI score were positively associated with sympathetic nervous activity, while gender and PSQI score were significantly associated with parasympathetic nervous activity.

Conclusions: Patients with comorbid insomnia and diabetes mellitus show significant autonomic dysfunction, marked by increased sympathetic activity and reduced parasympathetic activity. A possible synergistic interaction between sleep disturbances and diabetes-related metabolic abnormalities may contribute to the onset of autonomic dysregulation.

Subtyping and Prognosis of Insomnia Disorder Based on Clinical, Psychological, and Sleep EEG Features

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Introduction: Insomnia disorder (ID) is a clinically heterogeneous condition, limiting the effectiveness of standardized interventions. This study applied data-driven approaches to identify ID subtypes based on clinical, psychological, and sleep EEG features, and to assess their distinct profiles and treatment outcomes.

Materials and methods: Subjects aged 18–65 years, meeting DSM-5 criteria for ID without other sleep disorders, were included. Comprehensive clinical and psychological evaluations and polysomnographic (PSG) monitoring were conducted to collect clinical, psychological, and sleep EEG features. Clinical features included the Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HAMD), Hamilton Anxiety Rating Scale, and Multidimensional Fatigue Inventory (MFI); psychological characteristics included the Pre-Sleep Arousal Scale (PSAS), Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), Sleep Hygiene Index (SHI), Perceived Stress Scale (PSS), among others; sleep EEG features encompassed sleep structure and continuity, spectral power, and sleep spindle measures. Equivalent doses of benzodiazepine receptor agonists (BzRA) and antidepressants were recorded. PSQI and HAMD scores at 8 weeks post-treatment were used as outcome measures.

Feature selection was performed using a normalized correlation matrix, followed by dimensionality reduction via Uniform Manifold Approximation and Projection (UMAP). K-means clustering was employed based on optimal parameters based on silhouette coefficients and neighborhood preservation. Analysis of variance (ANOVA) and Kruskal-Wallis tests were utilized to compare subtype differences in characteristics and clinical outcomes, with significance set at two-tailed $P < 0.05$.

Results: A total of 220 participants completed baseline assessments. Feature selection yielded 7 clinical features, 9 psychological characteristics, and 57 EEG metrics. Three distinct subtypes emerged from UMAP dimensionality reduction and K-means clustering:

Subtype 1, labeled "Deep Sleep Deficient Insomnia" (28.2%), had significantly older participants

($F=4.78$, $p=0.009$), highest depression severity ($F=11.19$, $p<0.001$), shortest duration of N3 slow-wave sleep ($F=6.27$, $p=0.002$), and higher NREM β -band total power ($H=24.40$, $p<0.001$). This subtype received the highest equivalent dosage of BzRA ($F=14.74$, $p<0.001$) and showed significantly poorer improvement in PSQI scores at 8 weeks compared to other subtypes, as well as significantly worse HAMD outcomes compared to subtype 3 ($F=8.47$, $p<0.001$).

Subtype 2, "Stress Related Insomnia" (32.3%), displayed notable clinical anxiety ($F=4.00$, $p=0.020$) and fatigue ($F=9.24$, $p<0.001$), along with the highest insomnia vulnerability ($F=4.30$, $p=0.015$), pre-sleep arousal ($F=14.62$, $p<0.001$), rumination ($F=7.40$, $p=0.001$), and sleep hygiene issues ($F=10.91$, $p<0.001$). EEG analysis revealed reduced δ -band total power compared to other subtypes ($H=12.63$, $p=0.002$). This subtype received moderate BzRA dosages and demonstrated better overall improvement in PSQI scores at 8 weeks than subtype 1.

Subtype 3, "Spindle Deficient Insomnia" (39.5%), presented mild insomnia severity ($F=5.63$, $p=0.004$), lowest perceived stress ($F=14.18$, $p<0.001$), increased micro-arousals ($F=3.532$, $p=0.031$), and reduced spindle activity ($H=66.55$, $p<0.001$). Subtype 3 patients received the lowest equivalent dosages of BzRA and antidepressants, achieving the best overall outcomes in both PSQI and HAMD at 8 weeks.

Conclusions: This study identified three data-driven subtypes of insomnia with distinct EEG and clinical profiles, which were predictive of treatment response. These findings highlight the potential of personalized, subtypes-based management strategies for insomnia disorder.

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Temporal Subtypes and Characteristics of Insomnia Treatment Responses

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Introduction: This study aims to identify specific characteristics that can predict the treatment efficacy and onset time in patients with insomnia.

Materials and methods: A retrospective study was conducted on patients who visited the Sleep Disorders Clinic between January 1, 2016, and October 19, 2024 and underwent digital CBT-I. Data on demographic characteristics, Pittsburgh Sleep Quality Index (PSQI), Generalized Anxiety Disorder Scale (GAD-7), Patient Health Questionnaire (PHQ-9), Somatic Symptom Questionnaire (PHQ-15), Epworth Sleepiness Scale (ESS), and Eysenck Personality Questionnaire (EPQ) were collected. The PSQI score reduction rate was used as an indicator of treatment efficacy, where a reduction rate of more than 25% was generally considered effective. Since patients in this study underwent multiple assessments and exhibited varying degrees of treatment response, the average reduction rate was ultimately used to determine treatment effectiveness within this time dimension. Based on the time dimension, patients ($N=834$) were categorized into two groups: the early-response group (≤ 8 weeks) and the late-response group (> 8 weeks or non-responsive).

Results: The demographic characteristics and scale data of 834 patients indicated no significant differences between the two groups in terms of gender ($P=0.491$), family history of insomnia ($P=0.167$), and ESS score ($P=0.949$). However, significant differences were observed between the two groups in age ($P=0.005$), education level ($P<0.001$), duration of insomnia ($P<0.001$), GAD-7 score ($P=0.031$), PHQ-9 score ($P=0.044$), and neuroticism personality trait ($P=0.039$). The late-response group had a higher mean age, a lower education level, and a longer duration of insomnia than the early-response group. Additionally, the late-response group exhibited lower GAD-7, PHQ-9, and neuroticism personality trait scores compared to the early-response group. Multivariate logistic regression analysis indicated that higher education level (college or above), higher PHQ-9 and PHQ-15 scores, and a neuroticism personality trait were significant predictors of better treatment response and earlier onset of efficacy in insomnia patients. A longer duration of insomnia was identified as a risk factor for poor treatment response and delayed onset of efficacy.

Conclusions: Insomnia patients with higher education levels (college or above), higher PHQ-9 and PHQ-15 scores, and a neuroticism personality trait tend to have better treatment outcomes and an earlier onset of efficacy. Longer duration of insomnia, tend to experience poorer treatment outcomes and a delayed response to treatment.

The 2024 Canadian Recommendations for Chronic Insomnia Management: A Practical, Evidence-Based Consensus

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Introduction: Chronic insomnia is a serious disorder that usually follows a persistent course and should be managed as a long-term condition. While some individuals may experience periods of improvement or remission, the long-term impact on mental, physical, and occupational health is significant and should not be underestimated. The 2024 Canadian consensus recommendations for chronic insomnia were developed to assist healthcare providers, especially in primary care, with evidence-based recommendation for diagnosis and long-term management.

Materials and methods: The guidelines were established by 16 Canadian experts in sleep medicine representing family physicians, neurologists, psychiatrists, psychologists, pharmacists, and clinical researchers. The Delphi process, a common methodology to reach consensus on complex problems, was used to refine and arrive at a set of evidence-based recommendations and address practical needs.

Results: Among the recommendations that reached consensus, the experts agreed that:

- Chronic insomnia is highly prevalent, approximately affecting 1 in 7 Canadians
- Healthcare providers should proactively screen for chronic insomnia by routinely asking simple sleep-related questions about difficulties falling or staying asleep and functioning during daytime.
- Insomnia should be assessed and treated independently, even when comorbid with other sleep, mental, or physical health conditions.
- Comorbidities may potentiate insomnia's effects on physical and mental health.
- Tools such as ISI, PHQ-9, GAD-7, and STOP-Bang can help assess the nature and severity of insomnia and comorbidities.
- Sleep hygiene education alone is an insufficient treatment.
- Cognitive-behavioural therapy for insomnia (CBT-I) is the first-line treatment and can sometimes be combined with pharmacotherapy. CBT-I can be used in multiple modalities (virtual, self-help, face-to-face, group), although the efficacy varies across modalities.
- Dual Orexin Receptor Antagonists (DORAs) may have benefits that outweigh their risks for long-term use. Their side effect profile may be more favourable compared to BZRA agents, and other commonly prescribed pharmacotherapies.
- Ability of benzodiazepines and Z-drugs to improve sleep short term has been confirmed but are associated with potentially concerning adverse effects, e.g., daytime drowsiness, falls risk, motor vehicle accidents, addiction/abuse risk, rebound insomnia.
- Off-label and over the counter medications used in treating insomnia have unclear or hazardous safety and efficacy profiles that may outweigh their benefits.
- Outside of specialized subpopulations, there is a lack of evidence on the use of melatonin and long-term effect of cannabinoids for chronic insomnia.
- Key educational needs range from raising awareness of current treatment options to better understanding the balance of risk and benefits.

Conclusions: These guidelines for the management of chronic insomnia offer a pathway to more effective, evidence-based care. However, real-world implementation of the recommendations, particularly those related to novel therapies, will require a granular understanding of the evidence distinguishing the different classes of medication and identifying the most suitable treatment within

each class. This underscores the need to educate on the impact of insomnia and how to apply safe and effective evidence-based therapies to clinical practice for the benefit of patients living with insomnia.

The Association between Sleep Vulnerability and Autonomic Response to Nocturnal Arousals

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Introduction: Sleep vulnerability is an individual trait reflecting the tendency to experience sleep disturbances under stress. It's assessed via self-report using the Ford Insomnia Response to Stress Test (FIRST), which measures the likelihood of sleep disruption in response to everyday stressors. Higher FIRST scores consistently predict development of insomnia disorder. Although prior research links high sleep vulnerability to heightened physiological arousal, dynamic processes underlying autonomic nervous system (ANS) responses, especially recovery following nocturnal arousals, remain poorly understood. This study aimed to investigate how high versus low sleep vulnerability individuals differ in ANS reactivity and recovery patterns following experimentally induced arousals during nocturnal sleep, assessing their potential as physiological markers of insomnia risk.

Materials and methods: Forty healthy adults ($M = 24.1 \pm 3.1$ years) were recruited based on FIRST pre-screening, including a high vulnerability group (HV, $n = 19$; 10 females; $FIRST \geq 23$) and a low group (LV, $n = 21$; 12 females; $FIRST \leq 18$). During overnight polysomnography, auditory stimuli (1-second 1000 Hz pure tones) were presented via speakers during sleep in ascending intensity sequences (40–90 dB, 13-second intervals). Each stimulus sequence began when at least 10 seconds of stable EEG activity were presented and were terminated if EEG-defined arousal occurred. ANS reactivity was indexed by peak heart rate (HR) following arousal onset, while recovery reflected the efficiency of HR return to baseline. Baseline HR was calculated as the average of 2–12 heartbeats prior to cortical arousal. ANS reactivity was also quantified by the area under curve (AUC) from baseline to peak HR. Higher values indicated stronger reactivity. ANS recovery was assessed as the AUC across the 30 beats after the HR peak, divided by peak amplitude; larger values indicated slower recovery and poorer autonomic regulation.

Results:

During NREM sleep, the HV group exhibited significantly higher HR peak responses compared to the LV group ($t(38) = 0.858, p = .005$), while no group differences were observed during REM sleep or when all stages combined. In contrast, AUC-based reactivity showed no differences across NREM, REM, or combined sleep stages.

ANS recovery was significantly slower in the HV group when combining all stages ($t(38) = 2.351, p = .024$), while no group differences were observed during REM or NREM sleep.

Conclusions: Our findings suggest that ANS recovery, rather than reactivity, may better represent a physiological marker of sleep vulnerability. The discrepancy between peak HR and AUC-based ANS reactivity may reflect differences in arousal-to-peak latency, with the LV group showing a slower, more gradual HR rise that yields comparable AUC values to the HV group's sharper, faster responses. In contrast, the slower recovery process in the HV group likely reflects reduced parasympathetic modulation, impairing the ability to return to physiological homeostasis following arousal. These findings underscore the importance of recovery dynamics in understanding sleep vulnerability and support the potential utility of targeting ANS recovery for early detection and intervention of insomnia disorder. Future research is needed for understanding ANS reactivity mechanism.

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The associations between short-term changes in suicidal ideation and sleep disturbances in youth

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Introduction: Sleep disturbances are recognized as transdiagnostic symptoms that significantly increase the risk for mental disorders and suicide. Despite the emergence of sleep-related issues during adolescence and early adulthood, there is a paucity of studies examining the sleep-suicide association in youth. Given the importance of early detection, this study examines the associations between short-term changes in suicidal ideation (SI) and sleep disturbances in youth.

Materials and methods: This is part of an ongoing study on examining depression symptomatology in youth, which recruited Chinese individuals aged 18-24 years using convenient sampling, excluding those with neuropsychiatric disorders (other than depression and anxiety). At baseline, participants underwent a structured interview to assess SI and the presence of sleep disturbances, including difficulties falling asleep (DIS), difficulties maintaining asleep (DMS), and early morning awakening (EMA), based on the Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS). Participants also completed the Depression Anxiety Stress Scales-21 (DASS-21) to measure depression, anxiety, and stress levels. A week later, participants' SI was reassessed using HDRS interviews. The participants were classified into four groups, namely non-SI group (no SI at baseline and follow-up), SI remitted group (having SI at baseline but not at follow-up), incident SI group (no SI at baseline but having SI at follow-up), and persistent SI group (having SI at baseline and follow-up). Multiple logistic regression models were used to analyze the relationship between SI groups (outcomes) and sleep disturbances (predictor), adjusting for age, gender, and baseline levels of SI, depression, anxiety, and stress.

Results: The study included 328 individuals while 300 completed the study (mean age 20.68 years, SD 2.02; 76% female). Of these, 92 individuals (31%) exhibited at least one symptom, with 21% (n=63) experiencing DIS, 14% (n=41) having DMS, and 9% (n=28) showing EMA. In the completer analysis, there were 255 (85%) in the non-SI group, 15 (5%) in the SI remitted group, 16 (5%) in the incident SI group, and 14 (5%) in the persistent SI group. There were no significant differences observed in age and gender among the groups. Baseline sleep disturbances (OR= 4.79, 95% CI=1.50 to 16.93, p=.01) and depression severity (OR=1.18, 95% CI=1.08 to 1.30, p<.001) significantly predicted incident SI after one week. Baseline SI (OR=5.77, 95% CI=2.49 to 15.60, p<.001) increased the risk for persistent SI. Baseline anxiety severity (OR=0.86, 95% CI=0.75 to 0.98, p=.03) was negatively associated with SI remission. Baseline stress severity showed no significant links to short-term changes in SI.

Conclusions: This study identifies sleep disturbances as a significant predictor of incident SI in youths, alongside depressive symptoms. These results highlight the importance of focusing on sleep issues and depressive symptoms when developing strategies for suicide detection and prevention.

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The Contributions of Biological Sex to Sleep Microarchitecture: A Systematic Review and Meta-Analysis of Biological Sex Differences in Sleep Spindles and Slow Wave Activity in Adults With and Without Insomnia

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Introduction: Insomnia Disorder (ID) is the most prevalent sleep disorder in adults, particularly amongst females (1.5x more likely than males). In fact, insomnia symptoms may manifest more frequently during key reproductive life events marked by hormonal and physical changes (e.g., puberty, pregnancy, perimenopause). However, much less is known regarding sex disparities within sleep biomarkers associated with sleep quality, such as sleep spindle activity (SSA; spindle events and sigma-band spectral power) and slow wave activity (SWA; slow oscillations [SO], slow waves [SW], and delta-band spectral power). This systematic review and meta-analysis aimed to synthesize research on the impact of biological sex (female, male) and sleep condition (ID, healthy sleep [HS]) on SSA and SWA.

Materials and methods: A systematic search was undertaken on PubMed, Embase, Scopus, and PsycInfo from database inception to December 2022, using Medical Subject Headings (MeSH) terms and keywords associated with SSA, SWA, HS, and ID. We included published peer-reviewed studies involving both males and females over 18 years old. Eligible studies examined sex-based differences in SSA and SWA via event detection and/or spectral analysis. A meta-analysis was conducted using a random-effects model to pool effect sizes. Heterogeneity was assessed using the I^2 statistic. Risk of bias was evaluated using the Newcastle-Ottawa Scale. This study is registered on PROSPERO (CRD 42022355969).

Results: Of the 247 included articles, only 17% (41 articles) reported results on sex-based analyses (31 HS, 2 with ID, 8 HS+ID). Only 13 of the 31 HS articles (42%; N=668) had sufficient statistical data for meta-analysis, and none of the ID or HS+ID articles did.

In healthy sleep, evidence from the systematic review and meta-analysis indicated that, compared to males, females showed higher sigma power (5 studies, n=365, SMD=-0.29, 95% CI=[-0.50, -0.08], $I^2=0\%$), spindle density (2 studies, n=190, SMD=-0.65, 95% CI=[-1.95, 0.66], $I^2=85\%$), and delta power (6 studies, n=407, SMD=-0.50, 95% CI=[-0.70, -0.30], $I^2=0\%$). Sex differences were less consistent when considering ID alone, or when comparing ID with HS, likely due to the scarcity of studies examining group-by-sex interactions, and findings being highly dependent on method, age, and analysis type.

Conclusions: To our knowledge, this is the first systematic review and meta-analysis to examine the effects of biological sex on SSA and SWA in adults with and without insomnia, assessed with quantitative EEG measures (e.g., event-based detection, spectral analysis). Our review also highlights critical gaps in current sleep research. Sex-based differences in SSA and SWA characteristics are infrequently and inconsistently examined in sleep research, despite known hormonal influences on brain oscillations and sex differences in sleep quality. It also underscores inconsistencies in samples and the methodology used to study brain oscillations, including ID criteria, sample analysis (e.g., age stratification, use of hormonal treatment in covariate, balance in sex distribution), and brain oscillations detection methods. Further research that includes sex as a primary outcome, while considering relevant nuances, is imperative to clarify whether true sex-based differences exist in insomnia-related oscillatory activity, and to inform more precise, inclusive interventions addressing health disparities in ID.

The effectiveness of self-help cognitive behavioural therapy for insomnia in adults: a systematic review and meta-analysis

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Introduction: Uptake of cognitive behavioural therapy for insomnia (CBT-I) as a first-line treatment for chronic insomnia is limited due to a shortage of trained therapists, access barriers, and economic burden. Self-help CBT-I appears to be a viable alternative due to its promising scalability, accessibility, and affordability. To date, the effectiveness of self-help CBT-I on insomnia severity among adults with insomnia symptoms has not been extensively explored. This meta-analysis aims to evaluate the overall effectiveness of self-help CBT-I on insomnia severity and to identify potential characteristics associated with greater estimated treatment effects.

Materials and methods: We systematically searched PubMed, Embase, PsycINFO, CINAHL Plus, Web of Science, the Cochrane Library Core, and two Chinese databases (China National Knowledge Infrastructure [CNKI] and Wanfang Data) for articles published up to 4 April 2025. Randomized controlled trials (RCTs) comparing self-help CBT-I with a control condition were included if they involved adults with insomnia symptoms and reported insomnia severity as an outcome. Two independent reviewers screened the search records and extracted data from eligible RCTs. Hedges' g

was pooled using a random-effects model, with post-intervention insomnia severity as the primary outcome. Subgroup analyses and meta-regressions were performed to identify characteristics potentially associated with enhanced treatment efficacy. The Cochrane Risk of Bias 2.0 tool was used to assess study quality. This meta-analysis followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and was pre-registered on PROSPERO (registration number: CRD420251009153).

Results: A total of 33 RCTs (37 intervention vs. control comparisons) involving 6,187 participants (mean age range: 27.3–71.8 years), conducted in upper-middle- or high-income countries, were included. Self-help CBT-I interventions were mainly delivered via mobile apps or web platforms, with varying levels of support ranging from none to guided assistance. Compared with control conditions, self-help CBT-I demonstrated large effect sizes in reducing insomnia severity at post-intervention ($g = -0.97$, 95% CI: -1.19 to -0.75; $I^2 = 93.09\%$), moderate to large effects at 1–5 months post-intervention ($g = -0.67$, 95% CI: -0.83 to -0.51; $I^2 = 70.20\%$), and at 6–12 months post-intervention ($g = -0.78$, 95% CI: -1.03 to -0.52; $I^2 = 82.24\%$). Larger effect sizes were observed in trials that included relapse prevention components or were delivered via web platforms. No significant differences were found based on adaptation of CBT-I content, level of support, or provision of incentives. Of the included studies, 6 were rated as having a high risk of bias, 13 as having some concerns, and 14 as having a low risk of bias.

Conclusions: Compared with control conditions, self-help CBT-I demonstrated effectiveness in managing adult insomnia, regardless of the level of support or delivery format. Further rigorous research is warranted to evaluate the effectiveness of self-help CBT-I in low-income countries.

The effect of a tailored digital cognitive behavioural therapy for insomnia in people with co-morbid insomnia and sleep apnoea (COMISA): A pilot randomised controlled trial

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Introduction: Co-morbid insomnia and sleep apnoea (COMISA) is a prevalent and debilitating condition. Cognitive behavioural therapy for insomnia (CBTi) is an effective but largely inaccessible treatment in patients with COMISA. Self-guided digital CBTi programs may be one method to increase CBTi accessibility in people with COMISA. However, existing digital CBTi programs have largely been developed and tested in people with insomnia alone, and may not be as effective, appropriate, or safe in people with COMISA. We therefore aimed to develop and test a self-guided interactive digital CBTi program tailored for COMISA and insomnia-alone.

Materials and methods: An Australia-wide online pilot randomised controlled trial was conducted to investigate the effect of an interactive digital CBTi program, versus digital sleep education (control), on symptoms of insomnia, depression, anxiety, sleepiness, fatigue, and maladaptive beliefs about sleep in people with COMISA. Online questionnaires were administered at baseline, 8-weeks, 16-weeks and 24-weeks. The control group accessed the program after the 8-week follow up. Intent-to-treat mixed models and complete-case Fisher's exact analyses were used.

Results: Participants were 30 adults with COMISA (Age M [sd] = 61.0 [10.3], 60% female, BMI = 33.5 [6.5]). Compared to control, CBTi was associated with lower insomnia (M [95%CI] difference = 8.3 [5.0–11.6], $p < .001$, $d = 2.88$), depression (3.7 [1.0–6.5], $p = .008$, $d = 1.66$), anxiety (2.9 [0.9–4.9], $p = .005$, $d = 0.62$), sleepiness (2.7 [0.8–4.5], $p = .007$, $d = 0.71$), and maladaptive beliefs about sleep (13.9 [5.7–22.2], $p = .001$, $d = 1.16$), but not fatigue (1.9 [-1.2–4.9], $p = .229$, $d = 0.68$) at 8-week follow-up, controlling for baseline scores. The tailored CBTi group experienced greater rates of insomnia remission ($ISI < 8$; 42%, vs 0%, $p = .012$), and improvement (ISI reduction ≥ 6 ; 75% vs 14%; $p = .004$) by 8-weeks. Improvements in the tailored CBTi group were sustained by 24-weeks.

Conclusions: This digital CBTi program led to large and sustained improvements in insomnia, depression, anxiety, sleepiness, and maladaptive beliefs about sleep in people with COMISA. Larger trials are required to definitively understand the effectiveness of this program in diverse samples of people with COMISA, and "downstream" impacts of this program on acceptance and use of treatments for sleep apnoea.

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The Effect of Body Grounding on Sleep Quality of Cancer Inpatients, and the Relations between Body Voltage, Bedroom EMF and Sleep Quality: a Blinded Randomized Controlled Study

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Introduction: The prevalence of sleep difficulties or insomnia is high in cancer patients. Compared with healthy people, it is common for cancer patients to have a long sleep onset, short sleep duration, and poor sleep efficiency. Many studies have found that the higher the body voltage, the lower the vagal tone, suggesting that the high and low body voltage values have physiological significance and clinical importance, and grounding is an intervention that has been proven to reduce body voltage.

Materials and methods: We implemented body grounding therapy during the sleep period of cancer patients in two different environments: hospitalization (two nights) and after discharge (more than one week) through a randomized, controlled group experimental design. The Pittsburgh Sleep Quality Inventory (PSQI), Hospital Anxiety and Depression Scale (HADS), Stress and Somatic Symptom Scale (DSSS), Sleep Assessment Questionnaire (SEQ), and Sleepiness Scale (KSS) were used to evaluate the differences between the subjects before and after receiving the grounding therapy. In addition, the bed body voltage (BV) values before and during bed grounding in hospital and at home were obtained, and finally statistical analysis was performed using statistical methods such as paired sample T test.

Results: There were 14 people enrolled in the true grounding group (experimental group, Group 1) and 12 people enrolled in the sham grounding group (control group, Group 0) during their hospitalization. There were no significant differences between the two groups in age, gender, weight, height, BMI, age at onset, number of years of illness, and all pre-test assessment scale scores. Compared with Group 0, Group 1 had a significant decrease in PSQI scores ($p=0.03$ between groups), indicating that the degree of insomnia was significantly improved due to the intervention of the grounding patch, and similar significant differences were found under longer-term use after discharge and return home ($p=0.02$ within group 1). There was no significant difference in PSQI scores between the pre-test and the post-test in Group 0 ($p=0.22$). After using the grounding patch, there was a significant difference between the two groups ($p=0.000$ in hospital beds and $p=0.007$ in home beds). The body voltage drop rate of Group 1 was 99.3-98.8%, while that of Group 0 was only 3.6-7.1%.

Conclusions: *Conclusion: The improvement in PSQI confirm that the earthing patch did reduce insomnia severity in cancer patients, and similar effects are also seen under long-term use. The grounding patch produce a very noticeable and rapid drop in body voltage. The AC voltage present in the electric beds in hospital wards is one of the reasons for the high body voltage values and should be managed.*

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The Effect of CBT-I on Phasic/Tonic REM Microstructure in Patients with Insomnia: Preliminary Findings

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Introduction: The cognitive behavioural therapy for insomnia (CBT-I) is a widely recognised and tested method for the treatment of insomnia and reducing hyper-arousal. However, very few studies have explored its impact on the objective markers of nocturnal arousal and next-day emotion regulation, specifically the balance between phasic and tonic rapid-eye movement (REM) sleep microstructure. Therefore, current research presents preliminary findings of a pilot study conducted on patients with

chronic insomnia, exploring the effects of a six-week CBT-I programme on subjective and objective sleep characteristics.

Materials and methods: A total of 33 adult participants (21 – 59 years, $M = 39.7 \pm 9.5$) meeting the ICSD-3 criteria for chronic insomnia took part in the randomised, wait-list-controlled pilot trial. Participants were either allocated to an “Experimental” ($n = 17$) or “Waitlist” ($n = 16$) group. Participants completed two experimental nights separated by a 6-week intervention period, where participants in the “Experimental” group undertook a group CBT-I programme. During the experimental measurements, participants first undertook an evening exposure followed by a whole night polysomnography and subsequent morning exposure.

To contextualise the polysomnography findings, participants completed the Insomnia Severity Index (ISI), Beck Anxiety Inventory (BAI), Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), Hyperarousal Scale (HAS), Self-Assessment Manikin (SAM) at both pre- and post-intervention visits, providing trait-level and affective measures against which the effects of cognitive-behavioural therapy for insomnia (CBT-I) on REM-sleep microstructure could be interpreted.

Alongside this psychometric battery, each overnight polysomnography (PSG) night yielded several macro-structural indices—total sleep time (TST), wake after sleep onset (WASO), sleep efficiency (SE) and sleep-onset latency (SOL) as well as a profile of REM architecture, comprising REM latency, global phasic versus tonic REM percentages, REM arousal/density, and a band-specific micro-spectral decomposition of phasic and tonic REM (frontal/central alpha, beta, theta and delta relative power).

Results: The DBAS improved substantially - after CBT-I, the Time x Group interaction is statistically significant. BAI and ISI show promising trends, however, both interactions just miss conventional significance. Moreover, while non-significant hyper-arousal moves in the expected direction. SAM Intensity indicates a statistically significant Time x Group interaction while Valence and Arousal remain constant. Additionally, the Experimental group reports a statistically significant reduction in REM latency. Both phasic and tonic REM sleep percentages indicate a statistically significant Time x Group interaction, with phasic REM increasing and tonic REM decreasing in the Experimental group. A significant Time x Group interaction emerged in sleep-diary-based continuity (SOL, TST, SE and WASO) between the Experimental and Waitlist groups.

Conclusions: Along with the subjective and sleep-continuity outcomes, current findings suggest promising trends in exploring the REM sleep microstructure and indicate that the behavioural change of CBT-I potentially echoes the physiological change on the microstructural level. However, findings should be interpreted with caution due to their preliminary nature and the small sample size.

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The effect of home-based auditory sleep stimulation on chronic insomnia: preliminary findings

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Introduction: Closed-loop auditory stimulation (CLAS) is a promising non-invasive tool for studying and enhancing sleep. Chronic insomnia may be one candidate diagnosis that may be alleviated by CLAS. This study presents preliminary findings on the effectiveness and effects of a six-week CLAS program on both subjective and objective sleep characteristics in individuals with insomnia.

Materials and methods: A total of 14 participants (8 women, aged 21-44) with chronic insomnia took part in a within-subjects randomized crossover design. Each participant completed 3 weeks in the NREM stimulation condition and 3 weeks in the control condition. Sleep macrostructure indices assessed total sleep time (TST), wake after sleep onset, sleep efficiency, and time spent in each sleep phase. Furthermore, the slow oscillations amplitude and sleep spindle power were analysed. Analysed subjective sleep measures included the Insomnia Severity Index and Pittsburgh Sleep Quality Index.

Results: The effectiveness of CLAS in individuals with chronic insomnia was variable, with some patients demonstrating greater responsiveness than others. CLAS did not alter studied macro- or microstructural sleep indices. Notably, the overall TST was short due to limits of our data quality. Furthermore, CLAS showed no effect on subjective sleep quality or insomnia severity.

Conclusions: The study represents the first attempt to assess the long-term effects of CLAS on sleep in a home setting for individuals with insomnia. Preliminary results suggest that CLAS is effective but variable in delivery. CLAS did not alter artifact-free sleep macrostructure and did not produce any significant sleep improvements. However, these results should be interpreted with caution due to the small sample size and a high EEG signal variability, which may have introduced a measurement and stimulation error.

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The effects of Cognitive behavioral therapy for insomnia (CBT-I) and Tai Chi on mood symptoms and cognitive functioning in older adults with insomnia: A pilot study

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Introduction: Insomnia is prevalent in older adults. It is often accompanied by mood symptoms and poor cognitive functioning. While cognitive-behavioral therapy for insomnia (CBT-I) is considered the frontline treatment for adults with insomnia, Tai Chi (TC), a mind-body exercise, has emerged as a potential alternative intervention due to its documented health-related benefits, including improving sleep. However, there has been limited research comparing the effects of CBT-I and TC in addressing insomnia-related daytime symptoms and cognitive functioning among older adults. The present study aimed to compare the effects of CBT-I and TC on subjective sleep quality, mood symptoms, and cognitive functioning in older adults with insomnia.

Materials and methods: Forty-four participants with DSM-5 insomnia disorder (age:65.27±5.69, female:79.55%) were recruited. They received either CBT-I or TC (n=22 per group), both delivered over 3 months with two 60-min sessions each week. Sleep quality (Pittsburgh sleep quality index), mood symptoms (Hospital Anxiety and Depression Scale), and self-reported cognitive functioning (Cognitive Failure Questionnaire and Attention Function Index) were assessed at baseline and post-treatment. A mixed-design analysis of covariance (ANCOVA) was conducted, with time (baseline and post-treatment) as the within-subjects factor and group (CBT-I and TC) as the between-subjects factor, controlling for age and sex. Missing post-treatment data were imputed using the last observation carried forward method.

Results: There was a significant time*group interaction effect on sleep quality [$F(1, 42) = 7.102$, $p=0.011$, partial $\eta^2 = 0.165$] and cognitive failure [$F(1, 42) = 4.356$, $p=0.043$, partial $\eta^2 = 0.100$]. These results indicated that pre-post changes in sleep quality and cognitive functioning differed between the CBT-I and TC groups, where the CBT-I group showed greater improvement in sleep quality and the TC group showed greater improvement in cognitive functioning. In addition, there was a significant main effect of time on depressive symptom [$F(1, 42) = 5.428$, $p=0.026$, partial $\eta^2 = 0.138$] and anxiety symptom [$F(1, 42) = 4.183$, $p=0.048$, partial $\eta^2 = 0.107$], indicating mood symptoms improved significantly from pre- to post-treatment across both groups. There was a main effect of group on depressive symptoms [$F(1, 42) = 9.947$, $p=0.003$, partial $\eta^2 = 0.226$] and attention function [$F(1, 42) = 8.603$, $p=0.006$, partial $\eta^2 = 0.212$]. This result suggested that the TC group demonstrated fewer depressive symptoms and better attention across both pre- and post-treatment compared to the CBT-I group.

Conclusions: The findings of the current study highlighted the differential effects of CBT-I and TC in addressing sleep quality, mood symptoms and cognitive functioning. These findings collectively suggested that Tai Chi may serve as a valuable complementary intervention for elderly with insomnia, particularly for addressing mood and cognitive functioning. Further research is warranted to examine the sustainable effects of Tai Chi on mood symptoms and cognitive functioning and explore the potential mechanisms underlying these favorable outcomes.

The Effects of Lemborexant on Objective Sleep Parameters in Insomnia Patients Based on Sleep State Misperception

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Introduction: In insomnia patients, there is often a discrepancy between patient-reported (subjective) durations of sleep and objective sleep values. For those who underestimate their sleep, this may lead to high doses and/or multiple drug prescriptions, while those who overestimate their sleep may face increased mortality risk. For appropriate treatment of insomnia, improvement in objective sleep measures is necessary regardless of whether sleep state misperception is present. This is a challenge since polysomnography (PSG) is not standard of care and may not be reimbursable. However, no studies have examined the effects of hypnotics across different degrees of sleep state misperception. We investigated the effectiveness of lemborexant (LEM), a dual orexin-receptor antagonist, on objective total sleep time (TST), wake after sleep onset (WASO), and latency to persistent sleep (LPS) using PSG in groups with different degrees of sleep state misperception.

Materials and methods: Study E2006-G000-304 was a 1-month, randomized, double-blind, placebo (PBO)- and zolpidem extended-release (ZOL; not reported here)-controlled trial in patients aged 55 years and older who met *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, criteria for insomnia disorder with an Insomnia Severity Score ≥ 13 . Study drug (LEM 5 mg [LEM5]; LEM 10 mg [LEM10]; PBO; or ZOL) was taken immediately before bedtime. Participants completed a sleep diary each morning. Participants were classified into 3 groups of misperception index quartiles (Q; Q1: overestimation group, Q2-3: normal to moderate underestimation group, Q4: severe underestimation group) based on differences between baseline (BL) PSG (TST) and sleep diary values (subjective TST). Changes from BL (~2-week PBO run-in with BL PSG) in the average values of both days at Day 1/2 and Day 29/30 were compared for LEM5 and LEM10 versus PBO using a mixed-effects model for repeated measures. The trial was conducted with approval from the ethics review committee and with patients' voluntary consent, in accordance with relevant laws and regulations.

Results: A total of 712 patients were included (Q1/Q2-3/Q4: 183/353/176, respectively). Patient demographics were similar across the 3 groups, although Q1 had a higher proportion of patients aged over 75 years and Q4 had a higher proportion of females. At BL, mean TST for Q1/Q2-3/Q4 was 298.7/338.7/338.8 minutes, WASO was 135.8/104.6/105.8 minutes, and LPS was 50.1/42.9/41.0 minutes, respectively. Increases from BL in TST at each time point were greater in both LEM groups versus the placebo group across all Q1/Q2-3/Q4 groups. Decreases from BL in WASO and LPS at each time point were greater in both LEM groups compared with PBO across all Q1/Q2-3/Q4 groups. Changes in TST, WASO, and LPS tended to be greater in Q1 than in Q2-3 and Q4 for PBO and both LEM groups.

Conclusions: LEM improved objective sleep parameters in insomnia patients, regardless of the magnitude of sleep state misperception.

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The Effects of Lemborexant on Subjective Sleep Parameters in Insomnia Patients Based on Sleep State Misperception

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Introduction: It is reported that up to 56% of insomnia patients experience a discrepancy between subjective and objective sleep measurements (ie, sleep state misperception). There may be differences in treatment responsiveness depending on the degree of sleep state misperception. Under-estimators show better response to cognitive behavioral therapy for insomnia compared with over-estimators. However, no studies have examined subjective responses to pharmacotherapy across different degrees

of sleep state misperception. We investigated the effectiveness of lemborexant (LEM), a dual orexin-receptor antagonist, on subjective total sleep time (sTST), wake after sleep onset (sWASO), sleep onset latency (sSOL), and sleep quality (sQual) using sleep diaries in groups with different degrees of sleep state misperception.

Materials and methods: Study E2006-G000-304 was a 1-month, randomized, double-blind, placebo (PBO)- and zolpidem extended-release (ZOL; not reported here)-controlled trial in patients aged 55 years and older who met *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, criteria for insomnia disorder with an Insomnia Severity Score ≥ 13 . Study drug (LEM 5 mg [LEM5]; LEM 10 mg [LEM10]; PBO; or ZOL) was taken immediately before bedtime. Participants recorded sQual (scale from 1–9: 1=extremely poor; 9=extremely good) in a sleep diary each morning. Participants were classified into 3 groups based on baseline (BL) misperception index quartiles (Q) comparing objective values from polysomnography (TST) with sleep diary values (sTST; Q1: overestimation group, Q2–3: normal to moderate underestimation group, Q4: severe underestimation group). Changes from BL (7-day average during PBO run-in) in average values for the first and last 7 days of the month were compared for LEM5 and LEM10 versus PBO using a mixed-effects model for repeated measures. The trial was conducted with approval from the ethics review committee and with patients' voluntary consent, in accordance with relevant laws and regulations.

Results: A total of 712 patients were included (Q1/Q2–3/Q4: 183/353/176, respectively). Mean BL sTST for Q1/Q2–3/Q4 was 352.3/289.2/155.6 minutes, mean sWASO was 106.3/149.3/260.8 minutes, mean sSOL was 42.4/55.2/80.7 minutes, and mean sQual was 4.2/3.8/3.4 points, respectively. Increases (improvements) from BL in ratings of sQual at each time point were greater in both LEM5 (mean, first 7 days, Q1/Q2–3/Q4: 1.0/1.3/1.0; last 7 days: 1.5/1.6/1.1) and LEM10 (first 7 days: 1.0/1.2/1.2; last 7 days: 1.2/1.4/1.6) groups versus the PBO group (first 7 days: 0.3/0.7/0.6; last 7 days: 0.5/1.0/1.0) across all Q1/Q2–3/Q4 groups. Increases (improvements) from BL in sTST were greater in both LEM5 (least squares mean, first 7 days: 27.1/51.0/76.3; last 7 days: 43.2/60.6/93.4) and LEM10 (first 7 days: 37.3/60.2/111.9; last 7 days: 47.6/69.9/128.5) groups versus the placebo group (first 7 days: 11.7/30.5/57.7; last 7 days: 11.1/46.9/57.8) across all Q1/Q2–3/Q4 groups. Changes from BL in subjective sleep measures (sTST, sWASO, and sSOL) tended to be greater in Q4 compared with Q1 and Q2–3 for PBO and both LEM groups.

Conclusions: LEM improved subjective sleep parameters in insomnia patients, regardless of the magnitude of sleep state misperception.

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The Impact of Caregiving on Insomnia: Gender Differences, Long-Term Health Risks, Child Sleep Patterns, and Scalable Digital Interventions

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Introduction: Parents of young children often experience disrupted sleep due to nighttime awakenings, stress, and irregular schedules. These disturbances increase the risk of chronic insomnia and long-term health issues. Additionally, caregiver sleep behaviors significantly influence child sleep patterns, perpetuating an intergenerational cycle of sleep disruption.

While Cognitive Behavioral Therapy for Insomnia (CBT-I) is effective, caregivers face adherence challenges due to time constraints and competing demands. This study examines caregiver sleep behaviors, gender differences, long-term risks, and child sleep patterns while exploring scalable digital interventions to enhance treatment accessibility.

Materials and methods: A subset (20%) of 8,539 study participants were caregivers of young children. Their sleep patterns, behaviors, engagement with a digital CBT-I based program called Sleep Reset, and adherence were compared to non-caregivers (80%). Key variables included:

- **Sleep disruptions:** Nighttime awakenings, WASO, sleep efficiency, total sleep time.
- **Gender differences:** Variations in sleep disturbances, stress levels, and program adherence.
- **Behavioral factors:** Irregular schedules, caffeine/alcohol use, bedtime routines, wind-down activities.

- **Environmental influences:** Co-sleeping, bedroom noise, temperature, nighttime light exposure.
- **Psychological stressors:** Self-reported stress, racing thoughts, caregiving-related anxiety.
- **Health implications:** Fatigue, mood disturbances, weight changes, chronic stress.
- **Child sleep impact:** Consistency, nighttime awakenings, caregiver-reported disturbances.
- **Adherence analysis:** Sleep coaching engagement, confidence, dropout reasons.

Results:

- Caregivers had significantly higher sleep fragmentation than non-caregivers, with 70% waking at least once per night vs. 40% of non-caregivers.
- Gender disparities were notable. Female caregivers had longer WASO (45 min vs. 30 min for males), more stress-related awakenings, and lower adherence to structured sleep routines.
- Psychological stress was a major driver of sleep issues—78% of caregivers reported high stress and racing thoughts, leading to longer sleep latency and reduced sleep efficiency.
- Adherence to digital CBT-I based program was lower in caregivers (38% of females, 45% of males) compared to 60% of non-caregivers.
- Health risks included higher rates of fatigue (85%), mood disturbances (62%), and weight gain (45%).

Conclusions: Caregivers face persistent sleep challenges, with significant gender disparities and long-term health risks. Future digital insomnia interventions should be designed to meet caregivers' unique needs by integrating time-efficient, modular CBT-I based programs that fit into their demanding schedules.

The impact of insomnia disorder on the night and the day: analysis of polysomnography and subjective parameters from a large clinical trial database

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Introduction: Insomnia is a heterogenic disorder, and its characterisation could help tailor the management of subjects in clinical practice. Patients with insomnia disorder, in addition to sleep problems, also experience daytime impairment. However, studies investigating both the nocturnal and diurnal clinical profiles of patients with insomnia disorder are limited. This analysis aimed to comprehensively evaluate the demographic data and the objective and subjective clinical data assessing sleep and daytime functioning, collected from the large sample of subjects with insomnia disorder screened in the two phase 3 daridorexant trials.

Materials and methods: Both trials (NCT03545191, NCT03575104) were global, multicentre, randomised, double-blind, placebo-controlled trials that, when combined, screened approximately 7000 subjects aged ≥ 18 years with insomnia disorder (defined according to DSM-5 criteria, plus a self-reported history of ≥ 30 min to fall asleep, wake time during sleep ≥ 30 min, and subjective total sleep time [sTST] ≤ 6.5 h on at least 3 days/week and for at least 3 months). During the screening period (7-18 days), subjects performed a one-night polysomnography (PSG) assessment and completed a daily eDiary which included morning and evening visual analogue scales (VAS) and the Insomnia Daytime Symptoms and Impacts questionnaire (IDSIG; completed every evening). This analysis included all subjects screened with ≥ 1 data record on the selected parameters. Subjects with an apnoea or hypopnea index ≥ 15 events/hour or an event associated with oxygen saturation $< 80\%$, or with periodic limb movement index ≥ 15 events/hour, restless legs syndrome, circadian rhythm disorder, rapid-eye-movement behaviour disorder or narcolepsy were excluded.

Results: In total, 5474 screened subjects were included in the analysis (female: 66%, White: 83%; ≥ 65 years: 40%). Mean insomnia severity index score was 20.2 (SD 3.6), indicating moderate/severe intensity of insomnia symptoms (score ≥ 15). Among the objective PSG measures, mean latency to persistent sleep was 63.1 min (SD 61.7), mean wake after sleep onset was 102.6 min (SD 57.5), and mean TST was 320.5 min (SD 81.1). Subjects had on average 12.4 (SD 5.5) awakenings/night and 2.8 (SD 1.9) long wake bouts/night (> 6 min) with 92% having ≥ 1 long wake bout (PSG-assessed). Among

the subjective measures, patients reported a mean sTST of 325.5 min (SD 68.2), and poor quality and depth of sleep and moderate/severe morning sleepiness, as reflected by low mean VAS values (range 0-100; lower values indicate poorer outcomes) for all three parameters (quality of sleep: 38.7 [SD 16.9]; depth of sleep: 39.4 [SD 17.2]; morning sleepiness: 39.6 [SD 17.6]). IDSIQ total scores (range 0-140; lower scores indicate better patient-perceived daytime functioning) indicated moderate/severe daytime impairment (mean 71.6 [SD 22.5]). Mean VAS daytime ability to function (43.2 [SD 18.5]) and daytime alertness (41.6 [SD 18.8]) scores also indicated moderate/severe daytime impairment.

Conclusions: This large dataset provides much needed comprehensive data on the burden of insomnia disorder on daytime functioning and sleep from a broad population of patients. The further analysis of these data can help clinicians better understand the clinical profile and the needs of patients with insomnia disorder.

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The impact of insomnia disorder on the night and the day in males and females

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Introduction: Insomnia disorder, affecting approximately 10% of adults globally, is prevalent in both men and women, although it occurs approximately 50% more frequently in women. However, studies investigating potential sex-related differences in the clinical manifestation of insomnia and its impact on daytime remain limited. Using the large dataset of screened patients with insomnia disorder from the daridorexant phase 3 clinical program, this analysis assesses nocturnal and diurnal clinical characteristics of males and females with insomnia disorder.

Materials and methods: Analyses by sex (male: n=1845 [34%]; female: n=3629 [66%]) were performed on data from 5474 screened patients from the two global, randomised, double-blind, placebo-controlled trials (NCT03545191, NCT03575104) in adults (≥18 years) with insomnia disorder. Insomnia disorder was defined according to DSM-5 criteria, plus a self-reported history of ≥30 min to fall asleep, wake time during sleep ≥30 min, and subjective total sleep time [sTST] ≤6.5 h on ≥3 days/week and for ≥3 months. During the screening period, subjects underwent a one-night polysomnography (PSG) and completed a daily eDiary that included morning and evening visual analogue scales (100 mm VAS) and the Insomnia Daytime Symptoms and Impacts questionnaire (IDSIQ [range: 0-140]). This analysis included all subjects screened with data records on selected parameters and without an apnoea/hypopnea index ≥15 events/hour or an event associated without oxygen saturation <80%, periodic limb movement index ≥15 events/hour, restless legs syndrome, circadian rhythm disorder, rapid-eye-movement behaviour disorder or narcolepsy.

Results: At screening, mean (SD) insomnia severity index score was 19.8 (3.8) in males and 20.4 (3.5) in females, indicating moderate/severe insomnia in both subgroups. Among objective PSG measures, males had a numerically shorter TST than females (mean [SD]: 312 [82] vs 324 [80] min). This was due primarily to a longer wake after sleep onset (WASO) in males (110 [59] vs 99 [57] min), particularly during the last two quarters (Q) of the night (Q3: 31.6 [27.0] vs 28.6 [27.3] min; Q4: 43.2 [32.1] vs 36.4 [28.6] min). Latency to persistent sleep was comparable (male vs female: 65 [63] vs 62 [61] min). There were no notable differences in PSG-reported total wake bouts (32 vs 29) or wake-bout mean duration (4.7 vs 4.4 min).

No sex-related differences were observed among subjective measures. Unlike TST, mean sTST was comparable in males and females (325 [66] vs 326 [69] min). IDSIQ total score (male vs female: 73 [23] vs 71 [22]), and VAS scores for quality of sleep (38 [17] vs 39 [17]), depth of sleep (39 [17] vs 40 [17]), daytime alertness (41 [19] vs 42 [19]), ability to function (42 [19] vs 44 [18]) and morning sleepiness (39 [17] vs 40 [18]) were all comparable.

Conclusions: These data indicate that insomnia disorder negatively impacts sleep and daytime functioning in males and females with no apparent sex-related differences in subjective parameters. Additionally, PSG data suggest that males may tend to overestimate their sTST since they have longer WASO than females, mainly in the latter part of the night.

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The impact of insomnia disorder on the night and the day in older and younger adults

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Introduction: The burden of insomnia increases with age; however, it remains unclear whether differences exist in subjective and objective sleep parameters between older and younger adults. Furthermore, data on how insomnia disorder affects the day of older and younger adults are limited. The large dataset of screened patients with insomnia disorder from the daridorexant phase 3 clinical program provides comprehensive data to address these gaps. Using these data, this analysis assesses the nocturnal and diurnal clinical characteristics of patients aged ≥ 65 years ("older") and those < 65 years ("younger" adults).

Materials and methods: Analyses by age group (≥ 65 years $n=2178$ [40%]; < 65 years: $n=3296$ [60%]) were performed on data from screened patients from the two global, randomised, double-blind, placebo-controlled trials (NCT03545191, NCT03575104) in adults (≥ 18 years) with insomnia disorder. Insomnia disorder was defined according to DSM-5 criteria, plus a self-reported history of ≥ 30 min to fall asleep, wake time during sleep ≥ 30 min, and subjective total sleep time [sTST] ≤ 6.5 h on ≥ 3 days/week and for ≥ 3 months. During the screening period, subjects underwent a one-night polysomnography (PSG) and completed a daily eDiary that included morning and evening visual analogue scales (100 mm VAS) and the Insomnia Daytime Symptoms and Impacts questionnaire (IDSIQ; completed each evening [range 0-140]). This analysis included all subjects screened with data records on the selected parameters. Subjects with significant sleep comorbidities (obstructive sleep apnea, periodic limb movements, restless legs syndrome, circadian rhythm disorder, rapid-eye-movement behaviour disorder or narcolepsy) were excluded.

Results: At screening, mean (SD) insomnia severity index score was 19.5 (3.6) and 20.6 (3.5) in older and younger adults, respectively, indicating moderate/severe insomnia in both subgroups. Among objective PSG measures, mean (SD) total sleep time (TST) was numerically lower (298 [83] vs 334 [77] min) in older vs younger adults, due to a greater mean wake after sleep onset (123 [59] vs 90 [53] min); latency to persistent sleep was comparable (64 [64] vs 62 [60] min). Rapid eye movement duration was numerically shorter in older vs younger adults (53 [27] vs 63 [27] min). Among subjective measures, older and younger subjects reported a similar mean sTST (326 [67] vs 325 [69] min). Comparing objective to subjective measures, younger adults quantified the duration of sleep accurately, whereas older adults tended to overestimate it. IDSIQ total score was numerically lower (i.e. better) in older versus younger adults (66.3 [(21.9)] vs 74.9 [22.2]). VAS scores for quality of sleep (41.9 [16.5] vs 36.8 [16.8]), depth of sleep (42.4 [16.7] vs 37.6 [17.2]), daytime alertness (46.5 [18.2] vs (38.7 [18.6]), ability to function (47.6 [17.9] vs 40.5 [18.4]) and morning sleepiness (44.4 [17.2] vs 36.7 [17.1]) were all numerically higher (i.e. better) in older adults versus younger adults.

Conclusions: These data show that insomnia disorder negatively impacts sleep and daytime functioning in the two age subgroups, with more severe deficits in objective sleep parameters in older adults but less severe deficits in daytime functioning, as compared to younger adults.

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The Impact of Insomnia on Cardiometabolic Health: Importance of Sleep Assessment

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Introduction: Insomnia, characterized by difficulty initiating or maintaining sleep, or early morning awakenings, affects up to one-third of adults. Emerging evidence identifies insomnia as a significant, modifiable risk factor for cardiometabolic diseases, including type 2 diabetes, cardiovascular disease,

chronic kidney disease, and metabolic dysfunction-associated steatotic liver disease (MASLD). Insomnia is associated with increased sympathetic nervous system activity, dysregulation of the hypothalamic-pituitary-adrenal axis, and elevated inflammatory markers, all of which contribute to cardiometabolic risk. Evidence suggests that insomnia significantly impacts glucose metabolism, insulin resistance, and the development of type 2 diabetes. Additionally, insomnia is linked to obesity, MASLD, and cardiovascular diseases such as hypertension, myocardial infarction, and heart failure. Despite its prevalence and impact on health, insomnia remains underdiagnosed and inadequately managed. Integrating sleep health into cardiometabolic care is crucial for reducing the global burden of chronic diseases. Healthcare providers should prioritize screening for insomnia and implementing evidence-based management strategies to improve patient outcomes.

Materials and methods: Objective: This multiphase study aimed to assess the feasibility and need for sleep assessment in specialist clinics and to empower healthcare providers in primary care networks through knowledge translation of phase one of the study.

Methods: The study was conducted in two phases. Phase one involved assessing the feasibility and need for sleep assessments in specialty endocrinology clinic. Data were collected from 69 patients with diabetes and/or obesity, focusing on their sleep patterns, satisfaction with sleep, and the impact of sleep problems on daily functioning. Phase two involved knowledge translation to healthcare providers in primary care networks, aiming to empower them with the findings from phase one to improve sleep health management.

Results: Only 46% of patients reported that their sleep was assessed by their primary care physician or nurse practitioner before the study. Surprisingly, 9% of patients were required and agreeable to start on medication but 23% of patients preferred to talk to their primary care health providers (e.g. GP, NP) about their sleep issues. Around 70% of patients agreed that asking about their sleep helped them understand its importance. Overall, majority of patients were satisfied or very satisfied with their sleep being assessed at the specialty endocrinologist clinic.

The knowledge translation phase aimed to empower healthcare providers in primary care networks with the findings from phase one. This phase included training sessions and distribution of educational materials. Post survey revealed that the degree of comfort level increased after staff received education.

Conclusions: The study highlights the critical need for integrating sleep assessments into specialist clinics and empowering primary care providers through knowledge translation. Addressing insomnia in patients with cardiometabolic diseases can significantly improve patient outcomes and potentially reduce the global burden of chronic diseases. Healthcare providers should prioritize sleep health as a fundamental component of cardiometabolic care.

The Impact of Lemborexant on Gut Microbiota Composition in Insomnia Treatment

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Introduction: Emerging research highlights the gut microbiota's critical role in sleep regulation through the microbiota-gut-brain axis. While sleep restriction shows minimal microbiome alterations, insomnia is characterized by reduced microbial diversity. Lemborexant, an innovative insomnia treatment, has demonstrated promising improvements in sleep parameters. This study investigates how lemborexant might modulate gut microbiota composition and explores the intricate relationship between sleep medication and the microbiome.

Materials and methods: A prospective study was conducted on 29 adults aged 50 and older with insomnia. These individuals were participants in the FLUID study, which explored lemborexant's potential to improve sleep. Participants initially received a 5 mg dose of lemborexant for 12 weeks, with the option to increase to 10 mg if symptoms did not improve, after consulting with a physician. Throughout the study, existing medication doses remained unchanged, and participants' lifestyle and

dietary habits were monitored during each visit. The comprehensive study included sleep electroencephalography and stool microbiome analyses at baseline, 4 weeks, and 12 weeks of open-label lemborexant treatment. Researchers used 16S rRNA sequencing to examine microbial composition and performed metabolite analysis of short-chain fatty acids (SCFAs). The study received ethical approval from the Nagoya University Clinical Research Review Board.

Results: Beta diversity, assessed by Jaccard dissimilarity, significantly increased at week 12 compared to week 4. The Firmicutes/Bacteroidetes ratio was significantly elevated at week 12 relative to baseline. At the taxonomic level, *Tannerellaceae Parabacteroides* remained significantly different at week 12 after statistical correction. Notably, *Parabacteroides* showed a significant decrease throughout the study period. The *Anaerovoracaceae Family XIII AD3011 group* demonstrated persistent, albeit not statistically significant, increases. Additional exploratory trends included potential increases in *Streptococcus*, *Akkermansia*, and *Lactobacillales*, though these did not consistently reach statistical significance. No significant variations in SCFAs were detected during the treatment period.

Conclusions: Our findings suggest that prolonged lemborexant treatment in individuals with insomnia may induce subtle yet meaningful shifts in gut microbiota composition. The significant decrease in the genus *Parabacteroides* is particularly interesting given that it is associated with an increase when sleeping less than 6 hours in a mouse study. This highlights the potentially complex interactions between hypnotic medications and gut microbial ecology, offering a promising avenue for future research into the microbiota-sleep relationship.

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The impact of sleep duration, sleep debt and insomnia on infection risk: A longitudinal cohort study with one-year follow-up

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Introduction: Insufficient sleep is associated with increased risk of mental and somatic disorders, such as depression, anxiety, obesity, diabetes, cardiovascular disorders, and cancer. Whether insufficient sleep increases the risk of infections has received less attention. The objective of this study was to investigate whether self-reported short and long sleep duration, different levels of sleep debt (difference between subjective sleep need and sleep duration), and insomnia severity at baseline would predict increased prevalence of different types of infections at one-year follow-up.

Materials and methods: From March 2022 to January 2023, participants aged 25-70 years were recruited from the Norwegian Primary Care Research Network (PraksisNett) to complete a baseline survey about sleep. One year later, they were invited to a follow-up survey. In total, 861 participants completed the baseline survey and the response rate at follow-up was 60.5%, rendering 521 participants eligible for the present study. At baseline the participants completed questions about sleep habits and insomnia symptoms (Insomnia Severity Index, ISI), and at follow-up they responded to whether they had experienced various infections during the last three months and whether they experience more infections than peers. Data were analyzed with chi-square tests and logistic regressions, adjusted for gender, age, and children living at home.

Results: In general, participants with normal sleep duration (6-9 hours), no sleep debt and no insomnia (ISI <8) at baseline reported the lowest prevalences of infections at one-year follow-up. In the adjusted logistic regression analyses, long sleep duration (>9 hours) increased the odds of influenza-like illness (odds ratio 3.99, 95% confidence interval 1.13-14.11), gastrointestinal infection with vomiting and/or diarrhea (4.31, 1.25-14.86), and experiencing more infections than peers (3.74, 1.09-12.82), whereas short sleep duration (<6 hours) doubled the odds of skin infection (2.03, 1.22-3.38). Compared to no sleep debt, ≤2 hours of sleep debt doubled the odds of skin infection (2.13, 1.21-3.74) and >2 hours of sleep debt tripled the odds of experiencing more infections than peers (2.95, 1.46-5.96). Insomnia (ISI 15-28) increased the odds of any type of infection (1.95, 1.10-3.45) and influenza-like illness (1.96, 1.16-3.33), and more than tripled the odds of gastrointestinal infection (3.54, 1.84-6.79) and experiencing more infections than peers (3.09, 1.73-5.51). Subthreshold insomnia (ISI 8-14) increased

odds of gastrointestinal infection (2.35, 1.32-4.19) and experiencing more infections than peers (1.68, 1.01-2.79).

Conclusions: This longitudinal study supports the notion that people who have insufficient sleep are at increased risk of contracting infections. Sleep debt and insomnia severity dose-dependently increased the prevalence of some of the reported infections.

The Impact of Sleep Vulnerability on Sleep Misperception in Healthy Adults

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Introduction: Sleep misperception, defined as the discrepancy between subjective and objective sleep, is commonly observed in individuals with insomnia but remains poorly understood. It may represent a premorbid trait of insomnia or develop over the course of chronic insomnia. Stress-related sleep vulnerability, defined as the tendency to experience sleep disruption under stress, is considered a predisposing trait for insomnia. Previous studies have reported that various stress conditions can enhance sleep misperception. Thus, sleep vulnerability may be associated with heightened sensitivity to minor sleep disturbances under stress, leading to distorted sleep perception. Therefore, the present study aims to examine the association between sleep vulnerability and sleep misperception, to determine whether sleep misperception is a predisposing trait of insomnia linked to sleep vulnerability.

Materials and methods: Thirty-five healthy participants without reported sleep disturbances (M:F = 1.7:1.8; mean age = 23.91 ± 3.54) completed the Ford Insomnia Response to Stress Test (FIRST) to assess their sleep vulnerability. They also wore an actigraphy device and completed a sleep diary for seven days. Sleep onset latency (SOL), total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE) were derived from both actigraphy and sleep diaries. The 7-day average discrepancies between subjective and objective measures were calculated. The index of sleep misperception used included: 1) subjective values minus objective values, 2) the discrepancy between subjective and objective values divided by the objective values, 3) subjective values divided by objective values. Pearson's correlation between sleep vulnerability and indices of sleep misperception were conducted.

Results: The results showed no significant correlations between the FIRST score and all the indices of sleep misperception of SOL, TST, WASO and SE.

Conclusions: The findings suggest that sleep vulnerability under stress in healthy populations is not associated with sleep misperception. Sleep misperception does not appear to be a characteristic of individuals predisposed to developing insomnia, but rather may emerge over the course of chronic insomnia. Future research could benefit from investigating these relationships in clinical populations or under experimentally induced stress conditions.

The link between improvement in sleep and depressed mood: Exploring the role of repetitive negative thinking and behavioural activation

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Introduction: There is extensive evidence supporting a link between poor sleep and worse depression outcomes. Moreover, improvement in sleep disturbance contributes to enhanced depression outcomes. However, processes underlying this sleep–depression link are unclear. The current study examined whether changes in potential underlying processes, namely repetitive negative thinking (RNT) and behavioural activation (BA) can explain the relationship between improvement in reported sleep disturbance (reduction in the number of days participants experience sleep difficulties) is related to improvement in depressed mood.

Materials and methods: Data were analysed from 127 participants (mean [SD] age 39.16 [14.81], 60.6% women) who attended a group CBT mood management program at a government mental health

service. Pre and post-treatment changes in depressed mood were assessed using PROMIS-D, whilst the frequency of participants' sleep difficulties was assessed via CUDOS item 5 (sleep item).

Results: Our study found a significant association between improvement in sleep difficulties and improvement in depressed mood, however, this relationship was no longer significant (no direct association) when controlling for improvements in RNT, $ab = 0.56$, CI [0.21, 1.01], and BA, $ab = 1.08$, CI [0.41, 1.84]. Furthermore, 1 SD improvement in sleep was indirectly associated with a 1.83-point change in depressed mood (a 0.612-point improvement in depression via RNT, and a 1.22-point improvement in depression via BA).

Conclusions: The preliminary findings suggest that reduced RNT and enhanced BA may play an important role in explaining how improvement in sleep is related to improvement in depressed mood. Future research should investigate whether early improvements in sleep contributes to subsequent improvements in depressed mood via improvements in RNT and BA. To establish temporal ordering and assess causality, future studies should collect data across multiple time points and incorporate a more comprehensive measure of sleep.

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The mediating role of impulsivity on the association of insomnia with suicidal ideation: A national study of Chinese population

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Introduction: Increasing evidence suggests that insomnia is one of the key risk factors of suicidal ideation. However, the underlying mechanisms remain unclear. Previous studies indicated that impulsivity might be the associations of both insomnia and suicidal ideation. Therefore, the current study aimed to determine the mediating role of impulsivity in the association between insomnia and suicidal ideation.

Materials and methods: This study is a cross-sectional study, with data extracted from the national prospective cohort study, Digital multi-modal approaches to subtyping insomnia disorder (DiMOSI). A total of 1924 adult participants with diagnosis of insomnia disorder (65.9% female, age: 35.9 ± 12.1 years old) were recruited. All the participants were invited to accomplish the standardized questionnaires of severity of insomnia (Insomnia Severity Index, ISI), impulsivity (Barratt Impulsiveness Scale-11, BIS-11), suicidal ideation (Beck Scale for Suicidal Ideation, BSI), and demographics. Mediation analysis was conducted by the PROCESS in SPSS 26.0.

Results: A significant total effect of severity of insomnia on suicidal ideation was found ($\beta = 0.16$, 95% CI: 0.12-0.20). Impulsivity partially mediated the association, with a significant indirect effect ($\beta = 0.02$, 95% CI: 0.01-0.03). In the mediating model, the direct effect remained significant ($\beta = 0.14$, 95% CI: 0.10-0.18), suggesting additional pathways beyond impulsivity. The model explained 11.85% of the variance in suicidal ideation ($R^2 = 0.1185$). In terms of the two dimensions of impulsivity, including non-planning impulsiveness and motor impulsiveness, both of them partially mediated the association of severity of insomnia on suicidal ideation as well.

Conclusions: These findings highlight impulsivity as a modifiable target for suicidality intervention, especially among those suffering insomnia disorder. Moreover, interventions of each components of impulsivity might reduce suicidal ideation. Further cohort studies and randomized controlled clinical trials are warrant.

Acknowledgments: insomnia, impulsivity, suicidal ideation, mediation analysis

The Moderating Effect of Chronotype on the Relationship Between Insomnia Severity and Working Memory Performance in Youths

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Introduction: Insomnia is highly prevalent among youths and adversely affect their neurocognitive development and daily functioning. Youth is also characterized by an increased preference for eveningness, often leading to a misalignment between sleep schedule and early school times, as well as other societal demands. Increased eveningness has been linked to higher levels of insomnia severity and may compromise neurocognitive development. While both insomnia severity and chronotype have independently been linked to cognitive deficits in youth, the interplay between these factors—especially on working memory—remained underexplored. The present study aimed to examine whether chronotype moderated the association between insomnia severity and working memory performance in youth.

Materials and methods: A total of 154 participants meeting DSM-5 insomnia disorder (mean age: 19.87, SD = 2.10, 62.7% female) were included in the present analyses. 73 (47.4%) participants were classified as eveningness (E-group) (Reduced Morningness–Eveningness Questionnaire, rMEQ, rMEQ score ≤ 11), and 81 (52.6%) participants were classified as morningness or neither type as Non-Eveningness (Non-E group) (rMEQ score > 11). Participants completed self-reported measures for insomnia severity (Insomnia Severity Index, ISI), depression (Hospital Anxiety and Depression Scale–Depression subscale, HADS-D) and anxiety (Hospital Anxiety and Depression Scale–Anxiety subscale, HADS-A). Working memory was objectively assessed by Digit Span Task and Dual N-back Task. Multiple linear regression models were used to examine the moderation effect of chronotype on the relationship insomnia severity and working memory performance, controlling for timing of cognitive assessment, depression and anxiety.

[Table 1: Sample Characteristics](#)

Results: There were significant Chronotype $\times$ Insomnia Severity interactions on both forward digit span ($F(1,100) = 6.47, p = .013$), and accuracy in N-back task (2-back, $F(1,121) = 6.55, p = .012$). For the youths with eveningness chronotype, greater insomnia severity was significantly associated with worse working memory, including poorer performance on forward digit span ($\beta = -0.11, p = .015$) and lower accuracy on the 2-back d-prime score ($\beta = -0.09, p = .014$), whilst no significant association between insomnia severity and working memory performance was found among those with non-eveningness (all $p > 0.05$).

[Table 2: Multiple Linear Regression Outcome; Figure 1-2: Moderation Effect Graphs; Figure 3: Illustration of N-back Test.](#)

Conclusions: The findings showed the moderating role of chronotype on the association between insomnia severity and working memory performance in youths with insomnia disorder. This study underscored the need to consider circadian preferences when assessing insomnia-related cognitive deficits in youth. Future research may explore whether interventions integrating both sleep and circadian components could improve cognitive functioning in youths with insomnia and eveningness.

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Transcranial Alternating Current Stimulation (tACS) for Chronic Primary Insomnia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials on Efficacy

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Introduction:

Chronic primary insomnia is a pervasive sleep disorder with limited effective non-pharmacological treatments. Transcranial alternating current stimulation (tACS) has emerged as a potential neuromodulatory therapy, but its efficacy remains inconclusive due to variability in study designs and

small sample sizes. This meta-analysis synthesizes evidence from randomized controlled trials (RCTs) to evaluate the effects of tACS on sleep quality and architecture in chronic primary insomnia.

Materials and methods:

A systematic search of PubMed, Cochrane Library, ScienceDirect, and Scopus was conducted through May 2025, following PRISMA guidelines. Included were randomized controlled trials (RCTs) involving tACS intervention in chronic primary insomnia patients compared to sham. Four RCTs (n=131 participants) were included. Pooled mean differences (MD) with 95% confidence intervals (CI) were calculated using a random-effects model due to high heterogeneity. Outcomes were synthesized for PSQI, sleep onset latency (SOL) in minutes, total sleep time (TST) in hours, and sleep efficiency (SE) in percentage. Risk of bias was assessed using the Cochrane RoB 2 tool.

Results: tACS demonstrated significant improvements across all measured sleep parameters in patients with chronic primary insomnia. PSQI scores improved markedly with tACS (MD = -4.02, 95% CI [-6.55, -1.30], $p = 0.008$), though substantial heterogeneity was observed ($I^2 = 95\%$). SOL decreased by an average of 28.55 minutes (MD = -28.55, 95% CI [-35.56, -21.53], $p < 0.00001$), with moderate heterogeneity ($I^2 = 81\%$). TST increased by 0.62 hours (MD = 0.62, 95% CI [0.39, 0.86], $p < 0.00001$), similarly accompanied by high heterogeneity ($I^2 = 81\%$). SE also showed improvement (MD = -0.93%, 95% CI [-1.45, -0.42], $p = 0.0004$), but results were highly variable across studies ($I^2 = 91\%$). All studies have low risk of bias.

Conclusions: tACS appears to be a promising intervention for improving sleep quality, latency, duration, and efficiency in chronic primary insomnia, despite significant heterogeneity among studies. tACS likely improves insomnia by modulating hyperactive thalamocortical circuits and enhancing slow-wave/alpha oscillations, promoting sleep initiation and maintenance. Unlike pharmacotherapy, it offers targeted neuromodulation without systemic side effects. While high heterogeneity exists due to variable protocols, consistent improvements in sleep latency, duration, and quality support its therapeutic potential. These findings support further large-scale, standardized RCTs to optimize tACS protocols and confirm clinical applicability.

Treatment response, remission, and adherence across the delivery methods of cognitive behavioral therapy for insomnia: A systematic review and meta-analysis

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Introduction: Previous meta-analyses of cognitive behavioral therapy for insomnia (CBT-I) have not clarified the treatment response levels and dropout rates across different CBT-I delivery methods. This study aims to address these gaps in the literature and identify patients who would benefit most from various CBT-I formats.

Materials and methods: A literature search was conducted in PubMed, PsycINFO, and Embase on November 6, 2023 (The search is currently being updated, and more recent data will be available at the presentation.). CBT-I was defined as incorporating both sleep restriction and stimulus control techniques. This study included randomized controlled trials using individual, group, fully automated Internet-based, or supported Internet-based formats. Treatment response was defined as a decrease of 8 or more points in the Insomnia Severity Index from baseline to end of treatment (Morin et al., 2011). Remission from insomnia symptoms was evaluated at the end of treatment. When the number of remitters and/or responders were not reported in the original publications, it was estimated based on self-reported scale values at the end of treatment (Furukawa et al., 2005). Adherence was assessed using dropout rates, with dropouts were defined as participants who did not complete the assigned treatment. Odds ratio (OR) was used to synthesize outcome measures. In meta-regression analyses, each outcome measure was used as the dependent variable, and the delivery methods of CBT-I, comorbidities, and types of control groups were used as independent variables.

Results: A total of 120 trials from 110 studies were analyzed, with 15,060 participants (65.7% female, 27.9% male, 6.4% unknown/other). Treatment response was significantly higher in all delivery methods of CBT-I compared with the control group (overall: OR = 6.84 [5.56, 8.40]; individual: OR = 8.51 [5.94, 12.19]; group: OR = 8.12 [4.38, 15.05]; fully automated Internet-based: OR = 5.23 [3.95, 6.94]; supported Internet-based: OR = 8.54 [5.50, 13.27]). Meta-regression analysis showed that fully automated Internet-based CBT-I, presence of psychiatric diseases, and active treatment control were significantly negatively associated with treatment response. Remission was significantly higher in all delivery methods of CBT-I compared with the control group (overall: OR = 5.53 [4.62, 6.61]; individual: OR = 7.76 [5.70, 10.57]; group: OR = 5.13 [3.16, 8.35]; fully automated Internet-based: OR = 4.39 [3.39, 5.67]; supported Internet-based: OR = 7.31 [5.10, 10.48]). Meta-regression analysis showed that fully automated Internet-based CBT-I and presence of psychiatric diseases were significantly negatively associated with remission. Dropout rates significantly increased for Internet-based formats (overall: OR = 1.36 [1.14, 1.62]; fully automated Internet-based: OR = 1.87 [1.42, 2.47]; supported Internet-based: OR = 1.63, 95% CI [1.07, 2.49]; individual: OR = 0.94 [0.69, 1.27]; group: OR = 0.97 [0.73, 1.29]). Meta-regression analysis showed that Internet-based formats and presence of psychiatric diseases were significantly positively associated with dropout rate.

Conclusions: CBT-I is consistently effective in improving insomnia symptoms, regardless of the delivery method. Importantly, individuals who do not respond to the Internet-based format may require an individual approach. Additionally, it is necessary to devise strategies to prevent dropout, especially in Internet-based interventions.

Ultrasound-Guided Stellate Ganglion Block Combined with Cervicotemporal Myofascial Trigger Point Needling in Insomnia with Anxiety and Depression: A Retrospective Study

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Introduction: This retrospective study aimed to investigate the therapeutic potential of integrating ultrasound-guided stellate ganglion block (SGB) with cervicotemporal myofascial trigger point (MTrP) needling for patients with insomnia accompanied by anxiety and depression, proposing a novel multimodal intervention to enhance treatment outcomes.

Materials and methods: A total of 42 patients diagnosed with insomnia accompanied by anxiety and depression at the Anesthesia and Sleep Medicine Department of Shandong Second Provincial General Hospital between November 2024 and February 2025 were included. The patients were treated by ultrasound-guided SGB combined with MTrP needling. Ultrasound-guided SGB was performed through bilateral alternating injections of 4 mL 1% lidocaine, once daily for a total of 8 sessions. Cervicotemporal MTrP needling targeted the upper scalene (C2/C4 anterior tubercle), sternocleidomastoid (mid-internal border), upper trapezius, and temporalis trigger points. Disposable sterile 0.35 × 50 mm needles were used for percutaneous multidirectional stimulation of the targeted sites, followed by rapid punctures (7–10 insertions per MTrP) at twitch-response points, and then hemostatic compression was applied for 30 seconds to stop any bleeding. Needling was performed once per week for 3 consecutive weeks. The outcome of the combination therapy was evaluated by comparing changes in Pittsburgh Sleep Quality Index (PSQI), Hamilton Anxiety Scale (HAMA), and Hamilton Depression Scale (HAMD) scores after 4 weeks of treatment.

Results: All 42 patients met the inclusion criteria for insomnia with anxiety and depression. Post-treatment analysis revealed statistically significant reductions in PSQI ($P < 0.05$), HAMA ($P < 0.05$), and HAMD ($P < 0.05$) scores compared to pre-treatment values.

Conclusions: Ultrasound-guided SGB combined with cervicotemporal MTrP needling demonstrates clinically meaningful improvements in sleep architecture and symptoms of anxiety and depression, with minimal adverse reactions.

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Ultrasound-Guided Stellate Ganglion Block Combined with Myofascial Trigger Point Needling for Refractory Insomnia with Depression: A Case Report

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Introduction: To investigate the clinical efficacy of ultrasound-guided stellate ganglion block (SGB) combined with myofascial trigger points (MTrPs) needling in a patient with refractory insomnia and comorbid depression, and to explore the regulatory effects of this combined therapy on prefrontal cortex functional activity of the patient.

Materials and methods: The patient was a 58-year-old female, presented with a 10-year history of insomnia accompanied by depressed mood, exacerbated over the past year, with poor response to hypnotic medications and antidepressants. The diagnosis was refractory insomnia and depression. Following informed consent, the patient received ultrasound-guided SGB (administered alternately on left and right sides, once daily for 8 consecutive sessions) combined with MTrPs needling targeting the cervical and temporal regions (including the upper part of scalene muscle at C2 and C4 anterior tubercles, the medial border of the sternocleidomastoid muscle, the upper trapezius, and the temporal muscle; administered once a week for 3 sessions). Pre- and post-treatment Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Scale (HAMD), and Hamilton Anxiety Scale (HAMA) scores were collected and analyzed to evaluate the therapeutic effects on the sleep architecture and affective symptoms of the patient. Functional near-infrared spectroscopy (fNIRS) was employed to analyze prefrontal cortex functional activity.

Results: The patient demonstrated immediate sleep improvement on the day of initial treatment. After two weeks of intervention, significant improvements were observed in both insomnia and depressive symptoms. Comparative analysis revealed statistically significant reductions in PSQI, HAMD, and HAMA scores, indicating substantial improvements in sleep quality and affective symptoms. fNIRS data demonstrated markedly increased oxyhemoglobin (HbO) concentration in the prefrontal cortex region following treatment, suggesting enhanced prefrontal activation.

Conclusions: This case provides neuroimaging evidence supporting the "hyperarousal" hypothesis in insomnia with comorbid depression, confirming the pivotal role of prefrontal cortex in sleep-wake regulation. The findings elucidate the neurofunctional mechanisms underlying the therapeutic effects of ultrasound-guided SGB combined with MTrP needling, offering novel insights for treatment target selection in refractory insomnia.

Acknowledgments: The authors would like to thank Dr Zheping Chen, Shanghai Key Laboratory of Anesthesiology and Brain Functional Modulation, Translational Research Institute of Brain and Brain-Like Intelligence, Clinical Research Center for Anesthesiology and Perioperative Medicine, Department of Anesthesiology and Perioperative Medicine, Shanghai Fourth People's Hospital, School of Medicine, Tongji University, Dr Zhenzhen Li and Dr Lifeng Wang, Department of Anesthesiology, Shandong Second Provincial General Hospital for their helpful advice.

Validation and reliability of a Thai version of The Insomnia Severity Index

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Introduction: Insomnia is highly prevalent worldwide and has a significant impact on health outcomes. However, it is often underrecognized and untreated, as its diagnosis typically requires a comprehensive medical evaluation by experienced professionals. The Insomnia Severity Index (ISI) is a brief self-assessment tool specifically designed for screening and evaluating the severity of insomnia. This study aimed to translate and validate the ISI into a Thai version to enhance insomnia patient care in Thailand.

Materials and methods: Thai version of insomnia severity index (Thai-ISI) was developed under a standard linguistic translation protocol. Validity with Thai-Pittsburgh Sleep Quality Index (Thai-PSQI) and Thai-Athens Insomnia scale (Thai-AIS) was tested. Test-retest reliability was evaluated at 2–4-week interval.

Results: A total of 72 adult participants (70% female) with insomnia complaint were recruited. Twenty-nine percent had comorbid obstructive sleep apnea and 47.2% reported a history of sleep medication use. Based on the Thai-ISI, most participants ($n = 42$, 58.3%) were classified as having clinically significant insomnia. Thai-ISI demonstrated a strong correlation with the Thai-Athens Insomnia Scale (Thai-AIS) ($r = 0.784$, $p < 0.01$) and a moderate correlation with the Thai-Pittsburgh Sleep Quality Index (Thai-PSQI) ($r = 0.44$, $p < 0.01$). Cronbach's alpha of 0.703 indicated good internal consistency of the questionnaire items. Pearson's correlation for test-retest reliability of the total Thai-ISI score was 0.638 ($p < 0.01$) also reflexed good consistency.

Conclusions: We demonstrated validity and reliability of Thai-ISI. The data also supported the utility of Thai-ISI for capturing insomnia in Thai subjects with and without co-morbidity.

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Wearable sleep tracking in digital CBT-I: Clinical impact and the subjective-objective sleep discrepancy

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Introduction: Insomnia is a prevalent disorder, affecting up to 30% of the population, and is associated with poor physical and mental health outcomes. Cognitive Behavioral Therapy for Insomnia (CBT-I) is the first-line treatment, but its accessibility is limited by a shortage of trained providers and high costs. Digital Cognitive Behavioral Therapy for Insomnia (dCBT-I) has emerged as an effective and scalable alternative.

Wearable devices are increasingly used to track sleep patterns, offering objective data on sleep parameters. However, how well these wearable-derived sleep measures align with traditional subjective assessments remains unclear.

This study evaluates the combined effect of dCBT-I with wearable sleep tracking and examines discrepancies between subjective (sleep diaries) and objective (smart ring) sleep measures in individuals undergoing digital insomnia treatment.

Materials and methods: A single-arm, pre-post study was conducted to evaluate the clinical outcomes of an 8-week dCBT-I intervention with smart ring sleep tracking.

Inclusion:

- 30 adults with chronic insomnia (DSM-V)
- ISI score of 11 or above

Methods:

- dCBT-I for 8 weeks
- comparison of daily sleep data from smart ring and sleep diary

Results: Result 1: Insomnia severity improved significantly ($\Delta ISI = -6.16$, $p = 0.011$), while anxiety symptoms decreased ($\Delta GAD-7 = -2.38$, $p = 0.038$). No significant change was observed in depressive symptoms (PHQ-9, $p = 0.807$).

Result 2: Smart ring adherence was significantly higher than the sleep diary (52.5 vs. 44.5 days, $p = 0.002$).

Result 3: Significant discrepancies were observed between sleep diary and smart ring measurements. SOL, TST, SE WASO all showed significant improvements in sleep diaries ($p < 0.001$, $p = 0.004$, $p < 0.001$, $p = 0.007$, respectively), but no significant changes were detected by the smart ring. Interaction effects for SOL and TST indicate divergent trends between subjective and wearable-derived data.

Conclusions: • Digital CBT-I with smart rings reduces insomnia severity and anxiety symptoms.

- Smart ring adherence was significantly higher than the sleep diary.
- Smart rings did not capture improvements observed in sleep diaries.
- Significant discrepancies exist between subjective and wearable-derived sleep data.
- Subjective assessments remain essential in insomnia management.

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What is the optimal treatment for co-occurring insomnia and anxiety? An RCT comparing internet CBT for insomnia to internet CBT for anxiety

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Introduction: Insomnia and anxiety are highly prevalent and frequently co-occur. Given their comorbidity and bidirectional relationship, the study aimed to compare which treatment – internet CBT for insomnia or internet CBT for anxiety – leads to the best outcomes in individuals with comorbid insomnia and anxiety. We also examined mediators of treatment response.

Materials and methods: 120 participants with comorbid insomnia and clinical anxiety were randomized to receive internet-based cognitive behavioral therapy (iCBT) for insomnia or iCBT for anxiety. The primary outcome measures were the insomnia severity index and the generalized anxiety disorder 7-item scale. These were assessed before treatment, at mid-treatment, at post-treatment, and 3 months after treatment. Secondary outcome measures assessed depression symptoms, distress, and sleep diary parameters, as well as sleep effort, pre-sleep arousal, dysfunctional beliefs about sleep, and rumination.

Results: Large reductions in symptoms of insomnia, anxiety, depression, and distress were experienced by participants in both groups, as well as improvements in sleep efficiency and total sleep time. Critically, at the end of treatment, the insomnia treatment was more effective in reducing symptoms of insomnia than the anxiety treatment, and equally effective in reducing symptoms of anxiety. Treatment gains were maintained at 3-month follow-up, however, there were no differences between groups at that time point. Dysfunctional beliefs about sleep emerged as a key mediator of the differences between the interventions in insomnia symptoms at post-treatment.

Conclusions: These results suggest that in the common case of a patient presenting with comorbid insomnia and anxiety, treatment for insomnia may be the most efficient treatment strategy. Mechanisms of treatment will be discussed.

Memory

Age-Related Alterations in SO–Spindle Coupling and Their Impact on Sleep-Dependent Memory Consolidation: A Magnetoencephalography Study

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Introduction: Cognitive decline is common in aging, with memory loss reducing life quality. Sleep, especially the coupling of slow oscillations (SO) and spindles during NREM sleep, is vital for memory consolidation. How aging-related changes in SO–Spindle coupling affect this process remains unclear. Using MEG, this study examined age differences in neural information flow during SO–Spindle coupling. Findings shed light on sleep-dependent memory mechanisms and potential intervention targets.

Materials and methods:

A total of 99 healthy participants (aged 18–35 and 60–75) were recruited and assigned to nap or wake conditions. All participants completed an episodic memory encoding task. Those in the nap condition underwent a 120-minute MEG-recorded sleep session; wake participants remained at rest for an equivalent duration. Memory performance was assessed pre- and post-intervention.

1. Behavioral outcomes were analyzed using ANOVA to assess the interaction between age group and nap/wake condition.
2. Phase-amplitude coupling analysis was used to extract SO–Spindle coupling phases during NREM sleep, followed by group comparisons (Watson-Williams test) and circular-linear correlations with memory performance.
3. SO–Spindle events were source-localized to the hippocampus, thalamus, and medial prefrontal cortex (mPFC), including the medial orbitofrontal cortex (mOFC) and rostral anterior cingulate cortex (rACC). Granger causality was used to construct directed brain networks. Connectome-based predictive modeling with leave-one-out cross-validation and permutation testing was used to predict memory retention. Group differences in network-memory associations were tested using the Cocor package.

Results:

- **Behavioral Performance:**
Nap-related memory enhancement was age-dependent. Younger adults in the nap condition showed significantly better memory retention than in the wake condition ($p < 0.05$), while no such effect was observed in older adults.
- **SO–Spindle Coupling Phase:**
The mean coupling phase differed significantly between age groups ($p < 0.05$). In younger adults, spindles peaked near SO peaks and were significantly associated with memory retention ($r = 0.48$, $p = 0.047$). In older adults, spindles occurred earlier during the SO upstate and showed no significant memory association ($r = 0.18$, $p = 0.739$), suggesting disrupted temporal precision in coupling may contribute to age-related memory decline.
- **Neural Information Flow:**
 - **Temporal Dynamics:** Two key windows were identified: SO trough (-250 to $+250$ ms) and SO peak ($+300$ to $+800$ ms).
 - **Age-Group Differences:** During the SO peak period, younger adults exhibited significantly stronger directed connectivity from the right thalamus to the left medial orbitofrontal cortex (mOFC) and the right rostral anterior cingulate cortex (rACC) compared to older adults ($P_{FDR} < 0.05$).
 - **Predictive Value:** In younger adults, directed thalamus-to-mPFC connections during the SO peak predicted memory retention. These associations were absent in older adults. Cocor analyses revealed significantly stronger correlations in the younger group for right thalamus to left mOFC ($z = 2.317$, $p = 0.010$) and right rACC ($z = 2.013$, $p = 0.022$).

Conclusions: Sleep supports memory consolidation, but efficacy wanes with age. While younger adults benefit from napping via precise SO–Spindle coupling and thalamocortical connectivity, older adults exhibit decoupling and diminished directional connectivity, particularly in thalamus–mPFC circuits. These disruptions may underlie age-related memory impairment and represent potential targets for intervention.

An Sleep-Active Hippocampal Interneuron for Memory Consolidation

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Introduction: Sleep has been recognized as critical for memory. Research in recent decades has established that hippocampal memory replay during sharp-wave ripples is central to memory consolidation in sleep. However, the neural circuits that control ripple generation and memory consolidation remain poorly understood, particularly whether there are specialized cell types or dedicated neural circuits for this process. Here, we systematically investigated the involvement of specialized interneuron circuits for memory consolidation, as the interneurons are the fundamental building blocks of neural circuits that control hippocampal information processing.

Materials and methods: We have systematically examined the activity of different interneurons during the sleep-wake cycle in the hippocampus. Particularly, using a new strategy and single-cell RNA

sequencing data, we developed a new transgenic mouse model, specifically targeting the hippocampal sleep-active interneurons. We further examined its contribution to memory consolidation during sleep. **Results:** While the majority of hippocampus interneurons are more active during Wake or REM rather than NREM sleep, the primary state for memory consolidation, we identified a genetically defined interneuron population that is selectively active during NREM sleep and is essential for controlling ripple generation and memory consolidation.

Conclusions: We have identified a specialized neural circuit that is dedicated to memory consolidation in the hippocampus.

Aperiodic slope changes track encoding and sleep-based memory consolidation

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Introduction: Whilst ample research has investigated the relationships between oscillatory EEG, encoding and memory consolidation, the effects of the aperiodic component of the EEG are relatively undescribed in this realm. The aperiodic component of the EEG has been linked with brain state changes (i.e., different sleep stages) and memory performance, but not the two in conjunction despite their demonstrated link. Here, we assess the capacity of changes in the aperiodic slope to index learning and memory consolidation.

Materials and methods: 28 Participants (25F, age range 18-34) were required to learn different object-word paired associates on two separate days, then underwent either an afternoon nap (2-hour TIB) or 2 hours of wakefulness each session. They were tested on their recognition memory before and after the nap or wake intervention. EEG was recorded with a 64 channel EEG cap *in situ* throughout. The aperiodic slope was calculated through the IRASA method as implemented in the YASA toolbox. Linear mixed models were used to provide statistical analysis.

Results: The aperiodic slope steepened across learning and subsequently flattened across the nap ($\chi^2(1) = 15.20, p < .001$), but not across wake ($p > .05$) condition. Importantly, this renormalisation of the aperiodic slope was predictive of N400 amplitudes at delayed testing ($\chi^2(1) = 11.73, p < .001$). Learning-related, but not intervention-related slope changes were predictive of behavioural memory outcomes ($\chi^2(1) = 5.12, p < .023$).

Conclusions: These results provide first evidence for measures of aperiodic slope change as a method to track learning and consolidation-related changes across sleep, and suggest that this may be due to expectancy effects specific to sleep.

Associations between REM OSA, White Matter Microstructure, and Cognition in Community-Dwelling Cognitively Unimpaired Older Adults

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Introduction: Obstructive sleep apnea (OSA) severity increases Alzheimer's disease (AD) and cognitive decline risks. OSA during rapid eye movement (REM) sleep is sometimes more severe than non-REM OSA, however the relationship between REM-OSA severity and cognition is not well characterized. Emerging evidence also suggests that white matter microstructure alterations may contribute to cognitive deficits in patients with OSA. We examined associations between white matter tract integrity, cognition, and REM OSA severity in cognitively unimpaired older adults.

Materials and methods: This cross-sectional study included 70 community-dwelling cognitively unimpaired older adults (35 non-OSA, 35 REM-OSA; mean $\pm$ SD: age = 66.3 $\pm$ 4.9y) participating in NYU

studies of sleep, aging, and memory. Participants had diffusion-weighted imaging, neuropsychological battery tests, overnight polysomnography, and clinical data. REM-OSA was characterized as REM AHI4% (>15 events/hour). Neuropsychiatric testing included processing speed, working memory, and visuospatial ability measures. Cingulum, uncinate fasciculus (UF), and fornix microstructure properties were estimated using diffusional tensor imaging metrics. Multivariable linear regression models examined associations of white matter microstructure (exposure) on cognitive measures (outcome measure) between OSA and non-OSA, and white matter microstructure by REM-OSA severity on cognition. Models were adjusted for age, race, education, sex.

Results: Of the 70 participants (35 non-OSA, and 35 REM-OSA), 68.8% and 62.9% were female, respectively. Mean±SD education was 16.5±2.4y REM-OSA(vs. 16.3±2.5y controls). Participants with REM-OSA had lower attention (β [REM AHI4%]=-1.07[-2.1 - -0.04], $p<0.050$) and slower processing speeds (β [REM AHI4%]=0.29[0.05 - 0.54], $p<0.050$) compared to controls. REM-OSA was associated with white matter microstructure alterations within both hemispheres of the cingulum($p=0.01$) and fornix($p=0.040$). Furthermore, decrements in the UF were associated with worse working memory β [UF] = -0.25 [-0.45 - -0.05], $p < 0.050$) and slower processing speed β [UF] = 0.26 [0.04 - 0.50], $p < 0.050$). Moreover, REM OSA severity interaction with white matter microstructure demonstrated lower working memory β [REM AHI4% x cingulum, right]=-0.20[-0.37- -0.03], $p < 0.050$; β [REM AHI4% x cingulum, left]=-0.23 [-0.44 - -0.02], $p<0.050$) and reduced visuospatial ability β [REM AHI4% x fornix]=-0.23 [-0.44 - -0.01], $p<0.050$).

Conclusions: Our findings demonstrate the critical role of white matter microstructure in the relationship between REM-OSA and cognition. Longitudinal studies are needed to investigate the mediating role of white matter microstructure alterations between REM-OSA and cognitive decline.

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Auditory Suppression Cue Exposure During Sleep Promotes Targeted Memory Forgetting

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Introduction:

Previous research shows that individuals can intentionally suppress unwanted memories through retrieval suppression, leading to Suppression-Induced Forgetting (SIF). However, this training often requires prolonged exposure to memory cues, causing discomfort. Recent studies suggest that sleep, a period of memory consolidation and sensory processing, may offer a unique opportunity for memory manipulation. Auditory cues presented during sleep could reactivate inhibitory control training learned while awake, promoting the forgetting of specific memories. This approach may bypass discomfort and provide an efficient method for inducing the forgetting of unwanted memories. Thus, this study explores whether sleep-based auditory cues can reactivate retrieval suppression and induce targeted memory forgetting.

Materials and methods: Thirty-six healthy participants were recruited. Before sleep, participants engaged in declarative memory learning and underwent an initial memory test to establish baseline performance. Subsequently, while awake, they participated in Suppression-Induced Forgetting (SIF) training using the Think/No-Think (TNT) paradigm. This training involved two distinct auditory cues signaling the Think and No-Think conditions and the presentation of learned verb cues. The effectiveness of retrieval suppression was assessed through a memory test immediately after the TNT training. During the subsequent non-rapid eye movement (NREM) sleep phase, participants were exposed to continuous auditory cues, including the instructional cues and verb sounds used during the TNT paradigm. Upon awakening, participants completed another memory test and a Localizer task to assess the neural correlates of memory processing. Notably, the instructional cues presented during sleep were identical to those used in the wakeful TNT paradigm to reactivate retrieval suppression,

while the verb sounds following the cues differed to distinguish the effects of retrieval suppression between wakefulness and sleep. Throughout the experiment, 64-channel EEG monitoring was employed to explore the neurophysiological mechanisms underlying SIF during sleep.

Results: The study found that participants could effectively reactivate the Suppression-Induced Forgetting (SIF) process through auditory cues during sleep, leading to the active forgetting of targeted memories. Specifically, compared to the Think condition, the No-Think condition elicited greater electrophysiological potential changes after the instructional cues ended and inhibited the formation of sleep spindles, which are known to be associated with memory consolidation. Furthermore, cross-temporal representational similarity analysis (RSA) between EEG data from post-cue exposure during sleep and corresponding category-related EEG data from wakefulness revealed distinct neural correlates for the Think and No-Think conditions. While cues and stimuli in the Think condition successfully reinstated target category representations, the No-Think condition surpassed this reinstatement. This suggests that auditory cues presented during sleep can selectively modulate memory representations, supporting the hypothesis that sleep-based interventions can enhance targeted forgetting.

Conclusions: These results suggest that sleep-based interventions using auditory cues can enhance targeted forgetting, bypassing the discomfort associated with prolonged exposure to memory cues during wakefulness. This approach provides a novel mechanism for memory control and has significant clinical implications. Future research should further explore the long-term effects of sleep-based memory interventions and their applicability in clinical settings.

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Does intentional integration influence the fate of reactivated memories during sleep?

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Introduction: Growing evidence suggests that memories benefit from sleep. For example, neural investigations of new memory traces formed during learning show that they become reactivated during sleep, which offers a putative mechanism by which sleep benefits memories via rehearsal. Intriguingly, this process can be manipulated by presenting some stimulus (odor or sound) during learning and reinstating it again without waking the sleeper up. When this occurs, memories for simple associations generally improve, and the same neurons or neural regions that contributed to forming the memory become reactivated. Therefore, memory reactivation does not need to only occur spontaneously but can be targeted (in a technique known as targeted memory reactivation, or TMR). Many scientists have now realized that they can use TMR as a tool to understand how memories are formed and when/how they can be modified. For example, memories in these paradigms can be classified as simple (with one specific reactivation cue per tested memory) or complex (>1 cue per tested memory). Simple memories nearly always benefit from cueing, but it appears that the outcome of complex memories will depend on how they are learned. One hypothesis is that if memories were learned in such a way as to encourage integrating all the various elements together, such as with the creation of a concept map, all memories can benefit from reactivation. Conversely, if they were learned such that some information is prioritized over other information or if they were simply learned separately but contained overlapping associations, parts of the memories may get stronger while the other parts get weaker.

Materials and methods: Here, we tested whether a simple instructional manipulation – asking participants to integrate conflicting associations – would lead to different outcomes when memories are later cued during sleep. Participants learned A-B, A-C pairs with instructions to either integrate them or learn them separately, after which half of the associations were cued via low-volume sounds during an afternoon nap. All associations were then tested after the nap.

Results: In line with prior findings, behavioral results indicated that cued items were recalled better than uncued items ($p < 0.05$), though the extent to which instructions changed memory was unclear ($p > 0.1$). Physiological analyses showed typical post-cue responses like K-complex-influenced ERPs between 500-800 ms, theta bursts between 400-700 ms, and sigma (spindle) bursts between 1000-1500 ms.

Conclusions: These results have important implications for employing TMR in educational settings, as real-world learning involves complex networks of associations.

Effects of Intraindividual Variability in Sleep on Long-Term Memory Encoding

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Introduction: Greater variability in sleep across nights has been linked with poorer cognitive outcomes, but some recent evidence suggests that for sleep-restricted individuals, a variable sleep schedule that allows for prophylactic and/or recovery sleep might result in less impairment in some basic cognitive functions compared to a stable schedule. This study aimed to investigate whether multiple nights of curtailed sleep opportunities with either consistent or variable sleep duration affected declarative memory encoding differently.

Materials and methods: After two baseline nights of 8-h time-in-bed (TIB), in the following five nights, 44 participants (24 females, age: 21 – 26 years) had a nightly 8-h TIB (control group), a nightly 6-h TIB (stable short sleep group), or 8, 4, 8, 4, and 6 h of TIB from the first to the fifth manipulation night (variable short sleep group). Following the fifth manipulation night, participants performed a picture encoding task. Memory performance was measured after two recovery nights of 8-h TIB, thus minimising the effects of fatigue in the recognition test, where participants needed to indicate whether they had previously seen each picture by selecting one of five options: “definitely did not see”, “probably did not see”, “unsure”, “probably saw”, “definitely saw”. “Definite” and “probable” responses were combined to generate hits, misses, false alarms, and correct rejections. The numbers of unsure responses to new and old pictures were also derived.

Results: Compared to the control group, “no” responses to new pictures were more common and thus, correct rejection rate was higher ($p = .04$) in the stable short sleep group; a similar tendency was found for old pictures (i.e. miss rate, $p = .09$), suggesting that these participants adopted a more conservative response style. As for the variable short sleep group, they had significantly more “unsure” responses to old pictures than the control group ($p = .05$), and a similar tendency was observed for new pictures ($p = .09$), indicating that response certainty was reduced by this short sleep schedule. Between the two short sleep groups, for old pictures, the variable short sleep group had more “unsure” responses ($p = .003$) but fewer “yes” responses (and hence, a lower hit rate, $p = .02$); for new pictures, the variable short sleep group also had more “unsure” responses ($p = .003$) but fewer “no” responses (and hence, a lower correct rejection rate, $p = .01$).

Conclusions: In young adults, multiple nights of sleep restriction affected declarative memory encoding such that even after recovery sleep, performance was different from the well-rested control. These effects differed depending on the variability of sleep duration before memory encoding. A stable short sleep schedule induced a more conservative response style, whereas a variable short sleep schedule appeared to have weakened memory traces and increased uncertainty in responses. Consistent and sufficient sleep remains the most effective strategy for optimising declarative memory encoding.

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Effects of Monophasic and Polyphasic Sleep on Prospective Memory

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Introduction: Many struggle to sleep the recommended amount because of competing wake activities. In fact, some actively search for short sleep schedules to maximise their wake duration to cope with demands from their study and work. Polyphasic sleep—deliberately distributing multiple sleep episodes over a 24-h day, typically with the goal of reducing time spent asleep—has been claimed by its advocates to enable optimised performance, and improve productivity, memory and mood despite the short sleep durations. While neurobehavioural deficits, such as impairments in memory, induced by monophasic short sleep have been documented, the impact of polyphasic sleep on memory is unknown. This study aimed to determine whether prospective memory (PM) differed after following a monophasic and a polyphasic short sleep schedule for 24 h.

Materials and methods: Forty healthy young adults (22 females, age: 18-35) participated in this 29-h laboratory-based study. They were randomly assigned to either a monophasic sleep schedule consisting of a single 2-h sleep opportunity, or a polyphasic sleep schedule comprised of six 20-min sleep opportunities equally distributed across the 24-h manipulation period. At the beginning of the manipulation period (before the polyphasic group's first sleep opportunity), participants first performed a word categorisation (WC) task where they decided if a word is an exemplar of the given category in each trial. Task performance was indicated by accuracy and speed measures. The PM task was then introduced: participants were given a list of eight target words (e.g. "desk"), each paired with an action (e.g. looking under their table) which they needed to perform when they encountered the target word during the next WC task administered 24 h later (i.e. after the polyphasic group's last sleep opportunity). PM performance was indicated by the time taken to complete the action and the proportion of correct and on-time actions within the same trial.

Results: The monophasic and the polyphasic short sleep groups did not differ in the proportion of correct responses (mean $\pm$ SEM: 0.93 ± 0.01 ; 0.92 ± 0.01 , $p > .44$) and reaction times (1231.11 ± 115.82 ; 1236.52 ± 77.92 ms, $p > .97$) for the first WC task. Relative to the first WC task, during the second WC task, accuracy reduced slightly (monophasic: 0.90 ± 0.01 , $p < .001$; polyphasic: 0.88 ± 0.01 , $p < .001$), and reaction time increased prominently (1604.40 ± 150.51 , $p < .001$; 1510.69 ± 55.72 ms, $p < .001$), but no significant group difference was found for these two measures ($p > .57$). In the PM task, both groups did not differ in the proportion of correct responses (0.86 ± 0.03 ; 0.85 ± 0.03 , $p > .82$), on-time responses (0.75 ± 0.05 ; 0.80 ± 0.04 , $p > .41$), and the time taken to complete the correct action (9427.45 ± 746.74 ; 9606.95 ± 804.15 ms, $p > .87$).

Conclusions: Polyphasic and monophasic sleep schedule over a 24-h period resulted in similar PM performance. The increase in reaction time from the first to the second WC task might reflect both the effects of sleep curtailment and the efforts deployed in strategic monitoring for the target words, which did not differ between the two short sleep schedules.

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Impact of Melatonin on Progression of Cognitive Impairment

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Introduction: Melatonin is an antioxidant and anti-inflammatory molecule produced in the pineal gland. It has been proposed by animal models that exogenous supplementation of melatonin may act as a protective intervention in elderly participants with cognitive impairment and dementia. This study aimed to evaluate the impact of melatonin supplementation on cognitive function and the rate of progression from healthy to mild cognitive impairment (MCI), and from MCI to dementia postulating that melatonin could provide neuroprotection from the inflammatory state of the various dementia pathologies.

Materials and methods: Retrospective data was collected from the National Alzheimer's Coordinating Center (NACC) uniform data set (UDS) for this case-control study. Prevalence of melatonin use by demographic and clinical characteristics was analyzed in the cross-sectional portion of the study. Diagnosis codes were utilized to identify severity of cognitive status and Clinical Dementia Rating Sum of Boxes (CDR-SB) and Montreal Cognitive Assessment (MoCA) scores were analyzed for cognitive

function. Rates of conversion from normal cognition to MCI and from MCI to dementia at intervals of approximately 1 year were analyzed between melatonin and non-melatonin groups.

Results: A total of 17,264 participants aged 60 years and above (mean age 71.9, SD 7.0) from 2015-2024 completed the medication questionnaire and cognitive evaluations at the initial study visit. Of those, 1,120 (6.5%) reported melatonin supplementation (melatonin-group) compared to 16,144 who did not (non-melatonin group).

The melatonin group was 52.1% female, 88.7% white, and obtained a mean education of 16.3 years. Comparatively, the non-melatonin group was 58.3% female, 75.2% white ($p<0.0001$), and with a mean education of 15.3 ($p<0.0001$).

Of all participants at the initial visit, 45.5% had normal cognition, 4.2% had impaired cognition not MCI, 26.4% had MCI, and 23.9% had dementia. The melatonin group had a higher prevalence of cognitive impairment at baseline compared to non-melatonin, 64% vs 54% ($p<0.0001$). Mean CDR-SB was 2.4 among melatonin users and 1.8 in non-melatonin users. ($p<0.0001$). Mean MoCA total score was 22.2 among melatonin users and 22.4 in non-users ($p=0.64$).

A subset of 4,464 participants with normal cognition at baseline completed the second annual visit and 11.7% converted to MCI. Multivariate logistic regression was used to examine the association between melatonin use vs. non-use at baseline and conversion to MCI at subsequent annual visit after adjusting for covariates: age, sex, education, race, prevalence of sleep disorder, depression scale. The risk of conversion to MCI was not different between melatonin users vs non-users (Odds Ratio 1.18, $p=0.44$).

Conclusions: The large diverse NACC database was used to estimate prevalence of melatonin use among older adults with varying degrees of cognitive health. Melatonin users were more evenly distributed male and female and more likely White with longer education. Moreover, the melatonin-group had a higher prevalence of cognitive impairment than non-users at baseline. Melatonin use did not significantly impact the rate of conversion from healthy to MCI between baseline and annual evaluations.

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Impact of Post-Stroke Insomnia on Cognitive Decline: Evidence from the TriNetX Global Database

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Introduction: Insomnia is a prevalent sleep disorder among stroke survivors and is recognized as an independent risk factor for cognitive impairment. However, the longitudinal relationship between post-stroke insomnia and subsequent cognitive decline remains inadequately explored. This study aimed to investigate the association between post-stroke insomnia and the risk of developing cognitive impairment over time.

Materials and methods: We conducted a retrospective cohort study utilizing data from the TriNetX database, encompassing hospital-based records from January 1, 2004, to September 30, 2017. The study included patients aged 20 years and older with a diagnosis of stroke, insomnia, or cognitive impairment, as defined by the International Classification of Diseases. Stroke patients were categorized into two groups: those with insomnia (cohort 1, $n = 35,514$) and those without insomnia (cohort 2, $n = 1,309,838$). Propensity score matching (1:1) was employed to balance baseline characteristics, resulting in 35,144 patients in each cohort. Kaplan-Meier survival analysis was utilized to assess the risk of cognitive impairment.

Results: A total of 70,288 stroke patients (mean age: 67.3 years) were analyzed post-matching. During the follow-up period, 6,476 patients in the insomnia group and 5,197 in the non-insomnia group developed cognitive impairment. The analysis revealed a significantly higher risk of cognitive

impairment in the post-stroke insomnia group (hazard ratio [HR] = 1.288; 95% confidence interval [CI]: 1.242–1.336).

Conclusions: Post-stroke insomnia is associated with a significantly increased risk of subsequent cognitive impairment. These findings underscore the importance of early detection and management of insomnia in stroke survivors to mitigate long-term cognitive decline.

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Impact of Sleep Disturbance and Hypnotics on the Risk of Dementia: a longitudinal follow-up study

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Introduction: Sleep quality is often impaired in individuals with dementia. However, the relationship between sleep disturbances and dementia remains unclear. This study investigated the association between various sleep domains and the risk of developing dementia in older adults.

Materials and methods: In this retrospective longitudinal study, we enrolled 2,679 adults from three centers in Taiwan. We collected baseline data on age, gender, education, medication use, Clinical Dementia Rating (CDR) scale, Cognitive Abilities Screening Instrument (CASI), Neuropsychiatric Inventory (NPI), History-based Artificial Intelligence Activities of Daily Living (HAIADL), and History-based Artificial Intelligence Clinical Frailty Scale (HAICFS).

Results: We examined demographic, clinical, and neuropsychiatric differences between individuals who converted to dementia (Converters, N=957) and those who did not (Non-Converters, N=1,722) over an average follow-up of approximately 2.3 years. Compared to non-converters, converters were significantly older, had fewer years of education, lower CASI scores, and higher scores on the CDR-Sum of Boxes (CDR-SB), HAIADL, HAICFS, and NPI. Multivariate analyses identified nighttime awakenings and antipsychotic use as significant predictors of dementia conversion, whereas insomnia was associated with a reduced risk. Interestingly, the use of benzodiazepines and Z-drugs did not increase the risk of dementia.

Conclusions: These findings underscore the importance of early identification and monitoring of specific neuropsychiatric symptoms and medication use in older adults at risk of developing dementia.

Napping and Prospective Memory: Investigating Cue Type and the Selective Benefits on Memory Retrieval

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Introduction:

Prospective memory represents our ability to remember to do things in the future (Einstein & McDaniel, 1990) and is more prone to forgetting. Tasks ensuring attending meetings or taking medications punctually, require forming intentions to execute these tasks upon encountering relevant external cues like future events (visiting grocers while returning from work) or time (waiting for 6 pm). Napping is a natural practice that can provide insights into sleep organization. Research shows that daytime naps help effectively help process information that is often easily forgotten. (Dijk et al., 2014; Ficca et al., 2010; Duthiel et al., 2021; Sugawara et al., 2018).

Materials and methods:

Participants in the study were asked to memorize four letters (e.g., f, r, q, s). Each letter was presented for 2 seconds, followed by a 1-second interval without stimuli. The instructions for prospective memory tasks varied between event cue and mixed cue tasks. After memorization, participants either took a 90-minute nap or remained quietly awake in the laboratory. During the nap condition, participants wore an Actiwatch (PHILIPS Respironics, Inc.) and a Dreem Headband to record physiological data, including EEG activity and body movement. Following the distraction task, participants began the ongoing working memory task, which consisted of five blocks of experimental trials. Each block included 20 individual trials, and prospective memory cues appeared once in each block at the same position across all blocks. The entire experiment took approx. 45 minutes to complete, concluding with feedback.

Results: *Accuracy:* Responses were marked as correct if participants pressed the correct response key for the PM target in the WM task. Mixed factorial ANOVA was used for statistical analysis. Significant interaction effect between type of PM and nap [$F(1, 22) = 6.278, p < 0.05, \eta^2 = 0.22$] was found with mixed PM more benefited by nap. For event based PM task, no significant accuracy results were obtained. Significant main effect of pm type was also found [$F(1, 22) = 6.02, p < 0.05, \eta^2 = .02$]. *Reaction Time:* Significant main effect of nap [$F(1, 22) = 8.9, p > 0.05, \eta^2 = 0.01$] suggests that participants responses were quicker after nap ($M=0.82$ sec) as compared to no-nap ($M=1.2$ sec). Significant main effect of types of PM [$F(1, 22) = 10.08, p > 0.05, \eta^2 = 0.005$] was found indicating that participants were slower to respond in event based PM task ($M=1.4$ seconds) as compared to mixed PM ($M=0.9$ sec).

Conclusions: The study investigated the impact of napping on PM across type of cues. Despite established benefits of sleep on memory, napping did not significantly enhanced future memory performance in young adults. The research considered factors such as sleep stages (NREM and REM) and conscious monitoring of cues. The study emphasized the importance of contextual cues, particularly the association of mixed cues, and suggested a selective beneficial impact of naps on prospective memory cued by mixed cues. RT analysis indicated faster responses in PM trials after napping, supporting that sleep aids in the spontaneous retrieval of prospective memory over time.

Reactivating spatial memories during sleep using multi-sensory cueing and an immersive virtual environment

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Introduction: Sleep plays an active role in the consolidation of memories. During sleep, the neural traces supporting newly formed declarative memories are spontaneously reactivated. Targeted memory reactivation (TMR) is a technique that uses non-invasive sensory cues, such as odors or sounds, to preferentially reactivate associated memories during sleep. One avenue of TMR research that has not yet been explored involves the combined use of odors and sounds to selectively enhance memories.

Materials and methods: Here, we examine the interactive effects of multi-modal reactivation cues during sleep on consolidation in a realistic first-person memory task. We used the Minecraft Memory and Navigation task, a first-person, engaging spatial task that demonstrates sleep's contribution to spatial memory (Simon et al., 2022). Following memory encoding of unique object locations and the environment which we enriched with odors and sounds, we reactivated the encoded memories during NREM sleep using the odors, sounds, or both. We hypothesized that rich, multisensory synergetic reactivation during sleep, compared to the unisensory reactivation, would maximally benefit spatial memory recall. Additionally, we use EEG to explore the effect of different cueing regimes on sleep spindles and slow oscillations during NREM sleep.

Results: Data collection for this study is ongoing, with a target sample of 160 participants across two sites. Preliminary behavioral data ($N=60$) will show the effects of the different cueing regimes on object placement accuracy, as well as on other navigation metrics. Preliminary spectral data ($N=60$) will show the relative change in sleep spindles and slow oscillations, upon cue delivery, and will be compared across experimental conditions. Furthermore, we will evaluate the relationship between the change in spindle power upon cue delivery and subsequent spatial memory performance on our task.

Conclusions:

Our study reveals the contribution of memory consolidation during sleep to real-life spatial memories and provides insight into whether multisensory cueing has synergistic, additive, or competitive benefits for consolidation.

REM sleep promotes overnight emotional memory in a picture recognition task

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Introduction: World Trade Center (WTC) Disaster Responders suffer a high prevalence of obstructive sleep apnea (OSA), insomnia and mental health comorbidities such as post-traumatic stress disorder (PTSD), depression and anxiety. In picture tasks of emotional memory in OSA and PTSD, REM sleep instability impairs sleep-related consolidation of emotionally valenced images. We aim to test the effect of PTSD and sleep disorders on an overnight emotional picture recognition task and investigate whether REM sleep promotes emotional memory in WTC Disaster Responders.

Materials and methods: Nineteen (4 female) WTC Disaster Responders, mean age 61.8 (range 49-75) years encoded consensus-rated negatively valent and neutral pictures from the International Affective Picture System (IAPS) in the evening before sleep with attended polysomnography (PSG). Image recognition testing occurred within 1 hour of wake time. We compared memory performance for consensus and subjectively-rated negative and neutral image memory using paired signed-rank tests and 2-way ANOVA for comparisons between those with and without PTSD, insomnia symptoms, OSA or periodic limb movements of sleep (PLMs). We also investigated the relationship of memory performance to metrics of REM sleep (duration, proportion, REM bouts & latency) with Pearson's coefficients.

Results: Five participants (26%) had a diagnosis of PTSD and 9 (47%) had an insomnia severity index score ≥ 8 . On PSG, 11 participants (58%) had OSA ($AHI \geq 15$) and 7 (37%) had periodic limb movement disorder (PLMD) ($PLM \text{ index} \geq 15$). Correct image recognition (Hit Rate) was significantly greater for subjectively negative valenced compared to consensus neutral images ($p=0.01$). However, no effect of PTSD, insomnia, OSA or PLMD was observed. Accuracy (Hit Rate–False Alarms) for consensus negative images was correlated with %REM ($R=0.52, p=0.02$) and REM duration ($R=0.47, p=0.04$). Accuracy for subjectively negative images was not correlated with REM sleep metrics.

Conclusions: In this group of WTC Disaster responders, negatively valenced images are more readily recognized compared to neutral images, particularly for subjectively negative images. Proportion and duration of REM sleep appears to promote overnight memory of negatively valenced images but a greater understanding of REM sleep neurophysiology underpinning this observation may come from further analysis with the available 19 channel EEG. Additionally, the effect of sleep disorders, mood and PTSD on these findings in WTC Responders requires investigation with a larger sample.

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REM-sleep saw-tooth waves: cortical topography and associations with cognition

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Introduction: Saw-tooth waves (STWs) are a hallmark of rapid-eye movement sleep, reflecting widespread, coordinated brain activity (Frauscher et al., 2020). However, their function remains poorly understood. Given that STW were associated with altered thalamo-cortical connectivity (Peter-Derex et al., 2023) and that thalamo-cortical circuits play a crucial role in cognition (Filchenko et al., 2023,

2025), we investigated the associations between STW properties and cognitive functioning in an exploratory analysis.

Materials and methods: The “Sleep and cognitive functioning” study included volunteers in good or excellent health condition (Eastern Cooperative Oncology Group grade of 0-1) without known structural brain damage (e.g., previous stroke). Demographics, medical history, cognition, and sleep architecture by polysomnography were assessed at study inclusion. The neurocognitive battery (11 tests) assessed attention, executive functioning as well as short- and long-term visual and verbal memory. Electroencephalography (EEG) was recorded using either a 6-electrode setup (a montage with frontal, central, and occipital electrodes) or a 256-electrode setup. STW were detected using a custom feature-based algorithm in MATLAB (Manual of the American Academy of Sleep Medicine, v3). The detection was validated against the manual scoring of 5-second STW segments according to Simor et al., 2021. Associations between STW properties as dependent variables and cognition were explored using multivariate linear regression adjusted for age and arousal index. The significance level was set at $\alpha=0.05$.

Results: 60 participants were included (age: 52.7 [32.9, 64.6] years; 55% men; total recording time: 7.25 [6.50, 8.20] hours, apnea-hypopnea index: 5.1 [1.6; 15.9] events/hour; hd-EEG in 52%). STW were mostly expressed in the fronto-central areas, reaching there the maximal amplitude. 0.5–6 Hz and 20–40 Hz activity was dominating in the frontal regions, and 12–16 Hz activity was prominent in the posterior regions. EEG analysis based on the mean of 6 electrodes showed limited associations between STW and cognition (e.g., negative association of STW amplitude with reaction time in alertness and psychomotor vigilance task; negative association of EEG power in 8-12 Hz with task completion time in Bells test). HD-EEG analysis on the level of individual electrodes identified multiple associations of interest with a distinct topography, which were directionally consistent with the 6-electrode EEG analysis (e.g., STW amplitude in the fronto-central regions bilaterally with standard deviation of reaction time of Go-no-Go task [negative]; STW amplitude in the right frontal, temporal, and occipital region with the interference score of Victoria Stroop Task [positive]; STW amplitude and EEG power in 20-40 Hz in the right temporal and parietal region with immediate recall of Brief Visuospatial memory tasks [positive]).

Conclusions: This is the first description of the automatically detected STW in clinical polysomnography and in hd-EEG. STW properties showed distinct associations with cognition that depended on their underlying topography. Overall, higher STW activity was negatively associated with attention and executive functioning, but positively associated with visual memory. We will further investigate functional connectivity during STW.

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Sleep Disorders and Sarcopenia: Exacerbating Cognitive Decline in Chinese Women with Mild-to-Moderate Alzheimer's Disease

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Introduction: Sleep disorders and sarcopenia are both risk factors for cognitive deterioration and contribute to the development of Alzheimer's disease (AD). However, few studies have evaluated the relationship between sarcopenia and sleep disturbances in women with AD. The purpose of this study was to investigate the relationship between sarcopenia and sleep status in Chinese women with mild to moderate AD.

Materials and methods: This cross-sectional study recruited 112 female outpatients aged between 60 and 85 years. Demographic characteristics, appendicular skeletal muscle mass index (ASMI), grip strength, and gait speed were assessed. Sarcopenia was diagnosed according to criteria of the Asian Working Group for Sarcopenia. Pittsburgh Sleep Quality Index (PSQI) assessed sleep variables. Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) assessed cognitive function. Binary logistic regression models explored the relationship between sleep variables and cognitive function and sarcopenia, adjusting for potential cofounders.

Results: 门诊患者分为 36 例 AD 合并肌肉减少症 (ADSa) 和 76 例无肌肉减少症的 AD 患者 (ADNSa), 患病率为 32.1%。ADSa 的 ASMI 较低, 握力较弱, 步态速度较慢, 睡眠质量差的发生率较

高，认知功能较差。多因素二元 logistic 回归分析显示，PSQI 总分高（OR = 1.13）、睡眠质量差（OR = 2.73）、主观睡眠质量差（OR = 1.83）、低 MMSE（OR = 0.77）和 MoCA（OR = 0.76）评分与肌肉减少症的高几率相关。与睡眠时间 ≤ 15 min 相比，> 60 min（OR = 5.01）与肌肉减少症相关。与 7-8 小时相比，< 6 小时（OR = 3.99）、8-9 小时（OR = 4.48）和 ≥ 9 小时（OR = 6.33）的睡眠持续时间与肌肉减少症相关。

Conclusions: More sleep symptoms and cognitive impairment exist in female patients with sarcopenia. The higher total scores of PSQI, poorer subjective sleep quality, longer sleep latency, excessive and insufficient sleep duration and poorer cognitive function are associated with higher odds of sarcopenia in female patients with mild to moderate AD.

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Sleep quality, attitudes, cognition and APOE in older adults in the SleepQuest and Great Minds cohorts

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Introduction: Poor sleep quality impairs cognition and increases risk of neurodegenerative diseases such as Alzheimer's Disease (AD). Sleep disturbance is common in older adults, and poor sleep is a symptom of AD. Poor sleep and its adverse consequences have been linked with anxiety which may arise from unhelpful beliefs and attitudes about the importance of sleep. Apolipoprotein E (APOE) ε4 is an established genetic risk factor for AD, independently linked to both impaired sleep and behavioural disturbance. Here, we capitalise on two existing longitudinal datasets that probe sleep, cognition, sleep anxiety and APOE genotype to examine the relationships between these factors. We hypothesise that i) poor sleep predicts future cognitive decline; ii) APOE ε4 is associated with poor sleep independent of cognition; and iii) unhealthy beliefs about sleep predict poorer sleep and cognitive decline.

Materials and methods: A retrospective analysis was conducted on longitudinal data from the SleepQuest study and Great Minds register. Participants completed Pittsburgh Sleep Quality Index (PSQI), depression and anxiety (PHQ-8 and GAD-7) questionnaires at three timepoints (Spring 2020 – Winter 2022), Dysfunctional Beliefs about Sleep (DBAS-16) questionnaire twice, CANTAB Paired Associates Learning (PAL) task 1-9 times (median: 4, Winter 2020-2024), and baseline demographics and cardiovascular risk factors. The primary outcome was PAL score. Total PSQI score was a secondary outcome. Separate simple or mixed-effects linear models evaluated factors associated with mean and longitudinal PAL and PSQI scores, controlling for confounders such as age and sex.

Results: 585 UK adults without a cognitive diagnosis participated in both studies (mean age: 63 years, 71% female). 62 participants had a diagnosed sleep disorder. A sub-group (N = 276) underwent APOE genotyping; 89 carried at least one ε4 allele. There was no significant association between mean or baseline PSQI score on PAL score in the main- and sub-groups, and no significant effect of APOE allele status on sub-group PSQI score. Older age and being male were associated with poorer PAL performance. Increasing DBAS score was associated with a small decrease in PAL score over time ($p < 0.001$) – suggesting unhealthy attitudes to sleep, rather than the subjective sleep report itself, was associated with cognitive decline.

Conclusions: Sleep quality at baseline did not predict cognitive decline, in contrast to existing literature, however the robustness of the models was hampered by sample size and the limited follow-up period. There was insufficient evidence to support a link between APOE genotype and sleep quality. Unhealthy beliefs about sleep were associated with worsening cognitive performance. The presumptive link between attitudes to sleep and cognitive decline may be through disturbed objective sleep. A limitation is that the PSQI is a self-reported, subjective measure of sleep quality with reduced accuracy compared to objective measures such as polysomnography. The relationship between attitudes to sleep, subjective and objective sleep and future cognitive decline deserves future exploration as it may yield behavioural interventions that protect brain health.

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Targeted Memory Reactivation During NREM Sleep Selectively Modulates Fear Memory Extinction

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Introduction: Sleep plays a crucial role in memory consolidation, with neural oscillations during non-rapid eye movement (NREM) sleep, particularly slow oscillations (SO, 0.5-2 Hz) and sleep spindles (12-16Hz), considered key neurophysiological mechanisms facilitating memory integration. Targeted memory reactivation (TMR), which presents cues associated with specific memories during sleep, has been shown to selectively modulate memory processing. However, its effects on fear memory remain controversial: some studies suggest TMR promotes fear extinction, while others find it enhances fear memory consolidation. Importantly, whether and how TMR influences fear memory processing by modulating sleep-specific oscillatory features, and the precise neural mechanisms involved remain unclear.

Materials and methods: We employed a fear conditioning paradigm where participants learned to associate two distinct tones (CS+) with mild electric shocks, and a third tone served as a control stimulus (CS-). Following conditioning, participants were randomly assigned to either a sleep group (1.5-hour nap) or a wake group (reading task). During NREM sleep or wakefulness, only one CS+ tone (cued tone) was presented without the associated shock, while the other CS+ (uncued tone) served as a within-subject control. Throughout the study, we recorded electroencephalography (EEG) and skin conductance responses (SCR) to assess neural oscillations and autonomic nervous system responses to fear stimuli, respectively.

Results: Participants in the sleep group showed significantly reduced SCR to the cued tone, with no significant changes to the uncued tone; the wake group exhibited no significant response changes to either tone. Event-related potential (ERP) analysis further confirmed that neural response patterns to the cued tone gradually resembled those elicited by the CS- that was never paired with shock. Neural oscillation analysis revealed that presenting the cued tone during NREM sleep significantly enhanced slow wave activity (SW, 0.5-4 Hz) and SO, both of which positively correlated with post-nap fear expression. More importantly, TMR specifically promoted phase-amplitude coupling between SO and sleep spindles, characterized by spindle activity preferentially occurring during the SO up-state. This precise spatiotemporal coupling pattern was observed exclusively in the cued tone condition.

Conclusions: TMR during NREM sleep selectively attenuates fear responses through enhanced SW activity that correlates with fear expression and SO-spindle coupling that may facilitate extinction, demonstrating potential applications for fear-related disorders.

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Targeted memory reactivation during slow-wave sleep prompts systems-level changes in the neural basis of episodic memory

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Introduction: Slow-wave sleep (SWS) supports memory consolidation through the reactivation and reorganisation of newly formed memory traces. The emergence of a non-invasive memory cueing

technique known as targeted memory reactivation (TMR) has provided some of the most compelling evidence that episodic memories are reactivated during SWS. However, whether TMR prompts a reorganisation in the neural basis of episodic memory has yet to be established. In the current study, we used a multi-session, functional magnetic resonance imaging (fMRI) protocol to examine changes in the neural basis of episodic memories that were cued (vs not cued) with TMR during SWS.

Materials and methods: N=43 healthy young adults (27 female) learned adjective-object pairs—where the adjectives were presented both visually and aurally—in the evening before a night of polysomnographically-monitored sleep. TMR was administered throughout SWS, such that a subset of the adjectives was continuously replayed via loudspeaker in a bid to reactivate the adjective-object pairs. The next morning, while undergoing fMRI, participants were presented with each adjective in isolation and instructed to retrieve the associated object from memory. The same test was repeated in the fMRI scanner 24 hours later, allowing us to examine both immediate and delayed changes in the neural basis of episodic memories that had undergone TMR.

Results: An initial whole-brain analysis of object recall showed widespread activation, including bilateral hippocampus, at each test session. A contrast between object memories that were cued vs not cued with TMR revealed no significant difference in neural activity immediately after sleep. Critically, however, the same contrast performed at the 24-hour follow-up showed stronger activation for cued (vs non-cued) memories in bilateral precuneus, suggesting that TMR had initiated a systems-level change in the neural basis of episodic memory that emerged over multiple nights of sleep.

Conclusions: Our findings demonstrate that TMR delivered during post-learning SWS triggers a process of neural reorganisation that unfolds over multiple days. These data lend support to the idea that memory reactivation in sleep supports systems-level consolidation processes that extend far beyond the first night after learning.

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The Beneficial Effects of Sleep in Reducing Interference

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Introduction:

A steadily mounting set of findings suggests that sleep benefits memory, in part by reducing interference between competing memories. Indeed, prior findings suggest that sleep reduces retroactive interference (i.e., when later learning negatively affects earlier learning) (Ellenbogen et al., 2006; Abel et al., 2023) and proactive interference (i.e., when earlier learning negatively affects later learning) (Abel & Bäuml, 2014). However, the effects of sleep on retroactive interference and proactive interference have never been found within the same study, nor have they been compared to each other.

Materials and methods: Here, we investigated the effects of sleep on retroactive interference and proactive interference using a paired associate paradigm in which participants learned an initial list of word pairs (A-B; e.g., pious-slurp) followed by a list with new targets linked to the same cue (A-C; e.g., pious-west). Participants learned and tested on unrelated A-B word pairs in the morning or evening, after which they learned A-C pairs for half of the A-B words either immediately or after a 12-hour delay (which included either sleep or wake). After this, they took a cued-recall test on both A-B and A-C pairs.

Results: For groups that stayed awake during the 12-hour retention interval, interference for A-B pairs was significantly greater for those who learned A-C directly before testing ($p = 0.04$) than for those who learned A-C immediately after A-B, which accords with our prior findings and those of others (Antony & Bennion, 2022; Antony et al., 2022; Chandler, 1993). However, there was no difference in interference for A-B pairs for groups that slept during the 12-hour retention interval ($p = 0.51$). For A-C learning, we found main effects of sleep and timing (both $p < 0.01$), such that memory was better when the interval included sleep than only wake and when A-C was learned closer to the test (vs. immediately after learning).

Conclusions: In sum, sleep appears to protect both earlier-learned information overall and facilitate new learning relative to wake intervals. These results suggest that sleep reduces both retroactive and proactive interference, with implications for recommending quality sleep in educational contexts in order to improve memory performance.

The contribution of theta activity preceding cortical down-states to the slow oscillatory-spindle dynamics of human non-REM sleep

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Introduction: The sequential progression of cortical down-states, up-states, and spindle events constitutes a core electrophysiological basis for memory consolidation during non-REM sleep. Whether other oscillatory dynamics contribute to this well-characterized sequence has yet to be established. In this study, we applied phase-targeted auditory stimulation (PTAS) at cortical phases of maximal excitability (up-state, PTAS-up) or inhibition (down-state, PTAS-down) within the slow oscillation (SO) cycle, aiming to identify the spectral signatures associated with slow wave generation and their coordination with spindles. Moreover, by analyzing stimulus-evoked slow waves alongside spontaneous SOs and K-complexes, we investigated whether a shared spectral fingerprint differentiates these oscillatory events and accounts for their spindle synchronization.

Materials and methods: Twenty-six healthy participants (mean age $\pm$ standard deviation: 23.23 ± 2.61 years, 17 females) slept at home wearing a portable EEG system (Fpz-M1, AF8-M1) coupled with a laptop-based sine-fitting algorithm for real-time SO phase prediction. Pink noise bursts (50 ms, 45 dB) were delivered via loudspeakers and randomly alternated between the SO up-state (targeted phase angle: 90° , mean stimulations: 115.32 ± 40.69) and down-state (270° , 115.52 ± 40.99), with a minimum inter-stimulus-interval of 4000 ms. EEG responses were analyzed through event-related potentials (ERPs) and event-related spectral perturbations (ERSPs). Furthermore, slow waves were automatically detected post hoc throughout the night to characterize the spectral signatures of stimulus-evoked events, spontaneous SOs (stage N3), and spontaneous K-complexes (stage N2). Phase-amplitude coupling (PAC) metrics were computed to investigate the presence of cross-frequency dynamics surrounding SOs.

Results: The PTAS procedure accurately targeted the SO up-state (trial-level mean phase angle: $97.67^\circ \pm 37.95^\circ$, $R=0.78$) and down-state ($271.41^\circ \pm 44.94^\circ$, $R=0.69$). PTAS-up elicited larger ERPs than PTAS-down, with ampler negative and positive peaks at ~ 500 and ~ 1000 ms post-stimulation, respectively (both $p<0.001$). ERSP analyses indicated greater theta power (5-8 Hz) following PTAS-up in the 200 ms preceding the individual stimulus-evoked negative peak ($p<0.001$) and higher spindle activity (12-16 Hz) at ± 200 ms around the positive peak ($p<0.001$). Critically, pre-down-state theta response robustly predicted ERP peak-to-peak amplitude and subsequent spindle activity across stimulation conditions (both $r=0.70$, $p<0.001$), fully mediating the difference between PTAS-up and PTAS-down on spindle power ($p=0.001$, proportion mediated=75.27%).

An ERSP comparison of the three detected slow wave categories revealed that stimulus-evoked events and spontaneous K-complexes exhibited overlapping spectral profiles, with greater pre-down-state theta activity and higher up-state-coupled spindle power compared to spontaneous SOs (all $p<0.001$). Early theta strongly predicted subsequent spindle activity across all categories ($r=0.78$, $p<0.001$), fully mediating the spindle difference between K-complexes and SOs ($p<0.001$) and accounting for 95.16% of the effect.

Finally, PAC analysis confirmed the physiological integration of theta activity into slow oscillatory rhythms, indicating the existence of a SO phase-theta envelope coupling peaking at $245.06^\circ \pm 13.44^\circ$ ($p<0.001$, group-level $R=0.93$).

Conclusions: Findings indicate that PTAS-up maximizes cortical responsiveness by recruiting a theta-driven mechanism. Moreover, stimulus-evoked events primarily display the spectral fingerprint of K-complexes rather than resembling endogenous SOs. Finally, this study highlights theta activity as a previously unrecognized mechanism linking cortical down-states to spindle dynamics, expanding the electrophysiological landscape of non-REM processes supporting memory consolidation.

The Effect of Melatonin on Hippocampal Synaptic Plasticity in an Acute Sleep Deprivation Model

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Introduction: Sleep is essential for the consolidation of long-term memory. Consequently, sleep deprivation (SD) has well-documented detrimental effects on memory performance and overall cognitive function. Melatonin, a hormone primarily secreted by the pineal gland, plays a key role in regulating circadian rhythms and has also been implicated in modulating synaptic plasticity. Specifically, melatonin has been shown to influence the maintenance of long-term potentiation (LTP) in the hippocampus—a form of synaptic strengthening widely considered a cellular mechanism underlying long-term memory formation. Recent studies have demonstrated that melatonin supplementation enhances long-term memory in both non-sleep-deprived (non-SD) and chronically SD models. To further investigate the potential therapeutic role of melatonin, this study examined its effects on both long-term and associative synaptic plasticity in the hippocampi of non-SD and SD mice.

Materials and methods: For the SD procedure, mice were subjected to five hours of SD using the gentle handling technique. The functional properties of the hippocampal CA1 region were assessed through field electrophysiological recordings.

Results: Our findings indicate that five hours of SD significantly impairs LTP in the hippocampal CA1 region (mean fEPSP slope = $97.96 \pm 7.74\%$, $P = 0.1304$). Interestingly, melatonin supplementation in non-SD control mice led to a reduction in both long-term (mean fEPSP slope = $102.09 \pm 9.01\%$, $P = 0.8219$) and associative plasticity (mean fEPSP slope = $90.86 \pm 5.31\%$, $P = 0.1194$), suggesting that in the absence of SD, melatonin may exert a dampening effect on synaptic strengthening. However, in SD mice, melatonin supplementation effectively rescued the deficits in both long-term (mean fEPSP slope = $150.33 \pm 3.99\%$, $P = 0.0156$) and associative plasticity (mean fEPSP slope = $194.27 \pm 21.51\%$, $P = 0.0156$). These results suggest that melatonin can prevent or reverse the impairments in hippocampal synaptic plasticity and memory processes induced by acute SD.

Conclusions: Therefore, melatonin may hold promise as a therapeutic agent for mitigating memory deficits associated with sleep loss.

The Effects of Acute Evening Moderate-Intensity Exercise on Long-Term Declarative Memory in Sleep Restriction

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Introduction: Sleep enhances memory retention; conversely, sleep deprivation degrades brain functions and memory performance. Exercise may potentially counteract the detrimental effects of sleep loss on memory. However, there is limited evidence from human studies to indicate that exercise offsets the memory deficits caused by sleep restriction and whether sleep architecture, especially slow-wave sleep (SWS) mediates the compensatory effects. We evaluated whether acute moderate-intensity exercise compensates for the detrimental effects of nighttime sleep restriction on declarative memory and if SWS mediates the compensatory effect in healthy young adults.

Materials and methods: A total of 88 (52% female) healthy young adults (24.0 ± 3.8 years) were randomly allocated to one of four evening groups based on exercise and sleep opportunity: average sleep only (S_8 , 8.5 hours/night), sleep restriction only (S_5 , 4.5 hours/night), and moderate-intensity exercise before sleep restriction (ExS_5) or an average sleep (ExS_8). Groups either performed a 30-minute moderate-intensity exercise or rested in the evening (7:00 p.m.) prior to learning 80 face-name pairs (10:00 p.m.), followed by an immediate recall task (10:10 pm). In the morning after their respective polysomnographic-recorded sleep opportunity, a delayed recall task was administered. The discriminability index (d') during the recall tasks was used to assess long-term memory performance.

Results: Total sleep time differed between the average and restricted sleepers ($p < 0.001$). We found significant exercise-sleep interaction effects ($p = 0.033$, $\eta_p^2 = 0.056$) on d' at delayed recall and the difference between delayed and immediate recalls ($p = 0.012$, $\eta_p^2 = 0.077$). Post hoc analyses showed that the delayed retrieval d' of ExS_5 ($M = 0.07$, $SD = 0.89$) was not statistically different from those of the S_8 ($M = 0.58$, $SD = 1.20$, $p = 0.115$, $d = 0.48$) and ExS_8 ($M = 0.21$, $SD = 1.30$, $p = 0.747$, $d = -0.13$) but was significantly better than the S_5 (-0.60 ± 1.38 , $p = 0.028$, $d = -0.58$). Similarly, the delayed retrieval d' of S_5 was significantly lower compared to those of S_8 ($p < 0.001$, $d = 0.91$) and ExS_8 ($M = 0.21$, $SD = 0.30$, $p = 0.029$, $d = -0.61$). Likewise, the difference in d' of ExS_5 (0.36 ± 0.79) was comparable to those of the S_8 (0.23 ± 1.3 , $p = 0.699$, $d = -0.12$) and ExS_8 (0.63 ± 0.63 , $p = 0.516$, $d = -0.36$), but significantly higher than the S_5 (-1.13 ± 1.02 , $p < 0.001$, $d = -1.12$). The percentage of SWS mediated the compensatory effects of the ExS_5 vs. S_8 condition on long-term memory [$B = 20.38$, $SE = 16.49$, 95% bootstrap CI (5.70, 59.99)].

Conclusions: These results suggest that acute moderate-intensity evening exercise enhances sleep-dependent memory consolidation and compensates for the detrimental effects of sleep restriction on long-term declarative memory in healthy young adults. Slow-wave sleep provides a potential mechanism for conveying the effects of acute exercise on long-term memory in sleep restriction.

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The Role of Adenosine Receptors and Their Antagonist Caffeine in the Mouse Hippocampal CA2 Region Associated with Sleep Deprivation

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Introduction: Sleep plays a crucial role in facilitating learning and memory, and sleep deprivation (SD) has been associated with deficits in memory formation and consolidation. Research on rodents has revealed that as little as a few hours of experimental SD can interfere with the consolidation of hippocampal-dependent associative memory, object-place memory, and contextual fear memory. Numerous studies have also shed light on the biochemical and molecular pathways implicated in memory impairment caused by sleep loss. The CA2 subregion of the hippocampus plays a critical role in social memory and emotion processing and is involved in modulating brain activity and memory performance. The integrity of CA2 neurons is crucial for the normal functioning of this hippocampal subregion and is essential for social memory formation. Despite its importance, how sleep influences social memory through the CA2 region remains relatively unexplored. In this study, we investigated whether and how sleep deprivation affects synaptic plasticity and social memory in the CA2 region of mice.

Materials and methods: For SD procedure, mice were subjected to 5 hours of SD using the gentle handling technique. The functional properties of the hippocampal CA2 region were assessed using field electrophysiology. Field excitatory postsynaptic potentials (fEPSPs) were recorded from both the Schaffer collateral (SC) and entorhinal cortex (EC) pathways. Western blotting was performed to examine the expression of key plasticity-related proteins, including adenosine A1 receptors, PDE4A5, PKM ζ , ERK, and BDNF. In experiments involving caffeine administration, mice received a 0.3 g/L caffeine solution in their drinking water, provided *ad libitum* for 7 days prior to experimentation. The Direct Interaction Recognition Test was used to assess social recognition memory before and after SD.

Results: We found that 5-hour SD impaired long-term potentiation in the hippocampal EC-CA2 pathway, accompanied by an increased expression of adenosine A1 receptors. In addition, caffeine-induced synaptic potentiation in the CA2 subregion was significantly reduced following sleep loss. Adenosine A1 receptors are known to be coupled to the adenylyl cyclase-protein kinase A (AC-PKA)

signaling pathway, and several adenylyl cyclase isoforms—such as AC1, AC5, and AC6—are highly expressed in the CA2 region. Consistent with the observed deficits in synaptic plasticity, sleep-deprived mice exhibited impaired social recognition memory, failing to distinguish novel mice from familiar ones in the behavioral test compared to non-sleep-deprived controls. Sleep loss also led to reduced expression of key plasticity-related proteins in the CA2 region, including PKM ζ , ERK, and BDNF. Notably, caffeine supplementation reversed the impairments in both long-term synaptic plasticity and social memory in sleep-deprived mice.

Conclusions: In conclusion, our findings highlight the critical vulnerability of the hippocampal CA2 region to SD and its profound impact on long-term synaptic plasticity and social memory in mice. Moreover, our results reveal a key role for adenosine signaling within the CA2 area in mediating the effects of sleep on social memory, underscoring its potential as a therapeutic target for sleep-related cognitive dysfunction.

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Updating Social Evaluation During Sleep

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Introduction: Current research on sleep often focuses on memory consolidation, with limited exploration of its role in updating social images. Social images, including mental facial representations, significantly influence social biases and stigmatization. Addressing these biases is essential for promoting inclusive social relations. Recent studies have shown that sleep can modulate memory content and influence social attitudes. Building on these findings, we hypothesized that sleep could be leveraged to improve the social image of unattractive individuals by forming new associations through acoustic cues during slow-wave sleep (SWS).

Materials and methods: A total of 138 healthy adults (73 females, mean age 21.69 ± 2.75 years) were recruited, and 106 completed the study. The study consisted of four phases: encoding, baseline testing, sleep intervention, and post-sleep testing. During the encoding phase, participants learned two faces paired with names and personality traits (five positive and five negative). Baseline testing included memory recall and an Implicit Association Test (IAT) to measure initial attitudes toward the faces. During the sleep intervention, participants took a 90-minute nap while one group was exposed to name-positive description pairs during slow-wave sleep (SWS), and a control group was exposed only to names. Post-sleep tests included memory recall, IAT, an ultimatum game to measure social trust, and a reverse correlation image classification task to assess mental facial representations. The study aimed to determine whether sleep-based exposure to positive descriptions could enhance social perceptions of unattractive individuals.

Results: The study found that sleep-based exposure to name-positive description pairs significantly enhanced the attractiveness of mental facial representations for the SI-reshape target (mean $\pm$ SD; SI-reshape: 2.32 ± 0.54 , non-SI-reshape: 2.14 ± 0.55 , $p < .001$), while mere name exposure had no significant effect. This suggests that the positive associations formed during sleep specifically improved mental representations. Memory recall tests revealed that participants remembered more positive traits for the SI-reshape target after sleep (mean $\pm$ SD; SI-reshape: 0.52 ± 0.13 , non-SI-reshape: 0.42 ± 0.11 , $p < .001$), indicating a bias towards positive memory recall. Explicit attitude measures showed higher likeability and social willingness towards the SI-reshape target (mean $\pm$ SD; likeability: SI-reshape: 4.21 ± 1.01 , non-SI-reshape: 3.61 ± 1.10 , $p < .001$; social willingness: SI-reshape: 4.25 ± 1.18 , non-SI-reshape: 3.43 ± 1.19 , $p < .001$). Implicit attitudes, measured by the Implicit Association Test (IAT), also improved significantly after sleep (mean $\pm$ SD; pre-sleep: 0.00 ± 0.64 , post-sleep: 0.18 ± 0.67 , $p < .001$). Additionally, the number of slow oscillations during sleep was positively correlated with the attractiveness of mental facial representations for the SI-reshape target ($r = 0.40$, $p = .002$), suggesting that sleep-related neural activity supports the reshaping of social images. These findings collectively

demonstrate that sleep can be leveraged to enhance social perceptions through targeted acoustic cue exposure.

Conclusions: Our study demonstrates that sleep can be used to reshape social images through acoustic cue exposure, improving mental facial representations, memory of positive traits, and both explicit and implicit attitudes. Future research should explore the neural mechanisms and long-term effects of sleep-based social image reshaping.

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Wakefulness activity-dependent regulation of memory

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Introduction: Sleep plays a critical role in memory consolidation, however, both memory encoding and retrieval take place during wakefulness, underscoring its fundamental importance in maintaining and regulating these memory processes. In contrast to the extensive studies on the role of sleep in memory consolidation, there is a relative lack of studies addressing the impact of wakefulness and the specific circuits that support it on memory.

Materials and methods: We used in vivo calcium imaging, chemogenetics, optogenetics, multi-omics, electrophysiological recording, and EEG/EMG recording with memory behavior tests to explore how wakefulness regulates memory encoding and retrieval.

Results: We first found the structural basis of how wakefulness regulates memory, focusing on the wakefulness system's influence on brain regions involved in memory. Specifically, we targeted a hypothalamic wake-promoting region, the Supramammillary nucleus, which sends dense projections to the memory-related brain region, the dentate gyrus. Then, we highlight that wakefulness regulates memory in an activity-dependent manner, influenced by arousal levels from three perspectives: memory engram cells, synaptic plasticity, and neural oscillations. Additionally, wakefulness promotes memory by regulating adult hippocampal neurogenesis, which represents a novel mechanism to influence memory on a distinct timescale.

Conclusions: Our study demonstrates that wakefulness activity-dependently regulates memory via memory engram cells, synaptic plasticity, and neural oscillations.

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Movement Disorders

A diagnostic model for Parkinson's disease based on circadian rhythm-related genes

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Introduction: Circadian rhythm (CR) disturbance is intricately associated with Parkinson's disease (PD). However, the involvement of CR-related mechanisms in the pathogenesis and progression of PD remains elusive.

Materials and methods: A total of 141 PD patients and 113 healthy participants completed CR-related clinical examinations in this study. To further investigate the CR-related mechanisms in PD, we obtained datasets (GSE7621, GSE20141, GSE20292) from the Gene Expression Omnibus database to identify differentially expressed genes between PD patients and healthy controls and further selected CR-related genes (CRRGs). Subsequently, the least absolute shrinkage and selection operator (LASSO) followed by logistic algorithms were employed to identify the hub genes and construct a diagnostic

model. The predictive performance was evaluated by area under the curve (AUC), calibration curve, and decision curve analyses in the training set and external validation sets. Finally, RT-qPCR and Western blotting were conducted to verify the expression of these hub genes in blood samples. In addition, Pearson correlation analysis was utilized to validate the association between expression of hub genes and circadian rhythm function.

Results: Our clinical observational study revealed that even early-stage PD patients exhibited a higher likelihood of experiencing sleep disturbances, nocturnal hypertension, reverse-dipper blood pressure, and reduced heart rate variability compared to healthy controls. Furthermore, 4 CR-related hub genes (AGTR1, CALR, BRM14, and XPA) were identified and subsequently incorporated as candidate biomarkers to construct a diagnostic model. The model showed satisfactory diagnostic performance in the training set (AUC=0.941), an external validation set GSE20295 (AUC=0.842), and our clinical centre set (AUC=0.805). Additionally, the up-regulation of CALR, BRM14 and the down-regulation of AGTR1, XPA were associated with circadian rhythm disruption.

Conclusions: CR disturbance seems to occur in the early stage of PD. The diagnostic model based on CR-related genes demonstrated robust diagnostic efficacy, offering novel insights for future clinical diagnosis of PD and providing a foundation for further exploration into the role of CR-related mechanisms in the progression of PD.

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Age-Related Changes in Large Muscle Movements During Sleep and Their Impact on Sleep Architecture

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Introduction: Large Muscle Group Movements during sleep (LMM) are closely associated with sleep architecture instability and disruptions in sleep continuity. This study explores LMM across the lifespan, from school-aged children to older adults, examining their relationship with sleep architecture (REM and NREM) to better understand the factors contributing to age-related differences in sleep patterns and motor activity during sleep.

Materials and methods: The study included 141 healthy participants divided into five age groups: school-aged children (n=43), adolescents (n=31), young adults (n=27), adults (n=16), and older adults (n=24). Polysomnography (PSG) was used to record sleep data, with LMM, LMM associated with arousals (LMMA), and LMM associated with awakenings (LMMW) scored according to established criteria. LMM indices and durations were analyzed across groups, and statistical comparisons were made between age groups and between REM and NREM sleep.

Results: LMM indices increased significantly with age, with older adults showing the highest frequency of LMM, LMMA, and LMMW. Conversely, LMM duration was longer in younger participants and shorter in older adults. Significant differences in LMM patterns between REM and NREM sleep were noted, particularly in adults and older adults, where LMM and LMMA were more prevalent during REM sleep. No significant sex differences were observed across age groups. Overall, LMM increased in frequency and decreased in duration with age, with older adults exhibiting higher prevalence of these movements during REM sleep.

Conclusions: Our findings demonstrate an age-related increase in LMM indices, particularly in older adults, who also exhibited more frequent awakenings, potentially linked to heightened sympathetic activity. In contrast, children showed the lowest LMM indices, reflecting the more consolidated sleep and reduced motor activity associated with lower sympathetic activity. Adults displayed higher LMMA indices during REM sleep, suggesting a strong association between motor activity and arousal mechanisms, potentially influenced by cholinergic circuits. These results highlight the evolution of LMM

with age, its close relationship with changes in sleep architecture, and its potential neurophysiological underpinnings. Understanding these patterns provides valuable insights into the mechanisms of sleep-related motor activity and its implications for age-specific sleep management strategies.

Altered Circadian Patterns of Diurnal Blood Pressure in Clinical Phenotypes of Bruxism: A Signal of Autonomic Imbalance?

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Introduction: Bruxism, defined as repetitive masticatory muscle activity involving clenching or grinding of the teeth and/or mandibular thrusting, has recently been reclassified as a behavior rather than a disorder, with its circadian expression—awake bruxism (AB) versus sleep bruxism (SB)—increasingly recognized as clinically relevant. The impact of these phenotypes on systemic physiology remains underexplored. Given that blood pressure (BP) follows a circadian rhythm in healthy individuals—marked by a morning surge, postprandial dip, and afternoon stabilization—this study aimed to assess whether bruxism subtypes exhibit distinct patterns of diurnal BP variation that might reflect underlying autonomic dysregulation.

Materials and methods: A total of 178 healthy university students (mean age 21.3 ± 1.5 years; 74.6% female) were assessed using validated self-report instruments, including bruxism screening tools, the Morningness-Eveningness Questionnaire, Pittsburgh Sleep Quality Index, Insomnia Severity Index, and Epworth Sleepiness Scale. From these, a subsample of 59 participants with probable bruxism—confirmed via diary and clinical signs—was classified into circadian bruxism phenotypes: morning AB, evening AB, SB, and undefined. BP was measured at three standardized timepoints (morning, postprandial, and afternoon) on three non-consecutive days under controlled conditions using a calibrated manual sphygmomanometer.

Results: Overall, none of the bruxism subtypes followed the expected physiological BP circadian rhythm. The SB group demonstrated a significantly lower postprandial diastolic BP (mean 74.1 mmHg) compared to the AB group (79.6 mmHg; $p = 0.045$), consistent with a more pronounced parasympathetic-mediated dip. However, this phenomenon may reflect not parasympathetic integrity but rather an impaired autonomic compensation mechanism, mirroring dysautonomia features reported in insomnia and obstructive sleep apnea. Morning AB subjects also showed a postprandial dip followed by afternoon rebound—suggesting early sympathetic arousal with delayed recovery. The evening AB group, in contrast, presented a flattened BP profile, possibly indicative of diminished autonomic flexibility. Notably, over 40% of participants reported poor sleep quality or signs of circadian misalignment, both of which are known contributors to vascular autonomic dysfunction.

Conclusions: Bruxism phenotypes appear to disrupt normal diurnal BP rhythms, with distinct profiles emerging between AB and SB subtypes. These deviations suggest that bruxism may be more than a localized motor behavior, serving instead as a clinical signal of circadian-autonomic imbalance. Time-of-day-based bruxism phenotyping may thus offer a novel pathway for early identification of individuals at increased cardiometabolic risk—even within asymptomatic populations.

A Minimally Invasive Framework for Home-Based Sleep Tracking in Parkinson's Disease With Wearables

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Introduction: Sleep disorders are among the most prevalent and disabling non-motor symptoms of Parkinson's Disease (PD), significantly impacting patients' quality of life. Nocturnal hypokinesia and akinesia, characterized by reduced or absent movement during sleep, often emerge in the early stages of the disease, contributing to poor sleep quality and increased caregiver burden. Despite their clinical

relevance, clinical assessment of such disorders typically relies on infrequent neurological evaluations and subjective scales, which are susceptible to bias and often fail to capture nightly variability or symptom fluctuations. This highlights the need for objective, scalable, and reproducible frameworks for long-term monitoring of sleep-related motor disorders in PD patients in real-world settings. This study presents a lightweight approach for the unsupervised, home-based monitoring of sleep disturbances in PD using objective and reproducible metrics derived from wearable sensors.

Materials and methods: We included overnight recordings of 40 subjects (12 PD, 28 healthy/controls); data were collected during sleep with wearable inertial measurements units (IMUs) in home settings. The analysis pipeline followed two main objectives: (1) to automatically identify PD-specific sleep-related motor patterns and (2) to objectively evaluate sleep quality, with the Pittsburgh Sleep Quality Index (PSQI) as clinical reference. Given the current lack of standardized features to characterize PD sleep-related motor disorders, this study adopted a multi-domain approach that combines clinical features with motion-based parameters. The latter included both novel descriptors and features previously employed in night-time actigraphy studies. The raw IMU data were processed as follows: first, a series of features characterizing body movements throughout the night were extracted, related to axial movements, turning velocity, and overall nocturnal motility. Then, these were used as inputs to various Machine Learning models (Support Vector Machine, K-Nearest Neighbors, XGBoost), to carry out the two classification tasks. To ensure robust population-level analysis and mitigate potential bias, the dataset was stratified according to sleep quality (PSQI-based) and the presence of PD.

Results: Classification performance was evaluated through accuracy and F1 score, to counteract class imbalance. In automatic detection of PD, the SVM achieved the best results (accuracy: 96.2%, F1 score: 93.4%). Across all models, sleep posture and velocity of turns in bed emerged as the most discriminative features, reflecting the motor rigidity and reduced turning frequency typical of PD patients. For sleep quality assessment, the best performance was achieved with the XGBoost classifier (accuracy: 85.7%, F1: 82.5%). The nocturnal motility index and the time interval between movements, both indicative of sleep fragmentation emerged as most correlated features with PSQI. Subgroup analyses confirmed the significance of these specific features in differentiating between healthy and PD participants with poor sleep quality.

Conclusions: This study presented a home-based monitoring framework to objectively assess sleep-related motor symptoms in PD using wearable technology. The approach demonstrated high classification performance, supporting scalable and objective disease monitoring. Though preliminary, the findings highlight the potential to improve clinical follow-up and patient outcomes, moving toward continuous and personalized disease management, with positive impact on the quality of life for individuals with PD.

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Autonomic Function Test and Polysomnographic Findings in Parkinson's Disease and Multiple System Atrophy: A Comparative Correlational Study

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Introduction: Parkinson's disease (PD) and multiple system atrophy (MSA) are both α -synucleinopathies characterized by autonomic dysfunction and sleep disturbances. However, their clinical presentations and underlying pathophysiology differ considerably. This study aimed to compare polysomnographic (PSG) and autonomic function test (AFT) profiles between drug-naïve patients with PD and MSA, and to investigate disease-specific correlations between sleep-related and autonomic parameters.

Materials and methods: We retrospectively analyzed 136 patients with PD and 67 patients with MSA who underwent PSG, cardiac [I-123] MIBG scintigraphy, and standardized AFTs prior to initiating any treatment. All subjects reported sleep-related complaints (e.g., excessive daytime sleepiness, snoring, or dream enactment behavior). Group comparisons were performed for PSG and AFT parameters. Pearson or Spearman correlation analyses were used to identify significant associations between sleep and autonomic metrics within each disease group.

Results: Compared to PD, patients with MSA exhibited more severe respiratory disturbances and poorer sleep quality, as evidenced by higher apnea index, arousal index, and lower oxygen saturation and sleep efficiency. AFT measures indicated more advanced autonomic dysfunction in MSA across cardiovagal, cardiadrenergic, and sudomotor domains.

In PD, higher apnea-hypopnea index (AHI) correlated with greater cardiovagal dysfunction, while higher REM sleep percentage was associated with lower blood pressure variability. In MSA, greater AHI was correlated with higher composite autonomic severity scores, longer pressure recovery time (PRT), and exaggerated systolic and diastolic blood pressure (BP) drops. Additionally, reduced sleep efficiency, increased Stage 1 and decreased Stage 2 sleep percentage, and frequent arousals were associated with greater sudomotor dysfunction. Oxygen desaturation and AHI were inversely correlated with Valsalva ratio, reflecting compromised parasympathetic integrity.

Conclusions: PD and MSA show fundamentally different patterns of association between sleep architecture and autonomic dysfunction. Further studies are needed to clarify the mechanisms linking sleep and autonomic dysfunction. Given that sleep-related breathing disorders are potentially modifiable, investigating their impact on autonomic function and long-term clinical outcomes may offer valuable opportunities for early therapeutic intervention, especially in MSA.

Circadian Clock Gene *Per1/Per2* Knockout Leads to Motor Dysfunction in Mice

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Introduction: The circadian clock plays a crucial role in maintaining neurological function and behavioral rhythms. *Per1* and *Per2* are core clock genes essential for circadian regulation. Although many studies have reported altered expression of *Per1* and *Per2* in patients with movement disorders such as Parkinson's disease, direct evidence from animal models assessing motor function in *Per1/Per2* knockout mice remains limited.

Materials and methods: *Per1/Per2* double knockout (DKO) mice and age-matched wild-type (WT) C57BL/6J mice were assessed at 6 and 9 months of age. Behavioral tests included the open field test, rotarod test and pole test to evaluate locomotor activity, motor coordination, and bradykinesia-like features. Circadian rhythm disruptions were verified using ClockLab analysis.

Results: *Per1/Per2* DKO mice exhibited significant motor impairments compared to WT controls. At both 6 and 9 months of age, DKO mice performed worse in the rotarod and pole tests, with statistically significant differences indicating deficits in motor coordination and bradykinesia-like feature. In the open field test, no significant difference in locomotor activity was observed at 6 months; however, DKO mice demonstrated a marked reduction in spontaneous activity compared to WT controls at 9 months. Disrupted circadian activity patterns were also confirmed in DKO mice.

Conclusions: These findings suggest that deletion of *Per1* and *Per2* impairs motor function, with observable deficits in coordination and movement control. The results underscore the potential role of circadian clock genes in modulating movement disorders.

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Clinical and polysomnographic characteristics of periodic limb movements during sleep in obstructive sleep apnea patients and the effect of positive airway pressure therapy

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Introduction: Periodic limb movements during sleep (PLMS) are frequently observed in patients with obstructive sleep apnea (OSA). However, data on the clinical and polysomnographic characteristics of individuals with coexisting OSA and PLMS remain limited. Additionally, the effect of positive airway pressure (PAP) therapy on PLMS remains controversial.

This study aimed to investigate the clinical and polysomnographic profiles of patients with concurrent OSA and PLMS, assess the effect of PAP therapy on PLMS, and identify predictors associated with PLMS outcomes following PAP therapy.

Materials and methods: This retrospective analytical study included randomly selected patients diagnosed with OSA who underwent split-night polysomnography between January and December 2024. Clinical, demographic, and polysomnographic data were collected. PLMS was defined as a periodic limb movement index (PLMI) ≥ 15 events/hour. PLMI was compared between the diagnostic and optimal PAP portions of the study. Optimal PAP therapy was defined by a respiratory disturbance index (RDI) < 5 events/hour for at least 15 minutes, including supine REM sleep.

Results: A total of 155 patients were included, with mean age of 58.51 ± 15.33 years; 49.03% were male, and mean BMI was 26.59 ± 5.56 kg/m². Baseline polysomnographic findings included mean sleep efficiency of $79 \pm 12.02\%$, median AHI of 41 (25.9–62.8) events/hour, mean nadir oxygen saturation of $82.51 \pm 10.39\%$, and mean optimal CPAP pressure of 8.87 ± 2.48 cm of water. The median PLMI was 26.2 (18.2–35.8) events/hour. Only 4.5% of the patients met criteria for restless legs syndrome (RLS). During optimal PAP therapy, PLMS improved in 67.7% of the patients, remained unchanged in 1.9%, and worsened in 30.4%. Overall, PLMI normalized in 58% of the patients. Obstructive apnea index (OR 1.037, 95% CI 1.013–1.062; $p=0.003$) and hypopnea index (OR 1.022, 95% CI 1.006–1.039; $p=0.007$) were significant predictors of non-response to PAP therapy.

Conclusions: In patients with OSA and coexisting PLMS, most did not meet criteria for RLS. Notably, PLMS improved in nearly 70% of patients after effective OSA treatment with optimal PAP therapy. Obstructive apnea and hypopnea indices were significant predictors of persistent PLMS despite treatment.

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Clinical Research of Acupuncture and Medication Combined Treatment for Restless Legs Syndrome(RLS)

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Introduction: RLS is a neurological sensory and motor disorder characterized by an indescribable and irresistible lower limb discomfort during rest, which seriously affecting patients' sleep and quality of life. Clinical drug treatments often use dopaminergic drugs, but they may have side effects and unstable efficacy. This study aims to evaluate the clinical efficacy of acupuncture combined with Traditional Chinese Medicine (TCM) compared with Western medicine in the treatment of RLS.

Materials and methods: A total of 96 patients with RLS who visited the TCM outpatient department of Beijing Changping Hospital of Integrated Chinese and Western Medicine, from March 2022 to March 2024 were selected as the research subjects. They were randomly divided into an observation group and a control group according to the randomized controlled trial (RCT) method, with 48 cases in each group. The observation group was treated with modified TCM formula (Yangxue Roujin Decoction) and acupuncture (acupoints: Zusanli, Sanyinjiao, Yanglingquan, Taichong, etc.), while the control group was treated with oral Levodopa. The clinical efficacy and sleep quality of the two groups were observed after 8 weeks of treatment and followed up for 12 weeks. Evaluation indicators: International Restless Legs Syndrome Rating scale (IRLS); Pittsburgh Sleep Quality Index (PSQI).

Results: The total effective rate of the observation group (89.6%) was significantly higher than that of the control group (64.6%), and the difference was statistically significant ($P < 0.05$). After treatment, the improvement rate of the IRLS and PSQI score in the observation group were significantly better than those in the control group, and the difference was statistically significant ($P < 0.05$).

Conclusions: The combined treatment of acupuncture and medication for RLS can significantly improve clinical symptoms and sleep quality, with few adverse reactions. It provides new ideas for the future

integrated traditional Chinese and Western medicine therapy and precision targeted therapy of RLS, and is worthy of clinical promotion and application .

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Combined Cardiovascular Autonomic Failure and Cognitive Impairment as Independent and Additive Predictors of Progression and Phenoconversion in Isolated REM Sleep Behavior Disorder: A Prospective Cohort Study

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Introduction: Isolated REM Sleep Behavior Disorder (iRBD) is a prodromal state of α -synucleinopathies, where early identification of high-risk individuals remains a clinical challenge. While both cardiovascular autonomic failure (cAF) and cognitive impairment (CI) are established biomarkers of disease progression, their combined prognostic significance has not been fully explored. This study aimed to: (1) explore the cross-sectional and longitudinal interplay between autonomic and cognitive dysfunctions in iRBD; (2) assess their respective and combined roles in predicting phenoconversion.

Materials and methods: Seventy-four iRBD patients (73% male, mean age at onset 62.2 ± 8.1 years) were prospectively recruited and followed annually (mean follow-up: 3.17 ± 1.88 years). All underwent cardiovascular reflex testing (CRT) including Tilt Table Test, Valsalva Maneuver, Deep Breathing, Cold Face, and Handgrip tests, as well as a standardized neuropsychological battery. Cognitive and autonomic changes were assessed both cross-sectionally and longitudinally. Survival analyses (Kaplan-Meier and Cox regression) were used to estimate phenoconversion risk.

Results: At baseline, 17 patients (25.4%) had mild cognitive impairment (MCI), and 12 (17.9%) exhibited neurogenic orthostatic hypotension (nOH). No significant association was found between CI and nOH either cross-sectionally (MCI prevalence: 33.3% with nOH vs 23.6% without; $p = 0.484$) or longitudinally. Over time, we observed a significant increase in MCI with multiple domain involvement (OR = 1.65, 95% CI: 1.02–2.66; $p = 0.038$) and deterioration in visuospatial (OR = 1.17, 95% CI: 1.07–1.28; $p = 0.001$) and memory domains (OR = 1.50, 95% CI: 1.00–2.25; $p = 0.050$). Meanwhile, nOH showed a significant progression with time (e.g., OH at 3 min: OR = 1.66, 95% CI: 1.06–2.60; $p = 0.026$).

Fifteen patients (20.3%) phenoconverted (6 to DLB, 5 to PD, 2 to MSA, 2 to unspecified atypical parkinsonism) over a mean follow-up of 3.17 ± 1.88 years. Cox regression revealed that both MCI (HR = 3.71, 95% CI: 1.22–11.22; $p = 0.020$) and nOH (HR = 3.64, 95% CI: 1.20–10.98; $p = 0.022$) independently increased conversion risk. Their concomitant presence further amplified the hazard ratio to 12.12 (95% CI: 2.76–53.29; $p = 0.001$), indicating a four-fold higher risk compared to either factor alone.

Conclusions:

In iRBD, cognitive and autonomic dysfunctions follow parallel but independent progression pathways. While they do not significantly influence each other in their evolution, their coexistence markedly enhances the risk of developing α -synucleinopathies. These findings support the use of a multidimensional biomarker model integrating autonomic and cognitive assessments to improve phenoconversion risk stratification and patient monitoring in prodromal α -synucleinopathies.

Effects of Light Therapy on Parkinson's Disease-Related Brain Dysconnectivity and Sleep Disorders

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Introduction: Light therapy (LT) may improve the clinical symptoms of Parkinson's disease (PD), a common neurodegenerative disease, especially sleep disorders. The objective of this study was to verify the effect of LT and identify differences between bright light therapy (BLT) and dim light therapy (DLT) on the clinical symptoms, objective sleep parameters, and functional brain networks of PD patients.

Materials and methods: Thirty-three PD patients were randomized to receive either 1 month of BLT or DLT, separated by a 1-month washout period, in a crossover fashion. All patients filled out comprehensive clinical questionnaires and underwent polysomnography (PSG) at baseline and after each period of intervention. A subset (11 patients in each group) also underwent 64-channel resting-state electroencephalogram (EEG) recording.

Results: BLT and DLT both decreased the Pittsburgh Sleep Quality Index (PSQI) score of PD patients. Compared with DLT, BLT significantly reduced the excessive daytime sleepiness (ESS) score and sleep latency and increased the slow-wave energy (SWE) during sleep in PD patients. BLT significantly increased the phase locking value (PLV) between the frontal and temporal lobes. It also increased global efficiency in the delta, alpha, and beta bands and reduced the characteristic path length in the alpha and beta bands relative to DLT.

Conclusions: LT improved sleep disorders associated with PD. BLT, in particular, has therapeutic potential to enhance sleep stability and improve daytime sleepiness, possibly due to its ability to restore functional brain dysconnectivity and enhance information integration and transmission efficiency.

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Efficacy and tolerability of extended-duration tonic motor activation for treating middle of the night awakenings associated with restless legs syndrome

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Introduction: Restless Legs Syndrome (RLS) is often associated with symptoms during the middle of the night that increase sleep fragmentation and wake after sleep onset (WASO). Prior studies have shown that bilateral high-frequency peroneal nerve stimulation – also known as tonic motor activation (TOMAC) – reduces RLS symptoms and improves sleep quality. These studies evaluated a TOMAC device that stimulates for 30 minutes (TOMAC-30). Here, we tested if a novel investigational TOMAC device that stimulates for an extended duration of 180 minutes (TOMAC-180) could lead to greater improvements in WASO and middle of the night RLS symptoms.

Materials and methods: This two-phase open-label feasibility study enrolled 14 patients with RLS who reported RLS symptoms during middle of the night awakenings ≥ 3 nights per week. During weeks 1-2 (phase 1), all participants received TOMAC-30 and were instructed to activate stimulation whenever they had RLS symptoms at bedtime or during the sleep period. During weeks 3-4 (phase 2), all participants received TOMAC-180 and were instructed to activate stimulation each night at bedtime. To enable 180-minutes of stimulation on a single battery charge, a novel investigational device was developed. WASO was assessed objectively by calculating the average minutes awake during the sleep period based on wrist actigraphy (Philips Actiwatch 2). Participant-rated questionnaires assessed the frequency of middle of the night RLS symptoms. The analysis population comprised all participants who started phase 2 (n=11). Baseline data were collected for frequency of middle of the night symptoms but not for actigraphy.

Results: The frequency of middle of the night RLS symptoms decreased significantly during TOMAC-180 treatment relative to baseline (3.36 vs. 4.95 days per week, Difference: -1.69, $p < 0.01$) and relative to TOMAC-30 (Difference: -1.09, $p = 0.04$). The mean duration of WASO per night decreased significantly for TOMAC-180 relative to TOMAC-30 (56.2 vs. 85.5 minutes, Difference: -29.3 minutes, $p = 0.03$); 51% of this improvement (14.8min) occurred during the first 180-minutes of sleep (i.e. during TOMAC-180) and the remaining 49% (14.5min) occurred later in the sleep period. There were 3 dropouts during TOMAC-30 (none due to tolerability or adverse events), no dropouts during TOMAC-180, and no serious or severe device-related adverse events during either treatment.

Conclusions: Compared to 30-minute TOMAC, extended-duration 180-minute TOMAC improved WASO, reduced middle of the night RLS symptoms, and was similarly well-tolerated. These results support additional development and validation of extended-duration TOMAC. Further studies with additional baseline assessments would be helpful to characterize the extent of sleep improvement with extended-duration TOMAC relative to baseline.

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Efficacy of transcutaneous spinal direct current stimulation and pneumatic compression in restless legs syndrome and augmentation

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Introduction: Dopaminergic medications represent one of the most effective treatments for Restless Legs Syndrome (RLS). However, their use can lead to augmentation - a paradoxical worsening of symptoms characterized by an earlier onset, increased intensity, and spread of RLS manifestations with increasing drug doses. While some individual studies suggest the efficacy of non-pharmacological therapies for RLS, their impact on augmentation remains underexplored. The aim of this study was to assess the effectiveness of transcutaneous spinal direct current stimulation (tcSDCS) and pneumatic compression (PC) in patients with and without augmentation.

Materials and methods: A total of 40 patients with RLS were enrolled: 20 with augmentation and 20 without. The median age in the augmentation group (main group, MG) was 63.5 years (male/female: 5/15), and in the non-augmentation group (control group, CG) it was 62 years (male/female: 7/13). Among participants, 22 were taking pramipexole, 2 levodopa, 2 gabapentin, 1 pregabalin, while 13 were not taking any medications.

Patients were assessed using clinical examination and the International RLS Study Group rating scale (RS). All patients underwent the Suggested Immobilization Test (SIT) at 7:00–8:00 PM (SIT1) and 9:00–10:00 PM (SIT2) to evaluate the urge to move (via a 10-point numerical rating scale) and periodic limb movements while awake (PLMW). Twenty patients (10 with and 10 without augmentation) received tcSDCS, while the other 20 (10 with and 10 without augmentation) underwent PC therapy. Treatment effectiveness was evaluated based on changes in RS scores, NRS ratings of the urge to move, and PLMW counts during SIT.

Results: In the MG, tcSDCS significantly reduced PLMW during SIT1 (pre-treatment: 59 [15–105]; post-treatment: 11.5 [5–96], $p = 0.03$), NRS urge scores (pre: 7.0 [5.2–8.8]; post: 3.4 [1.8–6.8], $p = 0.03$), and RS scores (pre: 33.5 [30–35]; post: 25.5 [21–32], $p = 0.03$). In the CG, tcSDCS also led to RS score improvement (pre: 21 [20–28]; post: 21 [15–24], $p = 0.04$).

PC therapy in the CG resulted in a reduction of PLMW during SIT1 (pre: 10.5 [0–13]; post: 0 [0–5], $p = 0.048$) and a decrease in RS score (pre: 24 [20–29]; post: 21 [15–23], $p = 0.048$). However, neither tcSDCS nor PC showed any significant effect on SIT2 outcomes.

Conclusions: tcSDCS appears to offer symptomatic relief in both augmented and non-augmented RLS, particularly when administered before 8:00 PM. This effect may be related to reduced spinal excitability during earlier phases of the disease. PC demonstrated efficacy only in patients without augmentation, suggesting its role may be limited in more advanced or drug-complicated cases.

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Electroencephalographic slowing during REM sleep is a marker of cholinergic dysfunction in Lewy body disorders

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Introduction: Lewy body diseases, including Parkinson's disease (PD) and dementia with Lewy bodies (DLB), represent the second most common neurodegenerative disease in older adults. Recent work has implicated progressive cholinergic system dysfunction as a key contributor to cognitive decline and disease progression in Lewy body disorders. Despite this, simple, non-invasive biomarkers of cholinergic impairment are lacking. Given that cholinergic neurons are actively involved in REM sleep and play a central role in cortical activation, alterations in EEG during REM sleep may offer a unique window into cholinergic network dysfunction.

In this study, we investigated whether REM EEG slowing in particular reflects disruption of key cholinergic hubs, the nucleus basalis of Meynert (NBM) and pedunculopontine nucleus (PPN), and whether this electrophysiological marker relates to cognitive impairment in Lewy body disorders.

Materials and methods: This cross-sectional study included 105 participants: 25 with DLB (mean age = 74.6 ± 6.0 years), 40 with PD (mean age = 64.2 ± 8.6 years), and 40 controls without cognitive impairment (mean age = 66.3 ± 7.7 years). All participants underwent comprehensive neuropsychological assessment and overnight polysomnography. A subset of participants also completed structural and resting-state fMRI within 12 months of their other assessments. Absolute REM spectral power was computed across frontal, central, and occipital regions for standard frequency bands (δ , θ , α , σ , β), and a slowing ratio was defined as $[(\delta+\theta)/(\alpha+\sigma+\beta)]$. NBM volumes were extracted from T1-weighted images, and seed-based functional connectivity was assessed between the NBM and resting-state networks, and between the PPN and thalamus, using the Schaefer 400, Tian subcortical, and probabilistic NBM atlases. Group differences in REM spectral power were assessed using general linear models with permutation testing. Linear regressions were used to examine associations between neuroimaging variables and REM EEG slowing across α -synucleinopathies. All analyses included age and sex as covariates, applying FDR correction where appropriate.

Results: DLB participants showed significantly greater REM EEG slowing in occipital regions compared to PD and controls ($p_{FDR} = 0.006$). Power spectral changes were not associated with NBM volume. However, occipital REM slowing was significantly correlated with; aberrant NBM functional connectivity to the visual ($p_{FDR} = 0.034$), ventral attentional ($p_{FDR} = 0.034$), default mode ($p_{FDR} = 0.037$), and frontoparietal ($p_{FDR} = 0.037$) networks; and deficits in global cognition (MMSE; $p_{FDR} = 0.020$), verbal learning (RAVLT recall; $p_{FDR} = 0.009$), and executive function (Trails B; $p_{FDR} = 0.020$). Altered PPN connectivity to the thalamus was correlated with REM slowing across regions (frontal, $p_{FDR} = 0.008$; central, $p_{FDR} = 0.033$; occipital, $p_{FDR} = 0.033$).

Conclusions: This study demonstrates that REM EEG slowing is associated with cholinergic network dysfunction across Lewy body diseases, and correlates with cognitive impairment across multiple domains. These findings suggest REM EEG slowing may be a non-invasive and transdiagnostic marker of cholinergic dysfunction and cognitive decline in Lewy body disorders, with relevance for disease monitoring, prognosis, and stratification in clinical trials.

Exploring Sleep Bruxism through Sleep Physiology and Posture: Implications for Risk Prediction

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Introduction:

Sleep bruxism (SB) is a sleep-related behavior involving rhythmic masticatory muscle activity, classified into phasic, tonic, or mixed patterns. While traditionally viewed as a disorder, emerging evidence suggests SB may act as a compensatory mechanism to maintain airway patency or respond to arousals during sleep. Although SB has been linked to sleep disturbances, the relationship between its patterns, severity, and physiological sleep parameters remains unclear. Sleep posture may also influence SB expression, yet this factor is often overlooked. We hypothesized that SB severity and pattern are associated with specific sleep-related physiological markers and that body position modulates these associations. This study explores these relationships to provide insights for future risk assessment and predictive modeling.

Materials and methods:

We recruited 35 participants (mean age 29.2 ± 6.6 years) with self-reported sleep bruxism (SB). Exclusion criteria included neurological, respiratory, or systemic conditions and medication use affecting sleep or muscle function. Participants underwent overnight polysomnography (PSG) in a sleep lab (24 °C, 60% RH), with recordings including EEG, ECG (wireless patch), oxygen saturation, and body position. The sleep protocol included both **natural posture** and **controlled posture segments**, during which participants were instructed to maintain specific positions (supine, prone, left, right) using positioning aids and monitored in real-time. Body position was tracked continuously, and SB episodes were classified as phasic, tonic, or mixed, and quantified using the Bruxism Episode Index (BEI). Sleep architecture and spectral EEG parameters were analyzed by SB severity and posture.

Results: Our findings revealed that the frequency and type of sleep bruxism (SB) episodes—phasic, tonic, and mixed—differed significantly among groups classified by SB severity. Greater severity was associated with increased wake after sleep onset (WASO) and lower subjective sleep efficiency. Furthermore, variations in brain activity were observed, with significant differences in whole-night theta wave percentages and non-rapid eye movement stage 2 (N2) proportions among severity groups. Sleep position played a critical role: the frequency of SB events varied across natural, supine, prone, left, and right positions. Specifically, non-supine positions were associated with fewer SB events and better sleep quality metrics, such as total sleep time and reduced arousals. Correlation analyses showed that SB severity and type were inversely associated with poor sleep indicators in non-supine positions, while the opposite was observed in supine positions.

Conclusions: Sleep bruxism (SB) may not solely represent a pathological sleep disorder but could reflect a physiological response to airway instability during sleep. The present findings suggest that sleep posture may influence SB expression, with non-supine positions potentially associated with improved sleep continuity and fewer arousals. All three SB types—phasic, tonic, and mixed—exhibited posture-dependent associations with sleep parameters, indicating that body position might play a modulatory role in the occurrence and functional significance of SB.

Acknowledgments:

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Impact of Dopamine Agonists and Clonazepam on LMM and PLMS in RLS Patients

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Introduction: Restless Legs Syndrome (RLS) is a heterogeneous sensorimotor disorder characterized by disrupted sleep architecture. Evidence from numerous studies indicates that therapies for RLS can modulate various polysomnographic (PSG) parameters, aiming to restore normal sleep homeostasis. Recent findings suggest that Large Muscle Group Movements during sleep (LMM) are significantly increased in RLS and may have distinct neurophysiological and neurobiological mechanisms compared to Periodic Leg Movements during Sleep (PLMS). This study investigates the effects of dopamine agonists (DAs) and clonazepam (CLO) on LMM in patients with RLS.

Materials and methods: A retrospective analysis was conducted on 51 drug-free adult RLS patients, divided into three groups: 33 received a DA (pramipexole or ropinirole), 15 received CLO, and 18 received a placebo. Each patient underwent two consecutive nocturnal PSG recordings: one at baseline

and one following treatment administration. LMM and PLMS were scored. Between-group differences were analyzed using ANCOVA, with the International RLS Study Group severity scale as a covariate. Within-group changes were evaluated using paired t-tests.

Results: At baseline, no significant differences in LMM or PLMS were observed between groups. Post-treatment, DAs significantly reduced PLMS and periodicity indexes but had minimal impact on LMM indexes, except for a slight increase in LMM duration. The placebo group demonstrated a significant reduction in the LMM index during the second night, potentially due to a first-night effect (FNE). CLO did not significantly affect either PLMS or LMM.

Conclusions: This study underscores the complexity of motor disturbances in RLS, highlighting that while DAs effectively reduce PLMS, they have limited impact on LMM, suggesting distinct underlying mechanisms for these motor activities. These findings emphasize the need for a more comprehensive therapeutic approach in RLS that addresses the full spectrum of motor abnormalities. The persistence of arousals and NREM sleep instability despite DA treatment further suggests the inadequacy of current therapies in fully resolving sleep disruptions in RLS. Future research should prioritize the development of targeted interventions capable of addressing both PLMS and LMM to enhance treatment outcomes in RLS patients.

Impact of Large Muscle Group Movements on Sleep Neurophysiology in Restless Legs Syndrome

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Introduction: Restless Legs Syndrome (RLS) is a highly heterogeneous sensorimotor disorder rooted in a complex and interconnected network of neurotransmitters. These networks influence the clinical presentation, phenotype variability, severity of the disorder, and its response to treatment. Neurophysiological assessments, which reflect the functioning of neuronal and neurotransmitter systems, offer valuable insights into understanding RLS. Recently, criteria have been established for assessing Large Muscle Group Movements during sleep (LMM). This study aims to characterize LMM in RLS to better evaluate their impact on the sleep neurophysiology of the disorder in adults.

Materials and methods: Consecutive drug-free patients diagnosed with RLS and healthy controls aged 18 years or older were retrospectively enrolled. Leg movement activity was assessed and scored, including short-interval leg movements (SILMS), periodic leg movements during sleep (PLMS), isolated leg movements (ISOLMS), and LMM.

Results: A total of 100 RLS patients and 67 controls were included. All movement indices were significantly higher in RLS patients compared to controls. A significant positive correlation was observed between the LMM and ISOLMS indices in both groups, but not between LMM and PLMS indices. In RLS patients, the LMM index showed a significant negative correlation with total sleep time, sleep efficiency, and the percentage of sleep stages N3 and R. Conversely, it demonstrated a significant positive correlation with the number of awakenings and the percentage of sleep stages N1 and N2. No significant correlations were found between LMM or PLMS indices and RLS severity.

Conclusions: Different types of leg movements contribute uniquely to the sleep neurophysiology of RLS. LMM, in particular, are associated with sleep architecture instability, fragmentation, arousals, and awakenings, indicating potential clinical implications. These disruptions are supported by a complex neural network involving serotonergic and noradrenergic neurons and modulatory influences from glutamatergic, acetylcholinergic, dopaminergic, histaminergic, and orexinergic systems. Since homeostatic sleep pressure is regulated by neurotransmitters also implicated in RLS, targeting one or more of these systems to reduce LMM and their adverse effects on sleep neurophysiology could yield significant clinical benefits.

Impaired transition from wake to sleep and hyperarousal may not resolve with a dental guard in sleep-related bruxism

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Introduction: Sleep related bruxism (SB) is a common sleep-related movement disorder, defined by involuntary rhythmic recurrences of increased masticatory muscle tone during sleep. The present study aims to compare polysomnographic parameters and clinical assessments (oro-dental examination) along with daytime symptoms, in SB patients and a control group of similar age. In addition, exploratory associations between recorded sleep variables and clinical parameters are performed. An evaluation of the therapeutical impact of SB treatment with a dental guard (DG), has been conducted in a subgroup of SB patients. The main hypotheses are that, despite subjective symptom complaints, sleep structure does not show significant impairments in SB and that Rhythmic Masticatory Muscle Activity (RMMA) is not significantly associated with daytime symptoms or sleep variables.

Materials and methods: 22 SB patients and 13 good sleeper controls, of similar age, underwent polysomnography (PSG), clinical evaluations and assessments with structured symptom scales, in a cross-sectional observational study, between September 2024 and January 2025. Secondly, a clinical follow-up evaluation of SB patients, treated with DG (n=6) in comparison to untreated SB (n=11), has been conducted, at least 3 months after PSG.

Results: Excepted for a significant (p=.014) reduction of light sleep (Non-REM stage 1) and a significantly higher arousal index (p<.001), comparisons of sleep structure variables, revealed broadly similar sleep stage durations between groups. Sleep efficiency was significantly lower in SB patients (p=.028). Although being significantly increased in SB patients, apnea-hypopnea index did not show any association to the RMMA index. The latter was however significantly related to the decrease of N1 sleep duration (p=.033). SB patients displayed significantly greater teeth wear, higher levels of insomnia (p=.022) and daytime sleepiness (p=.012) than control subjects. While gingival recession was more frequent in untreated SB patients, comparative follow-up evaluations, solely showed significantly higher levels of insomnia complaints and higher levels of masseteric muscle hypertrophy among the DG treated subsample of SB patients.

Conclusions: The present study indicates that wake to sleep transitions may be impaired in SB patients. Our results also underline associated symptom intensities and suggest that hyperarousal or insomnia may not show sufficient therapeutic responses to purely mechanical treatments in SB patients.

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Real-world evidence of tonic motor activation (TOMAC) for refractory restless legs syndrome (RLS): Interim 180-day results from the THRIVE study

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Introduction: Tonic motor activation (TOMAC) is a therapeutic medical device for refractory restless legs syndrome (RLS) that transmits bilateral high-frequency electrical stimulation to the peroneal nerve in the legs. TOMAC has previously been demonstrated as safe and efficacious in randomized controlled trials. Here, we report interim results from the THRIVE study, which evaluates the real-world safety and effectiveness of TOMAC in clinical practice.

Materials and methods: Patients prescribed Nidra TOMAC (Noctrix Health, Inc.) after study initiation in November 2023 were invited to participate in the THRIVE multicenter prospective observational post-market study. The prespecified indicated intent-to-treat (IITT) population comprised participants who met the U.S. FDA indication of moderate-severe refractory RLS; data were imputed for participants who withdrew. Interim analysis was conducted on all participants enrolled ≥180 days before March 18,

2025, the date of interim database lock. Baseline measures were assessed prior to starting TOMAC and interim outcomes were assessed at Day-180 relative to baseline. The primary efficacy endpoint was mean change to International RLS Study Group (IRLS) score and key secondary outcomes included clinical global impressions of improvement (CGI-I) and mean change to Medical Outcomes Study Sleep Problem Index II (MOS-II) score. The frequency and nature of adverse events and medication changes were assessed.

Results: For IITT participants (n=73) at study entry, mean age was 66.4 years (SD: 11.0), average duration of RLS symptoms was 29.9 years (SD: 17.9), 63% were female, and mean IRLS score was 25.9 points (SD: 5.6). From baseline to Day 180, mean IRLS change was -8.5 (95% CI: -6.9 to -10.2), CGI-I responder rate was 60%, and mean MOS-II change was -14.1 (95% CI: -9.4 to -18.9). The only device-related adverse events were administration site skin irritation (5%) and administration site discomfort (4%), which were never serious nor severe. Of the 66 participants prescribed RLS medication at baseline, 24 (36%) reduced RLS medication dose and 9 (14%) increased RLS medication dose (odds ratio: 2.7). Participants who reduced medication had average dose reduction of 51%, mean IRLS change of -8.4 points (95% CI: -6.2 to -10.6) and MOS-II change of -9.3 points (95% CI: -2.5 to -16.1).

Conclusions: These interim results suggest that TOMAC treatment is safe and effective in real-world treatment of refractory RLS. After 180 days of TOMAC treatment, there were improvements to both RLS symptoms and sleep quality. Reductions to adjunctive RLS medication were more common than increases and were well-tolerated.

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REM sleep deprivation promotes the spread of pathological α -synuclein and dopaminergic neuronal degeneration in Parkinson's disease

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Introduction: Rapid eye movement sleep behavior disorder (RBD), as an important prodromal symptom of Parkinson's disease (PD), often emerges several years or even decades earlier than typical motor symptoms. Moreover, most RBD patients will gradually progress to synucleinopathies such as PD, suggesting that REM sleep disorders play a key role in the occurrence and development of PD. The latest research shows that the level of α -synuclein (α -syn) in cerebrospinal fluid shows obvious diurnal fluctuations, manifested as an increase during the awakening period and a decrease during the sleep period. Based on these findings, this study aims to explore the effects of chronic REM sleep deprivation on the pathological transmission of α -syn and the survival of dopaminergic neurons in a PD model.

Materials and methods: 12-week-old male C57BL/6J mice were randomly divided into four groups: 1) Normal sleep + PBS (CON+PBS); 2) Sleep deprivation + PBS (SD+PBS); 3) Normal sleep + α -syn preformed fibrils (CON+ α -syn PFF); 4) Sleep deprivation + α -syn preformed fibrils (SD+ α -syn PFF). The PD mouse model was established by stereotactic injection of 5 μ g α -syn PFF into the striatum. Beginning 48 hours post-injection, mice underwent daily REM sleep deprivation for 20 hours using the modified multiple platform water maze method, maintained for 4 consecutive weeks. At the 6-month endpoint, brains were collected for quantitative assessment of phosphorylated α -syn (Ser129) deposition and stereological counting of tyrosine hydroxylase-positive (TH+) dopaminergic neurons in the substantia nigra pars compacta (SNpc) using immunofluorescence microscopy.

Results: No obvious phosphorylated α -syn (pSer129) deposition was detected in the SNpc of PBS control groups (CON+PBS and SD+PBS). Compared with the CON+ α -syn PFF group, the SNpc of mice in the SD+ α -syn PFF group showed: 1) significantly enhanced immunopositive signals of phosphorylated α -syn; and 2) significantly reduced numbers of tyrosine hydroxylase-positive (TH+) dopaminergic neurons.

Conclusions: This study confirmed that chronic REM sleep deprivation can significantly promote the spread and abnormal aggregation of pathological α -syn in the SNpc of PD models and aggravate degenerative changes in dopaminergic neurons.

Restless arms syndrom - an uncommon presentation of restless-leg syndrom

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Introduction: Restless Legs Syndrome (RLS) also known as Willis-Ekbom-Disease is assigned to neurological disorders. It is characterized by an uncontrollable urge to move the legs, due to uncomfortable sensation. These conditions in term can lead to daytime sleepiness, fatigue and depression, which is mostly found in RLS patients. In extreme cases, these symptoms can be so stressful for patients that they develop suicidal thoughts. RLS may occur also in other parts of the body other than the legs. Especially, isolated restless arm syndrome (RAS) is very rare. Most commonly, the legs are in some way also affected by symptoms. These two following Case reports are about two patients with special forms of RLS.

Materials and methods: Overall 2 patients were included in this study. Diagnose was performed according to the International RSL Group (IRLSSG). All demographic and clinical data of patients were collected. Both patients received polysomnography. All demographical information and medical reports were examined. Polysomnography was available in both patients as well as follow up data.

Results: Both patients suffered from uncommon forms of RLS: The male patient, aged 50 years, suffered from isolated RAS of both arms. He suffered from depression and sleep disorder with consecutive day time sleepiness. The female patient, aged 66 years suffered from RLS isolated affecting the left body side. Iron-values were normal in both patients. Clinically, RAS presented with uncomfortable and painful burning sensation of the arms. The both patients were diagnosed using the IRLSSG-criteria and both met all criteria.

Conclusions: Restless arms syndrome is either a part of restless legs syndrome or a seldom variant of restless legs syndrome. It is part of discussions, if restless arms syndrome is a distinct disease. Due to its rarity, RAS is often underdiagnosed. Patients usually do not associate the distinct symptoms only affecting the arms or only one side of the body with restless legs syndrome. So far, clinicians are requested to ask patients with sleep disorders specifically about the distinct restless legs symptoms with regard to the arms. And they should consider, that RLS can appear one sided only. Especially the first case shows the effects of RAS on the quality of life. RAS can coincide with psychiatric disorders such as depression.

Restless Legs Syndrome during Pregnancy and Puerperium

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Introduction: Pregnancy is a significant risk factor for the development of Restless Legs Syndrome. Apart from it's negative impact on sleep and general quality of life, RLS is also associated with pregnancy complications and negative outcomes.

Materials and methods: To elucidate the prevalence, trajectory, severity, and risk factors of RLS throughout pregnancy and the postpartum period we analysed data from the multicenter Life-ON Cohort Study (NCT02664467) which recruited 439 pregnant women in the 10-15th gestational week and followed them up until 12 months after delivery.

Results: 26% of women (n=113) met the diagnostic criteria for RLS in at least one of the three visits during pregnancy. RLS severity was similar during all trimesters and during the postpartum period with however higher values in women who screened positive for RLS in all the three or two trimesters compared to those who screened positive in just one. A previous history of RLS was found in 50.68% of women who reported RLS during the current pregnancy and 18.7% had a positive family history. During the entire follow-up period out of 386 women, 134 were diagnosed with RLS, corresponding to a cumulative incidence of 34.7%. Previous history of depression, positive family history for RLS and previous RLS were statistically significant risk factors for RLS during pregnancy. Around 20% of women

experienced severe to very severe symptoms (IRLS >20 pts), representing a possible target to be carefully considered for a pharmacological treatment

Conclusions: The correct identification and treatment of RLS during pregnancy could potentially greatly improve women's sleep quality and generally quality of life during pregnancy and reduce associated pregnancy complications and negative pregnancy outcomes.

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Sex and Age Differences in PLMS Among RLS Patients: A Lifespan Perspective

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Introduction: Restless Legs Syndrome (RLS) and Periodic Leg Movements during Sleep (PLMS) are common sleep disorders with significant health impacts. While sex-related disparities in RLS and PLMS prevalence are well-documented, a comprehensive understanding of these differences across the lifespan remains limited. This study investigates sex differences in PLMS among RLS patients across various age groups, ranging from 2 to over 80 years, and explores the potential mechanisms underlying these differences, with important clinical implications.

Materials and methods: A retrospective analysis was conducted on drug-free patients diagnosed with RLS, comprising 95 females (ages 2–83.2) and 89 males (ages 2–79.5). Polysomnographic recordings were used to evaluate leg movement activity, including the PLMS index and Periodicity index. Exclusion criteria included other sleep disorders, psychiatric diagnoses, and central nervous system drug use.

Results: In females, the PLMS index showed a rapid increase starting before age 10, plateauing below male levels until about age 55, after which it rose significantly for over a decade. In males, the PLMS index increased steadily, peaking after age 75. The Periodicity index followed a simpler trajectory, progressively increasing from prepuberty to around age 35 in males and age 45–50 in females. Females maintained a slightly higher Periodicity index than males for over a decade after this period.

Conclusions: The findings highlight the complex interplay between PLMS, age, and sex, with critical differences emerging during puberty and menopause. These trends suggest a significant influence of sex hormones and autonomic nervous system modulation on sleep motor activity across developmental stages. Our results emphasize the importance of personalized approaches to managing movement-related sleep disorders, tailored to demographic and physiological differences across age and sex.

Sex-Related Differences in Dopamine Agonist Response in Restless Legs Syndrome: A PSG-Based Study

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Introduction: Restless Legs Syndrome (RLS) is a sensorimotor sleep disorder characterized by significant heterogeneity in clinical manifestations, symptom onset, progression, and response to pharmacological treatments. Epidemiological studies indicate a higher prevalence of RLS in women

compared to men from adolescence onwards. This study aimed to examine sex-related differences in the therapeutic response to dopamine agonists, specifically ropinirole and pramipexole, in adult patients with RLS. By analyzing clinical parameters and polysomnographic (PSG) findings, we sought to explore the potential implications of sex disparities on treatment efficacy and sleep quality in RLS management.

Materials and methods: A retrospective analysis was conducted on 41 drug-free RLS patients aged 18 years or older. All participants underwent two consecutive nocturnal PSG recordings, the first without medication (baseline) and the second following treatment. Prior to the second night, 26 participants received a single oral dose of 0.25 mg pramipexole, while 15 received a single oral dose of 0.5 mg ropinirole in the evening. After each PSG recording, patients assessed the severity of their previous night's symptoms using an ad hoc Visual Analogue Scale (VAS).

Results: On the treatment night, women exhibited higher sleep efficiency and a greater percentage of stage N2 sleep, whereas men experienced significantly higher wakefulness after sleep onset. Additionally, women showed significantly lower total leg movements during sleep (LMS), periodic LMS (PLMS), and periodicity indexes compared to men. While VAS scores decreased significantly across all patients after treatment, no significant sex differences were observed in subjective symptom relief.

Conclusions: Both pramipexole and ropinirole primarily act through D3 receptors, which exhibit sex-specific expression patterns. This differential expression may underlie the higher pharmacological response observed in women, particularly with respect to reductions in PLMS. These findings align with emerging research on sex differences in the pharmacokinetics and pharmacodynamics of cardiovascular therapies, underscoring the importance of considering sex as a critical factor in personalized medicine. Our study provides valuable insights for developing more tailored, sex-specific treatment approaches for RLS and highlights the need to incorporate sex differences into future pharmacological guidelines.

Sleep Disturbances and Quality of Life in Children with Developmental Coordination Disorder

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Introduction: Children aged 6–12 years with Developmental Coordination Disorder (DCD) often experience reduced health-related quality of life (QOL). While sleep disturbances are common in neurodevelopmental disorders (NDDs) and have been linked to lower QOL, little is known about this relationship in children with DCD. This study aimed to examine the association between parent-reported sleep behaviours and QOL in children with DCD or those showing symptoms but not yet formally diagnosed (probable DCD; pDCD).

Materials and methods: A total of 92 caregivers (97% mothers) of children aged 6–12 years with DCD or pDCD participated in an online survey. Child sleep behaviours were measured using the Children's Sleep Habits Questionnaire (CSHQ), and QOL was assessed using the KIDSCREEN-10 parent-proxy version. Descriptive statistics were used to summarise QOL and sleep. Spearman correlations were conducted to assess the strength and direction of associations between sleep and QOL.

Results:

Most children were male (67.4%), with a formal DCD diagnosis (83.7%), and aged 9–12 years. The majority had at least one comorbid condition (54.3%), most commonly ADHD (35.6%) and ASD (14.1%). Parents reported low QOL scores ($M = 34.10$, $SD = 6.49$), and 92% indicated their child experienced at least one sleep disturbance. The most commonly reported issues were daytime sleepiness ($M = 14.04$, $SD = 3.64$), bedtime resistance ($M = 8.63$, $SD = 3.20$), and parasomnias ($M = 10.36$, $SD = 2.59$). Overall sleep disturbance significantly and negatively correlated with QOL ($r = -.348$, $p < .001$), explaining 12.1% of the variance. Daytime sleepiness had the strongest association ($r = -.415$, $p < .001$; 17.2% variance explained), followed by parasomnias ($r = -.261$, $p < 0.001$). Bedtime resistance was not significantly correlated with QOL ($r = -.107$, $p > 0.05$).

Conclusions: Children with DCD or pDCD frequently experience both poor sleep and reduced QOL, particularly in relation to daytime sleepiness and parasomnias. These findings suggest that addressing sleep disturbances may be a promising avenue to support wellbeing in this population. Clinical

assessment and intervention planning for children with DCD should routinely consider sleep behaviours. Future research using objective sleep measures and child self-reports is recommended to strengthen and extend these findings.

Sleep Stage-Specific Aperiodic EEG Spectral Slope Alterations in isolated REM Sleep Behavior Disorder and Neurodegenerative Disorders

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Introduction: Quantitative electrophysiological biomarkers capturing alterations in neural activity during sleep hold promises for improving the early detection and monitoring of Parkinson's disease (PD) and its prodromal stages, isolated REM sleep behavior disorder (iRBD). The spectral slope of the EEG power spectrum provides a frequency-independent measure of cortical excitability. However, there has been limited data in characterizing stage-specific alterations of spectral slope in iRBD and PD populations and its association with the conversion risk of iRBD.

Materials and methods: 404 video-polysomnography recordings from 270 patients with clinically diagnosed iRBD (70.30 ± 6.62 years, 78% male), 46 patients with PD (70.68 ± 6.75 years, 83% male), and 88 age- and sex-matched controls (70.14 ± 7.66 years, 66% male) were studied. Among the iRBD patients, 25 patients eventually converted to neurodegeneration (16 PD, 7 dementia with Lewy bodies, 2 multiple system atrophy) at 5.21 ± 2.86 years follow up. Sleep stages were manually scored according to AASM criteria by experienced technicians. The aperiodic spectral slope, defined as the exponent of the $1/f$ decay in the EEG power spectrum, were estimated using the FOOOF package. The 1–45 Hz spectral slope was computed for each clean 8-second epoch. The spectral slopes were averaged across Wake (prior to sleep onset), N1, N2, N3, and REM stages and all EEG channels (F4,C4,O2). Group differences in mean slope values per stage were assessed via generalized linear model adjusted for age and sex with Bonferroni-corrected post hoc tests. The conversion risk was estimated via Cox proportional hazards regression model.

Results: Spectral slopes demonstrated a clear, progressive flattening from healthy controls to iRBD to PD across all sleep stages. In light sleep (N1), mean slopes were -1.70 ± 0.18 in controls, -1.53 ± 0.25 in iRBD, and -1.38 ± 0.26 in PD ($p < 0.001$). This pattern persisted in N2 (controls: -1.96 ± 0.17 ; iRBD: -1.73 ± 0.27 ; PD: -1.55 ± 0.28 ; $p < 0.001$) and slow wave sleep (N3: controls -2.33 ± 0.21 ; iRBD -2.14 ± 0.23 ; PD -1.88 ± 0.37 ; $p < 0.001$). During REM sleep, slopes averaged -1.74 ± 0.18 in controls, -1.56 ± 0.25 in iRBD, and -1.43 ± 0.29 in PD ($p < 0.001$). In contrast, wake stage showed only a slight flattening (controls -1.20 ± 0.46 ; iRBD -1.12 ± 0.45 ; PD -0.92 ± 0.44 ; $p = 0.011$), with post hoc tests revealing a significant difference between PD and controls (mean difference = 0.27, p -corrected = 0.003) as well as between PD and iRBD (mean difference = 0.204, p -corrected = 0.015). A more flattening spectral slope at wake stage was associated with significantly increased risk of phenoconversion (HR = 5.15; 95%CI: 1.73–15.3; $p = 0.003$), but not in other sleep stages (N1 $p = 0.152$, N2: $p = 0.104$, REM: $p = 0.095$).

Conclusions: There was progressive flattening of aperiodic EEG spectral slopes from healthy controls to iRBD to PD across all sleep stages. A more flattening of spectral slope at wake stage predicts phenoconversion in iRBD. These findings support the role of spectral slope as a non-invasive biomarker for both staging and risk stratification in prodromal neurodegeneration.

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Smartphone-based digital phenotyping of motor and non-motor biomarkers across early stages of α -synucleinopathies

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Introduction: Recent advances in smartphone-based digital measurements for neurodegenerative α -synucleinopathies, including Parkinson's disease (PD), have demonstrated promising results in symptom assessment. Nevertheless, existing applications generally have a narrow scope of symptom coverage (e.g., focusing solely on motor features). Thus, we developed a smartphone application *SmartBrainApp* in Hong Kong to comprehensively assess both motor (e.g., movement, speech and facial expression) and non-motor (e.g., psychomotor, cognition, impulsivity) functions of PD (26 tests total). In the current study, we aimed to: 1) validate *SmartBrainApp* among clinical PD patients, and 2) evaluate the ability of the App to detect subtle motor and non-motor changes in the prodromal stage of α -synucleinopathies, i.e., idiopathic/isolated rapid eye movement sleep behaviour disorder (iRBD).

Materials and methods: The validation study was conducted in 44 PD patients (mean age: 67.6 ± 5.5 years; 79.6% male) and 44 age- and sex-matched controls (67.1 ± 5.5 years; 79.6% male), who underwent clinical and traditional paper-and-pencil-based neurocognitive assessments and also completed the *SmartBrainApp* assessment. The content (expert review), construct (correlation with traditional tests), criterion (PD vs. control discrimination) validity, acceptability, and feasibility were evaluated. Test-retest reliability was assessed in a subset of 37 subjects (19 controls and 18 PD). A further assessment was conducted in 125 iRBD patients (68.4 ± 6.5 years; 72.8% male) and 95 age- and sex-matched controls (67.6 ± 5.4 years; 72.6% male), and a comparison of traditional and App features was carried out.

Results: Among 26 tests, 21 (81%) showed satisfactory validity (significant correlation with the traditional assessment and group differences), and 17 of these (81%) also showed acceptable test-retest reliability (intraclass correlation coefficient > 0.6). When combining all digital tests, the sensitivity and specificity for distinguishing PD patients from controls were 88.9% and 85.2%, respectively, reaching an area under the curve (AUC) of 0.93. Among them, pronation-supination movement (AUC = 0.88, accuracy = 84.1%) and leg agility (AUC = 0.84, accuracy = 80.7%) were the optimal App-based motor tests predicting PD. The feasibility was supported by high completion rates ($\geq 97.7\%$) across the assessments, with 97.0% of subjects indicating that the assessments were not difficult to complete and 75.8% preferred the digital format over traditional paper-based methods. In addition, our smartphone-based App was able to capture subtle but significant PD-like abnormalities of iRBD patients in some motor (leg agility, finger tapping, reading and monologue) and non-motor (executive and attentional cognitive functions) tasks that were not detected by conventional assessments. By using all the features of *SmartBrainApp*, the AUC for distinguishing iRBD from controls reached 0.72.

Conclusions: *SmartBrainApp* demonstrated satisfactory validation properties in most motor and non-motor tasks and effectively identified a series of early motor/non-motor deficits in iRBD that were not detected by conventional assessments. This innovative approach addresses the critical need for accessible and objective assessments that can capture the multifaceted nature of PD, potentially enabling earlier detection and more precise monitoring of symptom evolution compared to conventional clinical evaluations.

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The Double-Edged Pill: Pediatric Augmentation of RLS with Gabapentin

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Introduction: The American Academy of Sleep Medicine (AASM) updated its guidelines on restless leg syndrome (RLS), advising reduced use of dopamine agonists due to side effects like augmentation. While gabapentin shows low augmentation rates (~0.9%) in adults, limited data exist for pediatric cases. This report highlights treatment-resistant RLS in a 10-year-old male, potentially involving gabapentin-related augmentation.

Materials and methods: A 10-year-old with mild pediatric obstructive sleep apnea (OSA) and significant atopy presented with chronic nocturnal leg tingling relieved by movement. Adherence to PAP was reasonable. Family history included RLS in his father and pregnancy-related symptoms in mother.

Results: Labs were unremarkable, including ferritin at 85 ng/mL. X-rays ruled out lower extremity anatomic issue. Gabapentin was initiated and titrated with resolution of symptoms. After one year, symptoms worsened despite ongoing adherence to gabapentin, which was maximized at 600mg at night. The mother explored alternative therapies including transcutaneous electrical nerve stimulation unit, compression garments, massages, magnesium, and various homeopathic supplements with minimal relief. Repeat ferritin was 47 ng/mL and oral iron was started for 3 months without improvement. Given severity, intravenous ferric carboxymaltose therapy was ordered and also failed to improve symptoms. Symptoms escalated and began to occur earlier in the day and more persistent, raising concerns of gabapentin-induced augmentation. Neurology consultation yielded no additional guidance. Gabapentin was weaned, and pregabalin was considered but declined due to parental concerns of side effects. Benzodiazepines were also avoided due to a family history of substance misuse and parental concerns.

Conclusions: This adolescent initially responded to gabapentin, requiring higher and higher doses to control RLS. Occurrence of symptoms earlier in the day with increasing severity suggested augmentation. Unclear trigger. This case highlights a fairly underreported phenomenon of gabapentin-induced augmentation in pediatric RLS. This highlights the challenges of managing restless leg syndrome in children and emphasizes the need for more research and treatment strategies in the pediatric population.

Narcolepsy

Abnormal brain functional network dynamics in narcolepsy type 1 patients

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Introduction: To investigate the dynamic functional connectivity in narcolepsy type 1 (NT1) patients and whether clinical features are associated with abnormal connectivity.

Materials and methods: We investigated dynamic functional connectivity (dFC) of 80 drug-naïve NT1 patients, 30 idiopathic hypersomnia (IH) patients and 60 age- and sex-matched healthy controls using sliding-window approach, clustering state analysis and graph-theory methods. Relationships between clinical features and abnormal dFC properties were evaluated.

Results: Three dFC brain states were identified to characterize and compare dynamic functional connectivity patterns: a more frequent and sparsely connected State I (46.96%), a less frequent and more strongly connected State II (26.3%), and a less frequent and sparsely connected State III (26.74%). In NT1 patients, the occurrence of the State II increased, corresponding with a prolonged dwell time of State II. While State III are predominant for healthy controls and IH. The occurrence and dwell time of State III are negatively correlated with sleep latency in NT1 patients.

Conclusions: The abnormal temporal patterns and functional segregation coupled with the severity of sleepiness and abnormal local integration in topological properties confirmed the vulnerability of functional networks in NT1 patients.

Abnormal Connectivity between Visual and Intrinsic Networks as Biomarkers for Differentiating Idiopathic Hypersomnia from Narcolepsy Type 1

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Introduction: Differentiating between idiopathic hypersomnia (IH) and narcolepsy type 1 (NT1) remains challenging in clinical practice. This study aimed to investigate whether dynamic functional network connectivity (FNC) can effectively distinguish between NT1 and IH based on group differences.

Materials and methods: The study involved 36 drug-naïve NT1 patients and 14 age- and sex- group matched IH patients, employing group spatial independent component analysis, sliding-window techniques, and clustering state analysis methods. Logistic regression, support vector machines, and random forest algorithms were then utilized to develop models for distinguishing between NT1 and IH based on the group comparison results from dynamic functional network connectivity (FNC).

Results: The dynamic functional network connectivity (FNC) analysis revealed five distinct connectivity configurations. State III, which accounts for 52% of all windows, resembles a stationary FNC and represents a more frequent but relatively sparse connected state. State I (19%) is characterized by stronger interconnectivity, while State II (2%) shows robust interconnections between intrinsic connectivity networks (ICNs), featuring both positive and negative connections. State IV (13%) is notable for sparse internal connections within the frontal-parietal network (FPN) and limited external connections between the FPN and other ICNs. In contrast, State V (14%) is marked by strong internal connections within the dorsal attentional network, sensorimotor network (SMN), and visual network (VIN). Notably, NT1 patients were observed more frequently in State IV than IH patients, while IH patients were more prevalent in State V. In State V, functional connectivity between VIN and other ICNs shows significant group differences between IH and NT1. For these connectivity, three diagnostic models demonstrated exceptional predictive performance in detecting IH within both training and test sets.

Conclusions: Abnormal connectivity between VIN and other networks, such as auditory network, SMN and FPN, may serve as potential biomarkers to differentiating IH from NT1.

Amelioration of Sleep-Related Eating Disorder After Switching From Twice-to Once-Nightly Oxybate

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Introduction: In a disproportionality analysis (Merino D, et al. *J Clin Med.* 2022;11:3890), sodium oxybate (SXB) treatment was associated with sleep-related eating disorder (SRED), a parasomnia characterized by somnambulism and compulsive eating. Immediate-release twice-nightly oxybate (TN-OXB) formulations (ie, SXB and calcium, magnesium, potassium, and sodium oxybates [mixed-salt oxybates]) are administered at bedtime and again 2.5-4 hours later. SRED coincides with the first dose of TN-OXB if patients remain awake. This retrospective, single-site analysis assessed the effect of switching from TN-OXB to extended-release once-nightly SXB (ON-SXB) on SRED among individuals with narcolepsy.

Materials and methods: Retrospective chart review was conducted from a single clinical site. Data were collected from individuals with narcolepsy who experienced SRED while taking TN-OXB and were switched to ON-SXB from the time of switch to ON-SXB through currently available data. Patient demographics, medical history, oxybate treatment duration, dosage, and weight-related measures before and after the treatment switch were recorded. Data were described and analyzed descriptively.

Results: Of 8 individuals with narcolepsy who experienced SRED, the mean (SD) age was 21 (4.1) years, 6 (75%) were female, and 6 (75%) and 2 (25%) had narcolepsy type (NT) 1 and NT2, respectively. Before switching to ON-SXB, median (range) TN-OXB dose and mean (SD) treatment duration were 8.8 (4.8-10.5) g and 40.6 (21.1) months, respectively, with 3 individuals (37.5%) taking asymmetric doses. After switching to ON-SXB, median (range) ON-SXB dose was 9 (6-9) g. Sleep eating episodes were resolved in all individuals within 6 months of switching to ON-SXB. Five (63%) individuals experienced a reduction in BMI after switching to ON-SXB.

Conclusions: In this retrospective chart analysis, individuals with narcolepsy and SRED experienced positive clinical outcomes after switching from TN-OXB to ON-SXB. Individuals switching to an oxybate that did not require a middle-of-the-night dose had resolution of sleep eating, and nearly two-

thirds experienced a reduction in BMI. SRED is an underappreciated challenge with TN-OXB dosing that may be ameliorated with a single, extended-release dose of SXB, as provided by ON-SXB.

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A Phase 2, Randomized, Placebo-Controlled, Parallel-Group Study Evaluating the Safety and Efficacy of Alixorexton (ALKS 2680) in Patients With Idiopathic Hypersomnia: Study Design and Methods for Vibrance-3

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Introduction: Idiopathic hypersomnia (IH) is a rare, chronic central disorder of hypersomnolence characterized by excessive daytime sleepiness and frequently accompanied by sleep inertia, long and unrefreshing naps, and prolonged nighttime sleep. Alixorexton (ALKS 2680) is a highly potent, oral, and selective orexin 2 receptor agonist in clinical development as a once-daily treatment for narcolepsy and IH. In a phase 1b study, patients with IH experienced statistically significant, clinically meaningful improvements in mean sleep latency on the Maintenance of Wakefulness Test (MWT) and self-reported alertness on the Karolinska Sleepiness Scale (KSS) following single doses of alixorexton at 5, 12, and 25 mg. Alixorexton was generally well tolerated with no serious or severe treatment-emergent adverse events (TEAEs). The objective of the phase 2 Vibrance-3 study (NCT06843590) is to evaluate the safety and efficacy of alixorexton compared with placebo in patients with IH across 8 weeks of treatment.

Materials and methods: Vibrance-3 is a randomized, double-blind, parallel-group, dose-range-finding study. Eligibility criteria include age 18 to 70 years, a diagnosis of IH based on the International Classification of Sleep Disorders (ICSD-3-TR) criteria, a body mass index between ≥ 18 and ≤ 40 kg/m², no significant comorbid sleep-related illness that could interfere with the sleep-wake cycle, no unstable medical conditions, and no shift work or other activities that may disrupt regular nighttime sleep. Patients will undergo an initial 2-week washout period from current medications used to manage IH symptoms, after which approximately 96 patients with IH will be randomized 1:1:1:1 to placebo or 10, 14, or 18 mg dose of alixorexton once daily for 8 weeks. The primary efficacy endpoint of Vibrance-3 is the change in the Epworth Sleepiness Scale score from baseline to week 8. Change in the Idiopathic Hypersomnia Severity Scale score from baseline to week 8 is the key secondary endpoint. Safety will be assessed by TEAEs, laboratory assessments, vital signs, electrocardiograms, and the Columbia-Suicide Severity Rating Scale. Mean sleep latency (assessed across MWT sessions), Clinical Global Impression of Severity, and patient-reported outcomes, including the KSS, are exploratory endpoints of the study.

Results: Results of Vibrance-3 are pending study completion.

Conclusions: Findings from the Vibrance-3 study will inform further clinical development of alixorexton in patients with IH. The phase 2 Vibrance-1 (NCT06358950) and Vibrance-2 (NCT06555783) studies are evaluating alixorexton in patients with narcolepsy type 1 and narcolepsy type 2, respectively.

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Assessing Usability of Once-Nightly Sodium Oxybate Extended-Release Oral Suspension for Narcolepsy

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Introduction: Sodium oxybate, available in once-nightly and twice-nightly formulations, is indicated for treatment of cataplexy or excessive daytime sleepiness in narcolepsy. Once-nightly sodium oxybate extended-release oral suspension (ON-SXB; LUMRYZ™) may alleviate potential dosing challenges associated with immediate-release twice-nightly formulations. Human factors validation testing was conducted to confirm safe use of ON-SXB, using the product packaging, mixing cup, and Instructions for Use (IFU).

Materials and methods: Two summative studies evaluated simulated usability of ON-SXB in individuals (16–65 years of age) with narcolepsy, who were categorized as either experienced (having current or previous experience self-administering SXB) or naive (no current or previous experience). Both studies were conducted in lab settings modeled after a home bedroom environment. Study 1 (S1) assessed all critical and noncritical tasks related to storage, preparation, administration, and disposal of ON-SXB. After S1, IFU updates were implemented for additional risk control. Study 2 (S2) assessed tasks associated with these updates. Tasks were evaluated through observed performance or participant responses to a labeling comprehension activity.

Results: Of the S1 participants enrolled (mean [range] age, 37.0 [16–57] years; female, 77%), 77% (24/31) successfully prepared and administered the full ON-SXB dose. Critical use errors included failure to administer dose at bedside (experienced, 8/15; naive, 12/16) and preparing >1 dose packet (experienced, 1/15; naive, 1/16). Multiple critical use errors occurred during the label comprehension activity, which S1 participants attributed to difficulty in locating certain safety-critical warnings in the labeling. Using these data, the IFU was updated. In S2, 87% (26/30) of participants (mean [range] age, 35.8 [17–64] years; female, 83%) successfully prepared and administered the dose. Fewer S2 participants encountered critical errors observed in S1 (not administering dose at bedside [experienced, 4/15; naive, 5/15] and preparing >1 dose packet [none]), indicating that IFU updates effectively reduced the associated use risks. Only 2 use errors, which occurred with naive participants and were related to product storage, occurred in the S2 label comprehension activity.

Conclusions: Validation to confirm that individuals with narcolepsy can follow labeled instructions for safe use and self-administration of oxybates is important and has been conducted with ON-SXB.

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Attention and Inhibition Deficits in Narcolepsy Type 1 : Behavioral and Electrophysiological Markers

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Introduction: Cognitive impairments in narcolepsy type 1 (NT1) significantly compromise daily functioning, but their neural mechanisms remain unclear.

Materials and methods: This study employed multimodal electroencephalography (EEG) analyses to investigate electrophysiological substrates of attention and inhibition deficits in NT1 and their association with clinical characteristics, particularly orexin deficiency. High-density EEG recordings were acquired during a Go/NoGo task from 39 NT1 patients and 41 age-/sex-matched healthy controls. Behavioral analyses revealed that compared to controls, NT1 patients exhibited significantly prolonged reaction times and increased errors across both Go and NoGo conditions.

Results: Electrophysiological analyses demonstrated that NT1 patients showed: (1) delayed Go-P3 latencies, meaning impaired response preparation; (2) reduced NoGo-P3 amplitudes, reflecting deficient inhibitory control; and (3) attenuated theta-band power and inter-trial phase consistency across conditions. Notably, decreased theta-band power correlated with both lower orexin levels and slower reaction times.

Conclusions: These findings suggest that orexin deficiency may mediate theta-band oscillation impairments in NT1, which mechanistically contribute to cognitive dysfunction. Thus, we propose theta-band oscillations as a clinically translatable biomarker for NT1-related cognitive deficits, with

promising implications for objective monitoring of disease progression and developing EEG-targeted neuromodulation therapies.

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BP1.15205, a novel orexin-2 receptor agonist, demonstrates wake-promoting effects in monkeys and successfully completed the preclinical regulatory program

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Introduction: Narcolepsy is a chronic sleep disorder often caused by selective deficiencies in orexin, a brain neurotransmitter that regulates wakefulness. BP1.15205 is a novel, highly potent, and orally bioavailable orexin-2 receptor agonist that previously demonstrated wake-promoting and anti-cataplectic effects in a mouse model of type 1 narcolepsy. The objectives of the current studies were to confirm the wake-promoting effects of BP1.15205 in wild-type monkeys, and to complete the preclinical regulatory program prior to Phase 1 clinical studies.

Materials and methods: For the *in vivo* pharmacology study, polysomnographic recordings were performed in wild-type male Cynomolgus monkeys. Following regulatory studies were GLP-compliant. For general toxicity studies, BP1.15205 was administered orally to Wistar rats (30 to 1000 mg/kg/day) and Beagle dogs (10 to 100 mg/kg/day) for 13 weeks, followed by a 4-week recovery period. The different dose ranges were chosen after preliminary non-GLP 14-day toxicity studies. Safety pharmacology studies included Irwin and respiratory plethysmography in Wistar rats, cardiovascular telemetry in vigil Beagle dogs, and patch-clamp assay in HEK-293 cells expressing the hERG channel. Genotoxicity studies included the Ames mutagenicity test, and *in vitro* and *in vivo* micronucleus tests in human lymphocytes and rat bone marrow, respectively. Finally, phototoxicity was assessed on human fibroblasts.

Results: The polysomnography study in monkeys demonstrated BP1.15205 to produce a robust wake-promoting effect (increase in total wakefulness time at the expense of both NREM and REM sleeps), significant from the dose of 1 mg/kg. The 13-week toxicity studies in rats and dogs revealed no BP1.15205-related adverse changes in body weight, food consumption, hematology, coagulation, organ weights, gross pathology, or histopathology at the maximal doses (100 mg/kg/day in dogs, 300 mg/kg in female rats, and 1000 mg/kg in male rats). These top doses were thus considered as NOAEL doses and corresponding toxicokinetics data provided satisfactory safety margin estimates. The Irwin and plethysmography studies revealed no adverse effects of BP1.15205 on the central nervous system and respiratory function at doses up to 300 mg/kg and 1000 mg/kg in female and male rats respectively. No cardiovascular concern was raised for BP1.15205 with an IC₅₀ value >30 µM at the hERG channel and without any adverse effect on the cardiovascular function at the maximal dose of 100 mg/kg in dogs. The Ames, *in vitro* and *in vivo* micronucleus studies demonstrated the absence of genotoxicity induced by BP1.15205. Finally, no BP1.15205-related phototoxicity was depicted.

Conclusions: BP1.15205 wake-promoting properties were demonstrated across species, including wild-type and narcoleptic mice and monkeys. Moreover, the GLP preclinical program demonstrated that BP1.15205 was not toxic at the highest doses tested in two species, did not alter the central nervous system, respiratory or cardiovascular functions, and was neither genotoxic nor phototoxic. Taken together, these results will support an IND application submission, and Phase 1 clinical study is planned to start in H2 2025.

Characterization of the nature, severity, and subjective experience of Cognitive Symptoms Associated with Narcolepsy Type 1

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Introduction: Narcolepsy Type 1 (NT1) is a chronic neurological disorder marked by excessive daytime sleepiness, cataplexy, and fragmented nocturnal sleep. In addition to these hallmark symptoms, accumulating evidence indicates that cognitive symptoms are common, persistent, and clinically important in adults with NT1. Notably, cognitive symptoms can persist even when core sleep-related symptoms are well controlled and can adversely impact daily functioning and quality of life. Despite their clinical relevance, the nature and extent of cognitive symptoms in NT1 remain poorly understood. This analysis aimed to characterize these symptoms in adults with NT1 using validated tests of objectively assessed cognitive impairments and patient-reported cognitive difficulties.

Materials and methods: Baseline data were analyzed from three independent cohorts of adults with confirmed NT1 diagnoses. Each cohort was compared to a cohort of 120 healthy, age- and sex-matched controls with no evidence of any sleep disorder. Cohort 1 (N=111) was drawn from a Phase 2 clinical trial (NCT05687903), Cohort 2 (N=126) from a parallel observational study, and Cohort 3 (N=14) was a subset from a separate Phase 2 trial (NCT04096560). In Cohort 1, objective cognitive function was assessed using four validated neuropsychological tests: the Psychomotor Vigilance Task (PVT) for sustained attention, the Continuous Paired Associate Learning Test (CPAL) for visual learning and memory, the One-Back Test (ONB) for working memory, and the International Digit Symbol Substitution Test (IDSST) for processing speed. In Cohort 2, patient-reported cognitive function over the past week was measured using the validated Functional Impacts of Narcolepsy Instrument Cognitive Functioning domain (FINI CF). In Cohort 3, both PVT and FINI CF were assessed. For each NT1 Cohort, differences from normal performance were investigated for each outcome using independent-samples t-tests, and effect sizes were calculated using Cohen's *d*.

Results: In Cohort 1, individuals with NT1 performed significantly worse than healthy controls, with a large magnitude impairment in sustained attention ($d=1.34$, $p<0.001$), and moderate magnitude impairments in processing speed ($d=0.68$, $p<0.001$) and working memory ($d=0.73$, $p<0.001$); impairments in associate memory were not statistically significant ($d=0.14$, $p>0.1$). In Cohort 2, patient-reported subjective cognitive difficulties were significantly greater in the NT1 group than healthy controls with a large magnitude difference ($d=2.51$, $p<0.001$). In Cohort 3, large-magnitude differences were again observed in both sustained attention ($d=1.49$, $p<0.001$) and patient-reported cognitive difficulties ($d=2.58$, $p<0.001$).

Conclusions: This analysis of three independent cohorts show that cognitive symptoms are an important feature of NT1 as evidenced by large magnitude cognitive impairment on objective neuropsychological tests, particularly in attention, and substantial patient-reported cognitive difficulties on scales. The pattern of cognitive impairments observed in these well-characterized cohorts of adults with NT1 aligns closely with recent meta-analytic findings (Harel et al., *Sleep Advances*, 2024), supporting their robustness and replicability. These results suggest cognitive symptoms should be considered in the diagnosis and treatment of individuals with NT1.

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Clinical and Polysomnographic Differences Among Child-, Adolescent-, and Adult-Onset Type 1 Narcolepsy: A Chinese Cohort Study

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Introduction: The study aimed to evaluate the differences in clinical presentation and polysomnographic parameters across different onset-age groups of type 1 narcolepsy (NT1).

Materials and methods: This retrospective study included patients with definitive diagnosis of NT1. Participants were categorized into child-onset (<10 years), adolescent-onset (10-19 years), and adult-

onset (>19 years) groups. Demographic and clinical information were collected and statistically analyzed.

Results: 2,344 NT1 cases were included in the final analysis (Child-onset 1,160, adolescent-onset 902, adult-onset 282). A bimodal age distribution of narcolepsy onset was observed, with peaks at approximately 7 and 30 years of age. Diagnostic delays persisted across all three age-of-onset groups (median: 1 vs 5 vs 4 years, $p < .001$). An age-dependent progression was observed in symptom prevalence, with sleep paralysis and hallucinations showing increasing frequency from child- through adolescent- to adult-onset groups (sleep paralysis: 19.0% vs 56.2% vs 71.5%, $p < .001$; hallucinations: 47.2% vs 59.6% vs 62.1%, $p < .001$). Etiological patterns differed significantly among groups: childhood-onset cases were predominantly associated with infections and vaccinations (49.0%), while adult-onset cases mainly involved non-infectious/vaccination triggers (92.9%). Adolescent-onset patients demonstrated an intermediate clinical profile between these two patterns (71.6% non-infection/vaccination). Polysomnographic (PSG) and multiple sleep latency test (MSLT) analyses demonstrated gradual variations in apnea-hypopnea index (AHI) and sleep architecture across the three groups (AHI median: 1.2 vs 2.2 vs 9.2 events/hour). Although all groups showed similar objective sleepiness levels (as measured by PSG sleep latency [median: 1.5 vs 1.0 vs 1.0 minutes, $p = .144$] and MSLT mean sleep latency [median: 2.2 vs 2.0 vs 2.0 minutes, $p = .319$]), childhood-onset NT1 patients exhibited more pronounced rapid eye movement (REM) sleep dysregulation, evidenced by shorter REM latency in nocturnal PSG (median: 2.5 vs 3.5 vs 7.3 minutes, $p = .009$) and a higher frequency of sleep-onset REM periods (SOREMPs) in MSLT (median: 5 vs 4 vs 4, $p < .001$).

Conclusions: Child-, adolescent-, and adult-onset NT1 exhibit distinct clinical profiles, including differences in symptom presentation, etiological triggers, and polysomnographic features. These disparities may reflect divergent yet potentially overlapping pathogenic mechanisms.

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Clinically Meaningful Improvement in Daytime Sleepiness With ON-SXB in People With Narcolepsy and Severe Sleepiness

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Introduction: Efficacy of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) for narcolepsy was demonstrated in the phase 3 REST-ON trial (NCT02720744). Efficacy on daytime sleepiness in REST-ON participants with the most severe sleepiness at baseline was analyzed post hoc.

Materials and methods: Participants (≥ 16 years; narcolepsy type 1 [NT1] or NT2) were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. Sleep latency on the Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) scores were calculated in tertiles of participants from the modified intent-to-treat (mITT) population (randomized participants with ≥ 1 efficacy measurement after receiving 6-g dose) with lowest mean sleep latency on the MWT (MWT tertile) or highest ESS scores (ESS tertile) at baseline. Data are median (Q1, Q3) observed values.

Results: In the mITT population (ON-SXB, $n=97$; placebo, $n=93$), mean age for MWT tertile participants (ON-SXB, $n=33$; placebo, $n=30$) was 30.5 years (65.1% female, 76.2% NT1, 60.3% taking concomitant alerting agents), and for ESS tertile participants (ON-SXB, $n=33$; placebo, $n=41$), it was 32.4 years (63.5% female, 90.5% NT1, 37.8% taking concomitant alerting agents). Respective sleep latency on the MWT (min) for ON-SXB and placebo groups of MWT tertile participants was 1.5 (1.0, 2.3) and 2.0 (1.3, 2.5) at baseline and 7.0 (2.5, 15.0) and 4.9 (1.8, 8.3) at week 13 (9 g), and for ESS tertile participants was 4.7 (2.8, 7.5) and 4.6 (2.1, 6.6) at baseline and 11.5 (6.9, 21.7) and 5.0 (2.0, 13.0) at week 13 (9 g). Respective ESS scores for ON-SXB and placebo groups of MWT tertile participants were 16.0 (14.0, 19.0) and 19.0 (16.0, 20.0) at baseline and 10.0 (6.0, 16.5) and 16.0 (13.0, 19.0) at week 13 (9 g), and of

ESS tertile participants were 21.0 (19.0, 22.0) and 21.0 (19.0, 22.0) at baseline and 9.0 (6.0, 19.5) and 18.0 (14.0, 22.0) at week 13 (9 g).

Conclusions: The most severely sleepy REST-ON participants at baseline experienced clinically meaningful improvement in daytime sleepiness with ON-SXB treatment, as ESS scores were at or below the normal threshold at the end of the study.

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Clinical Phenotypes and Longitudinal Evolution Patterns in Narcolepsy: A Prospective Cohort Study Based on Symptom Cluster Analysis

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Introduction: To explore the heterogeneity and dynamic evolution of clinical phenotypes in narcolepsy by constructing a longitudinal subtype framework using prospective cohort data, and to assess the feasibility of phenotype-based prediction models in clinical practice.

Materials and methods: This study included 252 patients diagnosed with narcolepsy or idiopathic hypersomnia from a prospective cohort at Xuanwu Hospital, Capital Medical University (2021–2024). Baseline and follow-up data were collected at five time points, including clinical symptoms, Epworth Sleepiness Scale (ESS), Ullanlinna Narcolepsy Scale (UNS), REM Sleep Behavior Disorder Questionnaire (RBDQ-HK), polysomnography (PSG), Multiple Sleep Latency Test (MSLT), and cerebrospinal fluid (CSF) hypocretin-1 levels. Principal component analysis (PCA) was used to extract core symptom domains. Hierarchical clustering was conducted at each time point to define clinical phenotypes. The stability of cluster structures was evaluated by Adjusted Rand Index (ARI) and Feature Overlap Index (FOI). Symptom trajectories were visualized using Sankey diagrams. Generalized linear mixed models (GLMM) were used to model the longitudinal occurrence probability of cataplexy, hallucinations, and sleep paralysis. A random forest model was constructed to predict phenotypes based on clinical features.

Results: Five principal components were identified, representing cataplexy, hallucinations, sleep paralysis, sleep initiation/maintenance, and REM sleep behavior abnormalities. Four stable clinical phenotypes were observed across timepoints: (1) non-cataplexy, (2) hallucination-dominant, (3) isolated cataplexy, and (4) paralysis-dominant. These phenotypes demonstrated robust structural stability (baseline ARI=0.78; follow-up peak ARI=0.85) and external generalizability (validation cohort ARI=0.69; FOI > 0.95 across phenotypes). Longitudinally, phenotypes showed both symptom persistence and dynamic switching, with distinct trajectories in treatment-naïve vs. treated patients. The simplified prediction model using top 10 clinical variables achieved comparable accuracy to the full model (accuracy > 80%).

Conclusions: Narcolepsy exhibits diverse and evolving clinical phenotypes that are not fully captured by conventional NT1/NT2 classification. Our data-driven clustering approach reveals symptom-specific trajectories and provides a stable, generalizable framework for clinical subtype identification. These findings support the development of phenotype-informed diagnostic and treatment strategies for narcolepsy.

Comparison of Circadian Rhythm and Sleep Between Type 1 Narcolepsy, Delayed Sleep-Wake Phase Disorder, and Healthy Controls

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Introduction: This study aimed to compare the circadian rhythm and sleep parameters among individuals with Type 1 Narcolepsy (NT1), Delayed Sleep-Wake Phase Disorder (DSWPD), and healthy controls (HC) to explore their respective rhythm characteristics and potential differences in underlying mechanisms.

Materials and methods: The study enrolled 25 patients with NT1 and recruited 25 patients with DSWPD and 25 HC subjects as controls, with all three groups matched for age and gender. All participants underwent actigraphy to monitor sleep and had their serum melatonin levels measured via continuous 24-hour blood sampling to assess circadian rhythm parameters such as Dim Light Melatonin Onset (DLMO), offset (DLMOff), and peak time (Acrophase).

Results: Compared to the HC group, NT1 patients showed no significant difference in core circadian rhythm phase (DLMO), but their biological night duration (DLMOff - DLMO) was significantly prolonged ($12:07 \pm 1.5$ h vs. $10:51 \pm 1.6$ h). Their sleep efficiency (72.2%) was also significantly lower than that of the HC group (89.2%) and the DSWPD group (82.5%). The DSWPD group exhibited a significant rhythm phase delay (mean DLMO = 01:01), and the phase angle (SleepOnset - DLMO) was significantly shorter than in the NT1 group (0.7 ± 2.7 h vs. 2.9 ± 1.3 h).

Conclusions: This study found that the main difference between patients with Type 1 Narcolepsy (NT1) and healthy controls is the prolongation of their biological night. Although their DLMO is similar, the delayed melatonin offset (DLMOff) may contribute to increased daytime sleepiness. Compared to the DSWPD group, the circadian rhythm and sleep coupling in the NT1 group remained normal, suggesting different mechanisms of rhythm regulation in these two diseases.

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Consciousness Denied: The First Cross-National Autoethnographic Study of Diagnostic and Treatment Pathways in Type 1 Narcolepsy

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Introduction: Type 1 narcolepsy (T1N) is a rare neurological condition characterized by orexin deficiency, affecting approximately 1 in 2,000 individuals globally. While clinical features and diagnostic criteria are well established, real-world patient diagnostic journeys across different healthcare systems remain critically underexplored. This study presents the first autoethnographic account of a Type 1 narcolepsy patient navigating six healthcare systems over an 11-year period, validated by cerebrospinal fluid analysis confirming undetectable orexin levels (<50 pg/mL).

Materials and methods: Autoethnographic patient-researcher methodology documented Type 1 narcolepsy patient experience across mainland China, Singapore, Hong Kong SAR (China), Germany, Spain and Sweden (2014-2025). The dual patient-researcher position provided unprecedented access to institutional mechanisms typically unavailable to external investigators. Data included detailed clinical encounters, diagnostic procedure timelines, pharmaceutical access attempts, institutional accommodation responses, comprehensive medical correspondence, and comparative policy reviews. Cross-cultural analysis systematically compared diagnostic accuracy, treatment availability, financial barriers, accommodation provision, and medical literacy using identical patient presentation. Findings were triangulated with epidemiological and policy literature to contextualize individual experience within documented system-level patterns.

Results: Dramatic disparities emerged across systems, revealing systematic rather than individual barriers.

Diagnostic access: Sweden (free orexin testing) > China (affordable PSG+MSLT, orexin testing available) > Hong Kong (expensive, genetic testing only) > Singapore (prohibitive costs, orexin testing unavailable in public healthcare).

Cross-border medical recognition: Sweden immediately accepted China's sleep study documentation without requiring additional testing. Germany, Spain, and Hong Kong explicitly rejected identical clinical evidence, forcing expensive retesting.

Treatment availability: Sweden (heavily subsidized Modafinil at minimal cost, free sodium oxybate through public healthcare) > Spain (subsidized but heavier patient contributions) >> China (prohibitive Modafinil costs ~\$3000 monthly, accessible locally-manufactured Pitolisant) > Hong Kong/Singapore (Modafinil criminalized and unregistered, available only through regulatory appeals).

Institutional medical literacy: Sweden maintained sophisticated national patient database of ~1000 individuals. China updated comprehensive open-access national clinical guidelines in 2022, officially recognizing narcolepsy as rare condition since 2023, promoting locally-manufactured Pitolisant as first-line treatment. Singapore demonstrated concerning knowledge gaps, minimized condition as "person falls asleep suddenly" in official health communications, with senior medical experts describing orexin deficiency as "evidence suggests" while explicitly denying established autoimmune pathophysiology.

Employment and accommodation: Sweden's private insurance systematically denied work capacity protection of T1N patients while social insurance resisted permanent disability recognition. Singapore demonstrated institutional employment stigma with public sector HR personnel commenting employees "will get fired if seen napping".

Systematic patterns revealed developed nations without rare disease infrastructure created greater barriers than developing nations with targeted resources. Treatment criminalization in Singapore contrasted with near-free provision in Sweden for identical medical necessity.

Conclusions: This study provides the first autoethnographic, cross-national comparative analysis of Type 1 narcolepsy diagnostic pathways. Findings demonstrate that healthcare responses correlate with diagnostic literacy rather than national economic development. Results underscore urgent need for harmonized international diagnostic protocols, equitable pharmaceutical access, and evidence-based accommodation and compensation policies. Patient-researcher methodologies offer invaluable insights complementing traditional clinical research for future guideline development.

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Consistent Efficacy of Once-Nightly Sodium Oxybate on Disrupted Nighttime Sleep in People With Narcolepsy

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Introduction: Once-nightly sodium oxybate (ON-SXB; LUMRYZ™) demonstrated efficacy in treating narcolepsy symptoms, including disrupted nighttime sleep (DNS), in the phase 3 REST-ON trial (NCT02720744). This post hoc analysis assessed ON-SXB efficacy on DNS across various participant subgroups.

Materials and methods: Participants aged ≥16 years with narcolepsy type 1 (NT1) or 2 (NT2) were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. Least squares mean differences (LSMDs) in changes from baseline for ON-SXB vs placebo for number of sleep stage shifts and nocturnal arousals as measured by polysomnography, as well as patient-reported sleep quality and refreshing nature of sleep, were compared among demographic (age, sex, race, body mass index [BMI] category), narcolepsy type (NT1/NT2), and concomitant alerting agent use subgroups from the modified intent-to-treat population (mITT; participants with ≥1 efficacy measurement after receiving the 6-g dose).

Results: In the mITT population (ON-SXB, n=97; placebo, n=93), LSMDs for ON-SXB vs placebo demonstrated significant improvements from baseline ($P<0.001$) in number of sleep stage shifts at week 13 (9 g) across all participant subgroups, including age (<35, ≥35 years), sex (female, male), race (white, non-white), BMI (low [$<25 \text{ kg/m}^2$], high [$\geq 25 \text{ kg/m}^2$]), narcolepsy type (NT1, NT2), and alerting agent/no alerting agent use. LSMDs were significant in favor of ON-SXB 9 g vs placebo for change from baseline in number of nocturnal arousals ($P<0.05$) in all subgroups, except age ≥35 years. At week 13, ON-SXB was associated with significant improvement from baseline ($P<0.05$) in visual analogue

scale (VAS) sleep quality compared with placebo across all subgroups, except non-white. All subgroups exhibited significant improvements ($P \leq 0.01$) in VAS refreshing nature of sleep with ON-SXB 9 g vs placebo, except NT2. Comparable trends were observed with the 6-g dose at week 3 and the 7.5-g dose at week 8.

Conclusions: While the trial was not powered to test for subgroup differences, these post hoc analyses demonstrate the robust, consistent efficacy of ON-SXB in treating DNS, including reducing nocturnal arousals and increasing the refreshing nature of sleep, in patients with narcolepsy across various demographic and clinical characteristics.

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Correlation Between Maintenance of Wakefulness Test and Epworth Sleepiness Scale Scores in REST-ON

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Introduction: Low-to-moderate strength correlations between Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) scores have been reported in clinical trials in narcolepsy. This post hoc analysis of REST-ON (NCT02720744), which demonstrated the efficacy of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) for narcolepsy, assessed the correlation between mean sleep latency (MSL) on the MWT and ESS scores.

Materials and methods: REST-ON participants (age ≥ 16 years) with narcolepsy were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. Pearson correlation coefficients assessed the relationship between MSL (min) on the MWT and ESS score by treatment arm in the modified intent-to-treat (mITT) population (≥ 1 efficacy measurement after receiving the 6-g dose) at baseline (pretreatment) and weeks 3 (6 g), 8 (7.5 g), and 13 (9 g).

Results: In the mITT population (ON-SXB, $n=97$; placebo, $n=93$), respective baseline MSL (SD) on the MWT and baseline mean (SD) ESS score was 5.0 (3.1) and 16.6 (3.8) for ON-SXB and 4.7 (2.6) and 17.5 (4.1) for placebo. At baseline, no correlation was observed between MSL on the MWT and ESS score for either arm (ON-SXB, $r=0.015$; placebo, $r=-0.023$). At weeks 3, 8, and 13, respective MSL (SD) was 13.1 (8.8), 14.5 (9.8), and 15.5 (9.8) minutes and respective ESS scores were 13.3 (5.9), 11.6 (6.1), and 10.4 (6.2) for ON-SXB; for placebo, MSL (SD) was 7.8 (5.9), 7.8 (6.3), and 9.4 (7.9) minutes, with ESS scores of 16.6 (4.6), 15.4 (5.3), and 14.9 (5.5). Moderate strength correlations between MSL on the MWT and ESS scores were observed in the ON-SXB arm ($r=-0.419$, -0.305 , -0.394 at weeks 3, 8, 13, respectively). Weak correlations were observed in the placebo group ($r=-0.193$, -0.271 , -0.181 at weeks 3, 8, 13, respectively).

Conclusions: After initiating ON-SXB treatment, the correlation between MWT and ESS scores strengthened, suggesting that improved wakefulness enhances awareness of sleepiness levels in people with narcolepsy.

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Corticotropin-releasing hormone (CRH) in murine narcolepsy: What do genetic and immune models tell us?

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Introduction: Narcolepsy type 1 is a chronic sleep disorder of putative autoimmune aetiology, primarily caused by the loss of orexin-producing neurons in the hypothalamus. An additional 88% reduction in corticotropin-releasing hormone-immunoreactive neurons of the paraventricular nucleus has been recently observed in post-mortem brains of individuals with narcolepsy type 1. It is however unknown whether this reduction is specific to the paraventricular nucleus or involves other brain regions expressing corticotropin-releasing hormone, such as the amygdala, which plays a central role in mood regulation, stress response, and cataplexy. This study examined whether orexin neuron loss and/or hypothalamic neuroinflammation would affect the expression of corticotropin-releasing hormone and other neuropeptides, including melanin-concentrating hormone and histidine decarboxylase as a proof of concept.

Materials and methods: We measured mRNA expression levels of CRH, histidine decarboxylase MCH, and orexin in the hypothalamus and CRH in the amygdala using quantitative PCR, in three NT1 mice models: (1) Orexin-KO mice which lack orexin peptides due to the disruption of the prepro-hypocretin gene; (2) Orexin-DTR mice which experience rapid ablation of orexin neurons after diphtheria toxin administration; and (3) Orexin-HA mice which have an autoimmune-mediated orexin neuron loss accompanied by hypothalamic neuroinflammation.

Results: CRH mRNA expression levels were unchanged in both the hypothalamus and amygdala across all three NT1 mice models compared to controls, regardless of the timeline or mechanism of orexin loss. CRH mRNA expression in the hypothalamus and amygdala did not correlate with levels of orexin mRNA expression. Similarly, HDC and MCH mRNA expression levels were unaffected in NT1 mice models.

Conclusions: Despite the loss of orexin neurons, CRH expression remained unaltered in the hypothalamus and the amygdala. These findings indicate that orexin deficiency alone does not directly influence CRH expression, and additional mechanisms may underlie the reduction of CRH neurons observed in NT1 patients. Further studies are needed to elucidate the mechanisms and functional implications underlying CRH neuron loss in NT1 patients and to determine whether similar changes occur in other brain regions.

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Demographics and Comorbidities of Patients With Narcolepsy: A Propensity Score-Matched Cohort Study

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Introduction: Narcolepsy is a rare, chronic sleep disorder associated with decreased quality of life. Narcolepsy has a complex phenotype associated with multiple comorbid conditions. This study used aggregate electronic health record (EHR) data to characterize the demographics and comorbidities of patients with narcolepsy.

Materials and methods: An EHR-based search identified first-time Duke Health patients between January 1, 2012, to March 31, 2024. Included patients had ≥ 1 narcolepsy-specific ICD-9 (347.*) and ICD-10 (G47.4*) codes and ≥ 1 disease-supportive statement in clinical notes, identified using a natural language processing algorithm. A control cohort was propensity-matched for birth year, age at first institutional encounter, sex, race, number of diagnosis code instances, and mortality; ethnicity was not available for matching. Common comorbidities were compared and ranked between cohorts by odds

ratio (OR). Statistical significance was determined using a chi-squared test; *P* values were corrected for multiple comparisons using Bonferroni correction to control for a 5% false discovery rate.

Results: Within the EHR database of 2,617,188 patients, 1659 patients with a narcolepsy diagnosis were identified (mean age at first presentation to Duke Health, 32.4 years; white, 69%; female, 69%); the propensity-matched control cohort included 1659 patients (mean age at first presentation to Duke Health, 32.3 years; white, 69%; female, 69%). Comorbidities that occurred statistically significantly more frequently (all *P*<0.0001) among the narcolepsy vs control cohort (OR [95% CI]) included sleep disorders: sleep-related movement disorders (26.26 [10.71, 64.40]), hypersomnia (16.56 [12.54, 21.87]), circadian rhythm sleep disorders (15.43 [6.73, 35.38]), obstructive sleep apnea (4.64 [3.85, 5.60]), restless leg syndrome (4.17 [2.93, 5.94]); pain disorders: trigeminal neuralgia (6.63 [2.80, 15.70]), fibromyalgia (5.30 [3.58, 7.85]), chronic pain syndrome (3.37 [2.46, 4.61]), peripheral neuropathy (2.94 [2.04, 4.23]), myalgia (2.69 [2.20, 3.29]), headache (1.69 [1.43, 2.00]); and psychiatric or mood disorders: post-traumatic stress disorder (3.08 [2.10, 4.52]), attention deficit hyperactivity disorder (2.90 [2.28, 3.68]), depression (2.66 [2.27, 3.11]), anxiety (1.84 [1.58, 2.14]). Chronic fatigue syndrome (8.17 [3.22, 20.75]), postural orthostatic tachycardia syndrome (7.24 [3.59, 14.61]), irritable bowel syndrome (3.13 [2.30, 4.25]), memory disorders and dementia (2.69 [1.99, 3.64]), spondylosis (2.11 [1.64, 2.71]), syncope (2.08 [1.64, 2.64]), asthma (1.80 [1.44, 2.25]), and gastroesophageal reflux disease (1.50 [1.28, 1.76]) were also higher among patients with narcolepsy vs the control cohort (all *P*<0.0001). Hypertension and cardiovascular disease were not among the top 23 comorbidities that occurred more frequently among the narcolepsy cohort vs the control cohort.

Conclusions: The findings from this agnostic analysis of EHR records support and extend those of prior studies that reported increased frequency of sleep, pain, and psychiatric or mood disorders in patients with narcolepsy compared with matched controls. Consistent with prior EHR research, sleep, psychiatric, and pain disorders were among the most frequently reported comorbidities of patients with narcolepsy; cardiovascular disease was not. Real-world data identifying the most frequent comorbidities increased in a narcolepsy cohort informs clinicians of the most relevant concomitant disease states to consider when evaluating potential therapies.

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Development of a Novel, Oral Orexin Receptor 2 Agonist, ORX750 for Treatment of Patients with Narcolepsy (type 1 and 2) and Idiopathic Hypersomnia

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Introduction: Narcolepsy types 1 (NT1), 2 (NT2), and idiopathic hypersomnia (IH) are rare, life-long, disabling central disorders of hypersomnolence characterized by excessive daytime sleepiness (EDS). None of the currently available treatments target the orexin system, which is a core element of wake-promoting circuitries and specifically, of NT1 pathology. ORX750 is a novel, investigational, highly potent, oral orexin receptor 2 (OX2R) agonist in development for the treatment of narcolepsy and idiopathic hypersomnia. Strong wake-promoting effects were observed in preclinical studies of ORX750, supporting clinical investigation. The development program is ongoing and includes a first-in-human phase 1 study to evaluate the safety and wake-promoting effects of single and multiple oral doses of ORX750, a phase 2a study (ORX750-0201 [CRYSTAL-1]) in NT1, NT2 and IH patients, and a long-term extension (LTE) study (ORX750-202) for participants who complete ORX750-0201.

Materials and methods: In the phase 1 study, safety, tolerability, and pharmacokinetics (PK) of ORX750 are evaluated at single-ascending doses (SAD) and multiple-ascending doses (MAD) in a randomized, placebo-controlled design in healthy participants. In parallel, wake-promoting effects are evaluated in placebo-controlled Proof of Concept (POC) cohorts with a two-way crossover design in acutely sleep-deprived participants utilizing the Maintenance of Wakefulness Test (MWT).

ORX750-0201 (CRYSTAL-1) is evaluating the safety, tolerability, efficacy, and PK of ORX750 in NT1,

NT2, and IH patients. Initial dosing is 1 mg (NT1) and 2 mg (NT2 and IH) with adaptive, sequential dose selection between cohorts. Efficacy endpoints include the MWT, Epworth Sleepiness Scale (ESS), and weekly cataplexy rate (WCR, NT1 only). Other exploratory assessments include measures of overall symptom improvement, sleep, cognition, attention, memory, and general health. Participants who complete ORX750-0201 can enroll in the LTE study (ORX750-202). In ORX750-202, the primary endpoint is safety, with efficacy assessments including MWT, ESS, and WCR (NT1 only), alongside other exploratory endpoints.

Results: In the phase 1 study, as of the data cut-off date of December 5, 2024, five SAD (total N=45 active, N=15 placebo), four POC (N=8, N=10, N=8), and three MAD cohorts (N=24 active, N=6 placebo) have completed the study. Observed least squares (LS) mean (95% confidence interval [CI]) sleep onset latencies (minutes) in the MWT were 17.6 (12.1, 23.2), 32.0 (22.2, 41.8), 33.6 (27.1, 40.1), and 37.9 (31.7, 44.0) at 1.0 mg, 2.5 mg, 3.5 mg, and 5.0 mg once daily (QD), respectively. Average least square (LS) mean (95% CI) difference from placebo for mean sleep latency was 8.1 (0.3, 15.9), $p=0.04$ for 1.0 mg, 15.2 (4.7, 25.8), $p=0.01$ for 2.5 mg, 20.2 (15.2, 25.2), $p<0.0001$ for 3.5 mg, and 22.6 (17.0, 28.2), $p<0.0001$ for 5.0 mg. Treatment emergent adverse events were transient and mild or moderate in severity.

Conclusions: ORX750 showed a favorable safety profile and clinically meaningful and statistically significant improvements on wakefulness in the phase 1 study in acutely sleep-deprived healthy volunteers. ORX750 was well tolerated, and normative wakefulness (>30 mins on the MWT) was achieved at the doses ≥ 2.5 mg. The phase 1 study, ORX750-0201 and ORX750-202 are open, and results will inform future clinical development.

Does body mass index differentiate the clinical and sleep characteristics of Chinese children and adults with narcolepsy type 1 differently?

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Introduction: Narcolepsy is a rare sleep disorder caused by the deficiency of hypocretin neurons located in the hypothalamus. Children and adults with narcolepsy show different clinical picture especially for the obesity. The aim of the present study is to investigate whether body mass index (BMI) affect the clinical and sleep characteristics of Chinese children and adults with narcolepsy type 1 (NT1) differently.

Materials and methods: A total of 172 patients with NT1 were included from Peking University People's hospital. Patients with obesity, overweight and normal body weight were defined according to Chinese obesity and overweight criteria for children and adults. Clinical and sleep characteristics were compared between patients with obesity, overweight, and normal BMI in Chinese children and adults with narcolepsy, respectively.

Results: Age at disease onset, sleepiness onset, cataplexy onset and age at disease diagnosis were not significantly different among NT1 patients with obesity, overweight and normal BMI regardless of in children or adults with narcolepsy. Higher blood pressure was noted in children or adults with NT1 with obesity compared to patients with narcolepsy with normal BMI. Higher scores for abnormal eating behaviours, especially for uncontrolled eating behaviours were noted in children with obesity compared to children with normal BMI, whereas this abnormal eating behaviour was not observed in adults with narcolepsy with different BMI groups. A lower percentage of sleep paralysis was only noted in child NT1 patients with obesity compared to child NT1 patients with normal BMI but not in adult NT1 patients with different BMI groups as well. A higher percentage of stage N1 sleep and a higher apnoea hypopnea index (AHI) were noted in adult NT1 patients with obesity compared to adult patients with normal BMI, whereas these differences were not noted in child NT1 patients with different BMI groups. Shorter mean sleep latency on multiple sleep latency test (MSLT) was noted in children/adults with obesity or overweight versus children/adults with normal BMI.

Conclusions: Obesity is associated with lower hypocretin-1 levels and shorter mean sleep latency on MSLT regardless of in children or adults with NT1. Childhood obesity is associated with abnormal eating behaviours and lower percentage of sleep paralysis in NT1 patients. Adulthood obesity is associated with higher percentage of stage N1 sleep and higher AHI in NT1 patients. Obesity therefore affects the clinical and sleep characteristics differently in children and adults with NT1. Future

management of narcolepsy should be different in different age groups as shown by the different phenotype of obesity in children and adults with narcolepsy.

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E2086, a Selective Orexin Receptor-2 Agonist, Study for Promoting Wakefulness in Patients With Narcolepsy Type-1

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Introduction: There are approved symptomatic treatment options from several therapeutic classes to treat patients with narcolepsy type-1 (NT1). However, none addresses the root cause of NT1, orexin deficiency. E2086 is a novel orexin receptor-2 (OX2R) agonist. In vitro, E2086 activated OX2R with no strong off-target effects, indicating that E2086 is a highly selective agonist. E2086 is hypothesized to regulate the sleep/wake cycle by supporting wakefulness through the orexin neuronal pathway; its preclinical profile showed strong dose-dependent efficacy in promoting wakefulness and mitigating cataplexy. Here, results from the first clinical study of E2086 in patients with NT1 are reported.

Materials and methods: E2086-A001-101 was a multicenter, randomized, double-blind, double-dummy, single-dose, 5-period crossover study evaluating the efficacy, safety, and tolerability of three dose strengths of E2086 compared with placebo (PBO) and modafinil in adult subjects with NT1. Male and female adult participants with verified diagnoses of NT1 were randomized to receive study drug within an hour of waketime following an overnight polysomnogram. Forty-minute maintenance of wakefulness tests (MWTs) conducted based on standard criteria were commenced 2 hours after waketime and continued every 2 hours until ~9 hours postdose (4 total). The Karolinska sleepiness scale (KSS) was administered at the end of each MWT. Following a washout period of ≥3 days each, participants returned for the next 4 treatment conditions. Mean sleep latency (MSL) from the 4 MWTs was calculated. Using pairwise comparisons, each of the 3 doses of E2086 was compared with PBO and with modafinil. In addition, modafinil was compared with PBO to serve as assay sensitivity.

Results: Twenty-two subjects were randomized; 19 subjects were completers, defined as having received all 5 treatments and having efficacy data. In the safety analysis set of all randomized subjects who took study drug, 42.9% were female and 47.6% were White. The least squares mean (LSMean) sleep latency for E2086 was longer and statistically significant ($P=0.001$) compared with PBO and modafinil: MSL with modafinil was also significantly longer versus PBO, establishing assay sensitivity. LSmean KSS scores with E2086 were lower (improved) and statistically significant ($P=0.0001$) compared with PBO. LSmean KSS scores were also significantly higher than modafinil: E2086 was generally well-tolerated. Adverse events (AEs) demonstrated a dose-related trend with E2086. There were no discontinuations due to TEAEs, no serious AEs, and most TEAEs were mild to moderate in severity.

Conclusions: These data demonstrate that E2086 has the potential to improve daytime wakefulness in patients with NT1. The efficacy/safety profile supports continued investigation of E2086 in the narcolepsy patient population.

Effect of Narcolepsy and Idiopathic Hypersomnia on Relationships: A Social Media Analysis

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Introduction: Central disorders of hypersomnolence, such as narcolepsy and idiopathic hypersomnia (IH), contribute to quality-of-life challenges, including entering or maintaining relationships. A social

listening analysis was conducted to characterize the emotions and effects of narcolepsy and IH on romantic/social partners.

Materials and methods: This social listening analysis used natural language processing and other statistical techniques to analyze 447,347 posts and comments shared (August 2011 to September 2024) from 2 subreddits (r/Narcolepsy and r/idiopathichypersomnia) and the PWN4PWN Facebook group. The process used an Attributes of Daily Living (ADL) model to identify sleeping paragraphs and a span recognition model to filter paragraphs with spans labeled “relationship.”

Results: A total of 227,276 paragraphs that discussed sleeping were identified by the ADL model; of these, 8,871 (3.9%) also mentioned a partner. Across all conversations that mentioned both sleeping and a partner, the most common topics identified were sleep medication usage, narcolepsy journey, Xyrem/Xywav, falling asleep, medical diagnosis journey, and vivid dreaming. Of the most common sleep-related clinical topics identified, nighttime sleep disruptions were more likely to co-occur with the mention of a partner (OR [95% CI]; bad dreams, 2.8 [1.6-4.8]; night terrors, 2.2 [1.7-2.9]; rapid eye movement behavior disorder, 2.0 [1.3-3.0]; nightmares, 1.8 [1.5-2.1]; vivid dreams 1.4 [1.1-1.7]). The primary emotions expressed in paragraphs mentioning both sleep and a partner were fear (28.2%), anger (23.2%), and happiness (22.8%). In conversations that mentioned both sleep and a partner, the most associated sleep-related clinical topic and emotion (standardized pointwise mutual information squared [PMI²]) were sleep paralysis and fear (3.0). In paragraphs that discussed sleep and a partner, naps were associated with multiple emotions including frustration (2.6), love (2.5), anger (2.2), annoyance (1.7), and worry (1.6); sleepiness was associated with anger (1.9) and frustration (1.9); nightmares and night terrors were associated with fear (1.9 and 1.8, respectively).

Conclusions: These data suggest that nighttime sleep symptoms, including parasomnias, may be a source of concern within relationships of people with narcolepsy or IH. Sleepiness and bed sharing with a partner with narcolepsy or IH may cause relationship tension given the strong association with emotions with a negative connotation, such as anger and frustration.

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Effect of Oral Orexin Receptor 2 Agonist Oveporexton (TAK-861) on the Severity of Symptoms in Individuals With Narcolepsy Type 1: Results From Two Phase 3 Studies

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Introduction: Narcolepsy type 1 (NT1) is a chronic, rare, neurologic disorder of hypersomnolence caused by loss of orexin producing neurons in the hypothalamus, and is characterized by excessive daytime sleepiness, sudden muscle weakness triggered by emotions (cataplexy), disrupted nighttime sleep, sleep paralysis, and hypnagogic/hypnopompic hallucinations. Orexin receptor agonists target orexin signaling and are promising treatments for NT1. Oveporexton (TAK-861) is an investigational orexin-receptor 2 (OX2R)-selective agonist that stimulates OX2R signaling and addresses the underlying orexin deficiency. Following positive results from the NCT05687903 phase 2b study, the efficacy and safety of oveporexton were further evaluated in two phase 3 trials in participants with NT1.

Materials and methods: A prespecified analysis of two randomized, double-blind, placebo-controlled, phase 3 studies (TAK-861-3001 and TAK-861-3002) was conducted to investigate the effect of oreoprexton on NT1 symptoms severity. Eligible participants were aged 16–70 years with an International Classification of Sleep Disorders, Third Edition (ICSD-3) or ICSD-3-Text Revision diagnosis of NT1 (supported by polysomnography and multiple sleep latency test results or orexin cerebrospinal fluid concentration ≤ 110 pg/mL), Epworth Sleepiness Scale (ESS) score ≥ 11 , and ≥ 4 partial/complete episodes of cataplexy/week in absence of treatment. Participants received twice daily oral oreoprexton 1 mg (TAK-861-3001 only) or 2 mg, or placebo, at least 3 hours apart for 12 weeks. Key secondary efficacy endpoints were the Narcolepsy Severity Scale for Clinical Trials (NSS-CT; a validated, self-administered 15-item scale assessing sleepiness, cataplexy, sleep paralysis, hallucinations, and disrupted nocturnal sleep, score range 0-57), and the Patient Global Impressions Scales of Severity (PGI-S) and Change (PGI-C).

Results: Overall, 273 participants were randomized (TAK-861-3001, n=168; TAK-861-3002, n=105) to oreoprexton 1mg/1mg (n=61), oreoprexton 2mg/2mg (n=136), or placebo (n=76). Mean age for the TAK-861-3001 and TAK-861-3002 studies was 31.4 years and 30.7 years, respectively; 98 (58.3%) and 50 (47.6%) participants were female. Mean NSS-CT total scores at baseline were 30.9 and 31.1, respectively. In TAK-861-3001, 65.5% of participants (PGI-S) rated NT1 symptoms as severe/very severe at baseline, and in TAK-861-3002, 65.7% of participants rated the symptoms as severe/very severe. Statistically significant improvements ($P < 0.001$) in NSS-CT total score from baseline to week 12 were achieved with all oreoprexton dose groups vs placebo. In TAK-861-3001, least square (LS) mean (95% CI) changes from baseline vs placebo were -14.37 (-17.81, -10.93) with oreoprexton 1mg/1mg and -16.88 (-20.24, -13.52) with oreoprexton 2mg/2mg (both $P < 0.001$). In TAK-861-3002, LS mean (95% CI) change from baseline vs placebo was -18.11 (-21.25, -14.96) with oreoprexton 2mg/2mg ($P < 0.001$). At week 12, in TAK-861-3001, 73.7%, 96.9%, and 22.2% of participants in oreoprexton 1mg/1mg, oreoprexton 2mg/2mg, and placebo dose groups, respectively, reported 'much improved' or 'very much improved' on the PGI-C. At week 12, in TAK-861-3002, 91.0%, and 14.7% of participants in the oreoprexton 2mg/2mg and placebo dose groups, respectively, reported much/very much improved on the PGI-C.

Conclusions: In these two phase 3 studies, oreoprexton showed significant improvements in frequency, severity, and impact of narcolepsy symptoms, as assessed with the NSS-CT and PGI-C versus placebo in participants with NT1 over 12 weeks.

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Effect of the Oral Orexin Receptor 2 Agonist Oreoprexton (TAK-861) on Quality of Life in Individuals with NT1

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Introduction: Narcolepsy type 1 (NT1), a rare, chronic neurologic disorder that affects sleep-wake stability, is associated with detrimental effects on health-related quality of life (HRQoL). We evaluated the effect of oreoprexton (TAK-861), an orexin receptor 2 (OX2R)-selective agonist under investigation for the treatment of NT1, on measures of HRQoL (36-item Short-Form [SF-36] survey and EuroQoL 5-Dimensions 5-Levels [EQ-5D-5L] questionnaire), in two Phase 3 clinical trials.

Materials and methods: Results from two randomized, double-blind, placebo-controlled, Phase 3 studies (The First Light: TAK-861-3001 and The Radiant Light: TAK-861-3002) were evaluated to explore HRQoL with oreoprexton treatment in individuals with confirmed NT1. Eligible participants were aged 16–70 years with an International Classification of Sleep Disorders, Third Edition (ICSD-3) or ICSD-3-Text Revision diagnosis of NT1 (supported by polysomnography, multiple sleep latency test results or orexin cerebrospinal fluid concentration ≤ 110 pg/mL), Epworth Sleepiness Scale (ESS) score ≥ 11 , and ≥ 4 partial/complete episodes of cataplexy/week. Participants received twice daily oral oreoprexton 1 mg (The First Light only) or 2 mg, or placebo, at least 3 hours apart for 12 weeks. SF-36 Mental and Physical Component Summary scores were secondary endpoints (0-100 scale) and EQ-5D-5L visual analog scale (VAS; 0-100 scale) was an exploratory endpoint. Higher scores represented better quality of life. Efficacy and safety results are reported separately.

Results: Overall, 273 participants were randomized to ovesporexton 1mg/1mg (n=61), ovesporexton 2mg/2mg (n=136), or placebo (n=76). Mean age was 31.4 years (The First Light) and 30.7 years (The Radiant Light); 98 (58.3%) and 50 (47.6%) participants, respectively, were female. Mean baseline SF-36 and EQ-5D-5L VAS scores were similar across all study arms (SF-36 Mental Component Summary score [MCS]: 38.3-41.0; SF-36 Physical Component Summary score [PCS]: 46.9-50.5; EQ-5D-5L VAS score: 58.9-66.4). After 12 weeks, SF-36 MCS scores ranged from 47.1 to 49.2 with ovesporexton vs 38.2 to 38.5 with placebo, SF-36 PCS scores ranged from 54.7 to 55.8 with ovesporexton vs 49.1 with placebo, and EQ-5D-5L VAS scores ranged from 77.7 to 80.6 with ovesporexton vs 59.4 to 66.0 with placebo. Least square (LS) mean changes from baseline in SF-36 component summary scores were statistically significant for both ovesporexton dose groups vs placebo at week 12 (MCS score: The First Light: 6.79 [1mg/1mg], 10.11 [2mg/2mg], The Radiant Light: 9.32 [2mg/2mg], all $P < 0.001$, and PCS score: The First Light: 5.54 [1mg/1mg], 6.26 [2mg/2mg], The Radiant Light: 5.01 [2mg/2mg], all $P < 0.001$). Similarly, LS mean changes from baseline in EQ-5D-5L VAS score vs placebo were also nominally statistically significant (The First Light: 16.28 [1mg/1mg] and 20.15 [2mg/2mg], The Radiant Light: 14.65 [2mg/2mg], all $P < 0.001$).

Conclusions: In these Phase 3 clinical trials, ovesporexton showed statistically significant and clinically meaningful improvements in HRQoL, assessed with the SF-36 and EQ-5D-5L VAS compared with placebo in participants with NT1 over 12 weeks.

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Effects of Once-Nightly Sodium Oxybate on Apnea-Hypopnea Index: Post Hoc Analysis From the Phase 3 REST-ON Clinical Trial

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Introduction: Sodium oxybate (SXB) is a central nervous system depressant used to treat narcolepsy and has the potential to cause respiratory depression. Registrational trials of SXB have generally excluded patients with respiratory depression, including those with an apnea hypopnea index (AHI) > 15 . This post hoc analysis of REST-ON evaluates the effect of once-nightly SXB (ON-SXB) compared to placebo on AHI in individuals with narcolepsy with either no sleep apnea or mild sleep apnea.

Materials and methods: REST-ON (NCT02720744) was a phase 3, double-blind, placebo-controlled randomized clinical trial. Participants (age ≥ 16 years) with narcolepsy and AHI < 15 were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2–3, 6 g; weeks 4–8, 7.5 g; weeks 9–13, 9 g) or placebo. AHI was measured using polysomnography at baseline and weeks 3, 8, and 13, and analyzed post hoc. Adverse drug reactions (ADRs) were assessed at each visit.

Results: Respective mean (min, max) AHI values were similar for the ON-SXB (n=97) and placebo groups (n=93) at baseline (2.7 [0, 15] and 2.8 [0, 13]), week 3 (0.1 [0, 5] and 0.1 [0, 2]), and week 8 (0 [0, 0] and 0 [0, 0]). At week 13, mean (min, max) AHI values were 0 (0, 0) and 0.2 (0, 10) in the ON-SXB and placebo groups, respectively. Least squares mean (LSM) change from baseline in AHI with ON-SXB and placebo was -3.0 and -2.9 , respectively, at week 3 (LSM difference [LSMD; 95% CI], -0.11 [-0.46 to 0.24]; $P=0.522$); -3.0 and -2.9 , respectively, at week 8 (LSMD [95% CI], -0.11 [-0.46 to 0.23]; $P=0.518$); and -3.0 and -2.9 , respectively, at week 13 (LSMD [95% CI], -0.12 [-0.46 to 0.23]; $P=0.515$). In the safety population, 1 (0.9%) and 1 (1.0%) participant in the ON-SXB and placebo arms, respectively, experienced ADRs of sleep apnea, and 1 (0.9%) participant receiving ON-SXB reported snoring; all were mild or moderate in severity.

Conclusions: Treatment with ON-SXB was not associated with worsened AHI at any tested dose. ON-SXB was well-tolerated, as the reported respiratory-related ADRs were minimal, and mild or moderate in severity.

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Erectile function in Male patients with Narcolepsy

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Introduction: Explore the nocturnal erectile function of male patients with narcolepsy, and whether there are any changes after taking medications for narcolepsy.

Materials and methods: Eighteen adult male patients with narcolepsy admitted to Peking University People's Hospital from September 2024 to April 2025 were selected. Among them, 9 patients took Methylphenidate 9mg and Venlafaxine 75mg per day, and the other 9 patients took Methylphenidate 9mg and Clomiphen 12.5mg per day. Polysomnography (PSG) and RigiScan tests were performed at night after admission, and the examination was re-conducted 3 days after medication. PSG data were staged strictly according to the standards of the American Academy of Sleep Medicine. RigiScan data were converted and exported using the Spyder software. Meanwhile, questionnaires such as the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Athens Insomnia Scale (AIS), International Index of Erectile Function-5 (IIEF-5), Erectile Hardness Score (EHS) questionnaire, and the 19-item Morningness-Eveningness Questionnaire (MEQ-19) were used to collect and analyze scores related to insomnia, anxiety, depression, erectile dysfunction, etc. of the included patients.

Results: About **16.7% (3/18)** of the patients were diagnosed with erectile dysfunction after undergoing tests on two nights. **83% (15/18)** of the patients had an IIEF-5 questionnaire score of less than 21, indicating erectile dysfunction. **88% (16/18)** of the patients had an EHS of less than or equal to 3 and considered that their erections were not firm enough. After the linear regression test, it was found that patients with higher scores in AIS ($p=0.004$), ESS ($p=0.025$) and EHS ($p<0.001$) have lower scores in IIEF-5 and shorter erectile duration after taking medication ($p=0.026$). Meanwhile, patients with higher AIS scores ($p=0.044$) also have higher EHS scores. The results of the paired samples t-test suggest that after taking the medicine, the patients' REM sleep time ($p < 0.001$), proportion ($p = 0.002$), and erection time ($p = 0.001$) all decrease significantly, and the REM sleep latency ($p < 0.001$) significantly prolongs.

Conclusions: There is a close connection between the psychological state of the patients and their erectile function, most male patients subjectively believe that they have erectile dysfunction, a small number of patients objectively have erectile dysfunction. Commonly used medications such as Methylphenidate, Clomiphen and Methylphenidate can significantly inhibit their REM sleep while affecting the erection of patients.

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Estimating the Clinical and Economic Effects of High- and Low-Sodium Oxybate Agents among the US Population with Narcolepsy: Microsimulation Cost Analysis

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Introduction: Excess sodium intake is associated with increased risk of cardiovascular (CV), cardiometabolic (CM), and cardiorenal (CR) disorders. People with narcolepsy have a higher prevalence and risk of development/progression of certain CV/CM/CR conditions/events than people without narcolepsy. High-sodium oxybate agents, indicated to treat narcolepsy, contain 1640mg of sodium per nightly 9g dosage, while low-sodium oxybate agents contain 131mg per nightly 9g dosage. This study evaluated potential clinical and economic benefits associated with taking low-sodium versus high-sodium oxybate agents.

Materials and methods: A microsimulation model was developed to estimate the 10-year clinical and economic impacts of sodium intake in US adults with narcolepsy. Using US Census Bureau population data and published US prevalence estimates, the simulated cohort included 101,135 adults with narcolepsy. Two treatment scenarios were modelled (assuming continuous treatment over the 10-year horizon or until the patient reached 100 years of age): 1) taking a high-sodium oxybate agent (1640mg of sodium added to daily dietary sodium intake [based on age- and sex-stratified NHANES data]) and 2)

taking a low-sodium oxybate agent (131mg of sodium added to daily dietary sodium intake). Patients entered the model with or without a chronic condition (atrial fibrillation, chronic kidney disease [CKD], diabetes, heart failure, hypertension, non-alcoholic fatty liver disease), based on literature-identified, narcolepsy-specific prevalence estimates. Every 3-month cycle, individuals were at risk of developing new-onset chronic conditions or acute events (oedema, haemorrhagic stroke, ischaemic stroke, myocardial infarction) and were modelled with risk (hazard/odds ratios) adjusted based on treatment scenarios. Each cycle, patients could die from an acute event or overall mortality, aligned with risk estimates from published literature. The effect of sodium on each outcome was sourced from network meta-analyses or individual studies. US-based cost data from administrative claims and the Healthcare Cost and Utilization Project were applied per condition/event per cycle. Model outputs included clinical event counts and total and event-specific direct costs (2025 USD) over 10 years for each treatment scenario.

Results: Over the 10-year horizon, total direct healthcare costs among people with narcolepsy treated with a high-sodium oxybate agent were \$16.48B versus \$15.32B for individuals treated with a low-sodium oxybate agent, representing \$1.16B in cost savings. Reduced chronic condition costs with low-sodium agents accounted for most of these savings (\$1.15B). The largest cost reductions were observed in CKD (\$527.1M), diabetes (\$153.0M), and hypertension (\$82.5M). Savings among people with narcolepsy treated with a low-sodium agent were observed for all modelled health outcomes and driven primarily by avoidance of 4979 cases of hypertension, 2924 cases of diabetes, and 2490 cases of atrial fibrillation. Among acute events, 504 ischaemic strokes, 130 myocardial infarctions, and 92 haemorrhagic strokes were avoided with a low-sodium agent, as were 107 event-specific deaths.

Conclusions: This microsimulation suggests that treatment with a low-sodium versus high-sodium oxybate agent was associated with a notable reduction in negative health outcomes among US adults with narcolepsy, translating to \$1.16B in healthcare cost savings over 10 years. These findings underscore the importance of treatment strategies that minimise excess sodium exposure to mitigate elevated CV/CM/CR risks in this population.

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Evaluating Progressive Learning Using Meta-Analytic and Claims Data: A Case Study in Narcolepsy

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Introduction: Between 2022 and 2024, Haymarket Medical Education (HME) launched 7 narcolepsy-focused online educational activities for sleep clinicians to address ongoing gaps in knowledge and practice. Using meta-analytic methodology, we compared single- and multiple-activity learners to evaluate the impact of repetition and reinforcement and environmental factors on knowledge, competence, and real-world behavior, using pre- and post-test, and claims data.

Materials and methods: Pre-/post-test responses from learners for 7 online narcolepsy educational activities conducted 2022-2024 were tagged by topic to ensure comparison of similar topics across questions. Pre- to post-activity changes were evaluated across years to show general trends or by year to highlight year-over-year differences. Within the group of sleep clinicians, we compared two cohorts: those who participated in 1 activity versus those who participated in >1 (repeat learners). The goal was to identify differences between the groups and assess whether repeated learning led to greater improvements in knowledge, competence, and practice.

We also evaluated whether the education resulted in performance (clinical) change, using real-world claims data from the PurpleLab database, matching learners using NPI numbers. Differences in use of diagnostic codes for narcolepsy and changes in recommended treatment selection prior to and after exposure to the education were measured.

Results: We included 1,773 sleep medicine learners from 7 activities; 331 (18.67%) were repeat learners.

Learners showed significant knowledge and competence gains across all topics, with the largest improvement in Use of Guidance (19%), Treatment Efficacy and Safety (14%) and Treatment Strategy (14%). Baseline scores dipped in 2023 (19–24%) compared to 2022 (28–40%), but recovered in 2024. We postulate this occurred due to novel guidelines and new trial data and approvals that occurred prior to 2023.

Repeat learners showed significant and greater improvements from pre- to post-test than single activity learners. Repeat learners had the largest gains in Use of Guidance (21%), Treatment Efficacy and Safety (15%) and Treatment Strategy (15%). Single activity learners showed significant but smaller gains in: Use of Guidance (18%), Treatment Efficacy and Safety (13%), and Treatment Strategy (14%). Year-over-year, positive trends were observed, except in Treatment Efficacy and Safety, where both groups saw baseline knowledge declines, possibly attributed to the number and complexity of questions, and uncertainty caused by emerging data and therapies during this period.

Using real-world claims data, we found that repeat learners versus single activity learners showed: differences in diagnosis of narcolepsy (increase by 67% vs. 40%); and prescription of recommended treatments (17% increase vs 17% decrease)

Conclusions: We demonstrated that serial learning strengthened clinical decision-making, boosted long-term knowledge retention, and optimized clinical behavior in sleep clinicians through repetition and reinforcement, whereas single exposure appears to result in suboptimal practice. Serial learning approaches are crucial for adapting to evolving environments and ensuring sustained, impactful learning. A limitation of this study is the failure to account for bias introduced through learner exposure to education beyond our activities.

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Excessive adrenergic stimulation triggers narcolepsy and Food Protein Induced Enterocolitis (FPIES) along with increased Respiratory Effort during sleep (RE), tissue hypoxia, and oxidative stress through transformed foods and emerging allergens. Which allele should be explored in narcolepsy cases negative for HLA DQB1*06:02?

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Introduction: Cataplexies have been linked to the presence of the HLA-DQB1*06:02 allele, which predisposes individuals to progressive destruction (autoimmune type) of orexin neurons. However, the type 2 narcolepsy group is characterized by the absence of SOREMP, and negative HLA-DQB1*06:02. In narcoleptic children, diagnosis is delayed by a minimum of one year. A delay in diagnosis could be a pivotal cause of the disease as it provides time for the ongoing reaction to destroy hypocretin neurons. For children younger than 6 years, current recommendations focus on providing adequate sleep time, taking naps during the day, treating comorbidities and accompanying medical disorders such as OSA, and sleep fragmentation. Food protein-induced enterocolitis (FPIES) is a severe non-IgE-mediated allergy of unknown origin, with an estimated incidence gradually increasing to 0.45%.

Materials and methods: We describe a 3-year-old child with FPIES positive for HLA-DQB1*03:02 and HLA-DRB1*04 suffering from cataplexies triggered by alimentary and drug excipients and a 14 year-old suffering narcolepsy positive for HLA DQB1*06:02.

Results: Case 1: A polyallergic child is nourished with amino-acid-formula since the age of 4,5 months.

3-year-old: Treatment with lactose and galactose-containing lactulose containing **polysorbate 80, maltodextrin, and sorbitol** induced severe hypnagogic hallucinations, nightmares, hyperactivity, aggressive behavior, excessive daytime sleepiness, persistent itching, crying, skin reactions and facial cataplexies which ceased after laxation cessation. **4-year-old:** a multivitamin sirop containing **maltodextrin** and **amidon** induced hypnagogic hallucinations, nocturnal terrors, nightmares, facial cataplexies, and neck hyperextension that reoccurred on food reintroduction, despite normal iron levels. She experienced FPIES, skin hyperextensibility, alopecia, dopamine dysregulation, increased pilosity, and 3-methylhistidine levels. CPAP helped better tolerate food reintroduction and occasionally adopted neck hyperextension. CPAP cessation led to an acute increase in the hydroxybutyrate and TNF- α levels. **HLA was positive for DQ8 (HLA-DQB1*03:02) and HLA-DRB1*04, negative for HLA-DQB1*06:02. The mother confirmed that, during cataplexies, the child consumed some gluten and gluten-free products. The early diagnosis and adequate treatment initiated for the 3-year-old child ceased narcolepsy signs and FPIES with no recurrence. Case 2:** A 14-year-old child underwent allergy consultation because of severe repercussion signs (Epworth scale 22/30), hypnagogic hallucinations, and chronic rhinitis. He had secondary nocturnal enuresis since the age of 11. PSG two months earlier revealed mild OSA, mainly in the dorsal position, and restless legs syndrome. The patient fell asleep

during the consultation and had the jaw dropping involuntarily. We performed PG at home, which revealed moderate OSA, aggravated in the non-dorsal position, severe sleep fragmentation, and increased RE during sleep. The child had low coefficient iron saturation, folate, Vit-D values, and increased noradrenaline and Eosinophilic Cationic Protein (ECP). We explored HLA which was positive for **HLA DQB1*06:02**. Both children experienced persistently increased respiratory effort during sleep despite a low apnea-hypopnea index (AHI).

Conclusions: Constant adrenergic stimulation through increased RE during sleep can trigger the onset of FPIES and narcolepsy in children with HLA predisposition. The industrialized mode of nutrition could detrimentally alter the gut microbiota through allergens such as polysorbate 80 and maltodextrin, and facilitate the lack of nutrients, vitamins, and antioxidants essential for protecting neurons and restraining the onset of FPIES and narcolepsy.

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First-Line Treatments for Children with Narcolepsy Type 1: Retrospective Comparison of Pitolisant and Modafinil

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Introduction: Narcolepsy Type 1 (NT1) is a rare, chronic neurological sleep disorder characterized by excessive daytime sleepiness (EDS) and REM sleep-related phenomena, including cataplexy, sleep paralysis, and hallucinations. Over 50% of NT1 cases manifest before the age of 20, highlighting the critical need for safe and effective pediatric therapies. Although Modafinil has been widely used to manage EDS in children, its use lacked formal pediatric approval. More recently, Pitolisant, a histamine H3 receptor inverse agonist, has been approved for NT1 in children, following randomized controlled trials demonstrating its efficacy in reducing EDS and cataplexy. This study aimed to retrospectively compare the efficacy and tolerability of Modafinil and Pitolisant as first-line pharmacological treatments in children with NT1.

Materials and methods: We included all children diagnosed with NT1 between 2009 and 2025 at the National Reference Center for Narcolepsy in Lyon, France. Patients systematically completed validated questionnaires assessing EDS (Adapted Epworth Sleepiness Scale for children, AESS) and depressive symptoms (Children's Depression Inventory, CDI). Anthropometric parameters, polysomnographic (PSG) data, multiple sleep latency test (MSLT) results, and adverse events were collected. Comparative analyses between groups treated with Modafinil or Pitolisant as first-line therapy were conducted using Wilcoxon rank-sum tests, Fisher's exact tests, and multivariable mixed models for ranked variables.

Results: A total of 90 patients (52 boys) were included, with 56 treated with Modafinil and 34 with Pitolisant. Compared to the Pitolisant group, patients treated with Modafinil were younger at disease onset (median 8 vs. 11 years; $p = 0.03$) and diagnosis (median 10 vs. 14 years; $p < 0.001$), with a shorter diagnostic delay (median 1 vs. 2 years; $p = 0.005$). The Modafinil group also exhibited shorter sleep latency on MSLT ($p < 0.001$), lower sleep efficiency on PSG ($p < 0.001$), greater N3 sleep proportion ($p = 0.001$), fewer arousals ($p = 0.01$), and fewer depressive symptoms ($p = 0.005$). No significant differences were observed in baseline AESS scores, cataplexy prevalence (91% vs. 88%), or BMI Z-scores.

After 1 to 5 months of treatment, AESS scores decreased by a median of 5 points with Modafinil and 4 points with Pitolisant (non-significant). The median dosage for Modafinil was 200 mg (range 100–400 mg) and for Pitolisant, 27 mg (range 9–36 mg). Adverse events were reported in 48% of Modafinil-treated patients and 61% of Pitolisant-treated patients, though Pitolisant-related side effects were mostly transient (headaches, insomnia). Treatment discontinuation was significantly higher with Modafinil (81% vs. 31%; $p < 0.001$). Only the Pitolisant group demonstrated a significant reduction in cataplexy frequency (88% to 61.7%; $p < 0.05$). No significant BMI Z-score changes were observed. Adjusted models revealed higher baseline depressive scores and more arousals in the Pitolisant group, with lower treatment discontinuation rates.

Conclusions: This retrospective, real-world study supports Pitolisant as a first-line treatment for NT1 in children, showing comparable efficacy in reducing EDS, additional benefits in reducing cataplexy, and significantly lower discontinuation rates than Modafinil. Prospective, long-term studies are needed to further guide pediatric NT1 management.

Gender differences in Chinese with narcolepsy type 1: comparison of clinical manifestations and sleep characteristics

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Introduction: Narcolepsy type 1 (NT1) is a chronic sleep disorder due to a hypocretin/orexin deficiency induced by immunological process. Given the male predominance and earlier age at disease onset of narcolepsy in China versus other ethnic groups, whether the gender contributes to different phenotypes of narcolepsy in Chinese remains to be determined. Accordingly, the present study aims to address the effects of gender on clinical and sleep characteristics in a large population of Chinese children and adults with NT1, respectively.

Materials and methods: A total of 1415 patients with NT1 were included from Peking University People's hospital and other sleep centers in China. Clinical and sleep characteristics were compared between girls and boys with narcolepsy according to age at both disease onset and diagnosis < 18 years, women and men with narcolepsy according to age at both disease onset and diagnosis ≥ 18 years, as well as patients with narcolepsy according to age at disease onset < 18 years but with age at disease diagnosis ≥ 18 years, respectively.

Results: Age at disease onset, sleepiness onset, and cataplexy onset were not significantly different between girls/women and boys/men with narcolepsy. Girls/women with narcolepsy have longer diagnostic delay than men with narcolepsy. Boys/men with narcolepsy showed a higher body mass index (BMI) than girls/women with narcolepsy. Girls with narcolepsy present a higher percentage of hypnagogic/hypnopompic hallucinations and a higher spontaneous arousal index than boys. Men with narcolepsy had a higher percentage of stage N1 sleep, a lower percentage of stage N3 sleep and a higher apnoea hypopnea index (AHI) on nocturnal sleep as well as a shorter mean sleep latency and more sleep onset rapid eye movement periods (SOREMPs) on multiple sleep latency test (MSLT) than women. HLA-DQB1*06:02 positivity is higher in boys with narcolepsy than in girls with narcolepsy and is tended to be higher in men with narcolepsy than in women with narcolepsy. Hypocretin-1 levels were tended to be lower in boys or men with narcolepsy versus girls or women with narcolepsy. No differences in terms of diagnostic delay, stage N1 sleep, stage N3 sleep, MSLT characteristics, hypocretin-1 levels and HLA-DQB1 06:02 genotype positivity were noted between different gender groups in patients with narcolepsy according to age at disease diagnosis during adulthood but with symptoms onset during childhood.

Conclusions: Men with narcolepsy present more severe clinical picture than women with narcolepsy, probably to some extent promoting sooner diagnosis of men with narcolepsy. However, girls with narcolepsy present a more severe clinical picture than boys with narcolepsy, suggesting gender affects differently children and adults with narcolepsy. Patients with narcolepsy have disease diagnosis during adulthood but with symptoms onset during childhood constitute a specific phenotype of narcolepsy different from those children or adults with narcolepsy. Prospective longitudinal study is warranted to investigate the disease progress between different sex to better understand the underlying pathology and to ensure a proper management of narcolepsy.

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Hormonal Contraceptive and Pitolisant CYP3A4 Induction

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Introduction: Some narcolepsy treatments (e.g. modafinil) are contraindicated in narcoleptic patients taking oral contraceptives as they reduce their plasma levels by inducing CYP3A4. Pitolisant is a wake-promoting and anticataplectic agent approved in Europe, USA, Canada, Israel, China, Taiwan for the treatment of narcolepsy. We assessed its CYP3A4-inducing potential *in vitro* and *in vivo* to possibly

offer a therapeutic alternative for patients with narcolepsy wishing to continue their hormonal contraceptive treatment.

Materials and methods: In cultured human hepatocytes, pitolisant inducing potential was evaluated on CYP3A4 mRNA and enzyme catalytic activity. *In vivo* induction was evaluated in volunteers receiving pitolisant oad at 36 mg for 7 to 28 days with two approaches. In the traditional one the metabolism of midazolam was evaluated. In the second and more recent one (Goodenough, 2011) formation of a characteristic cholesterol metabolite (4- β -hydroxycholesterol, 4 β HC) was measured using a novel LC/MS method requiring only 50 μ L serum samples.

Results: Pitolisant demonstrated only minor changes in CYP3A4 mRNA levels whereas CYP 3A4 catalytic activity was not induced in hepatocytes across six subjects. In 18 volunteers receiving 36 mg pitolisant oad for 8 days, minor midazolam exposure modifications were evidenced without change in metabolite formation via CYP3A4. In another group of 48 volunteers receiving 18 to 45 mg oad for up to 28 days, 4 β HC level were not modified. This new test was validated in 18 other volunteers receiving for 8 days 600 mg/day of rifampicin, a prototypic CYP 3A4-inducer, in which 4 β HC levels were increased ($P < 0.00001$).

Conclusions: Pitolisant at therapeutic dose is devoid of any inducer activity on CYP3A4 and, therefore, represents a valuable alternative for treating Excessive Daytime Sleepiness and cataplexy in female patients with narcolepsy taking hormonal contraceptive drugs

Hypnagogic/Hypnopompic Hallucination Types Among Participants With Narcolepsy Type 1 From the Phase 3 REST-ON Trial

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Introduction: Limited information is available to quantify hypnagogic/hypnopompic hallucination (HH) events people with narcolepsy (PWN) may experience. This post hoc analysis from the phase 3 REST-ON trial evaluated individual HH types.

Materials and methods: REST-ON (NCT02720744) participants (age ≥ 16 years) with narcolepsy were randomized 1:1 to once-nightly sodium oxybate (ON-SXB) (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. HH events were assessed in participants with narcolepsy type 1. Modified intent-to-treat (mITT) population (≥ 1 efficacy measurement after 6-g dose) data were analyzed. Nocturnal HH types were evaluated via 6 yes/no questions and recorded in daily diaries. Daytime HHs were not assessed.

Results: In the mITT population with HH at baseline ($n = 112$ [ON-SXB, $n = 55$; placebo $n = 57$]), baseline mean [SD] number of HH events/day was 0.60 [0.35] and 0.66 [0.35] in the ON-SXB and placebo groups, respectively. Respective mean change from baseline (95% CI) in HH events/day to weeks 3, 8, and 13 was -0.16 (-0.21, -0.11), -0.28 (-0.37, -0.19), and -0.29 (-0.40, -0.18) with ON-SXB (all $P < 0.001$) and -0.14 (-0.20, -0.08), -0.18 (-0.26, -0.10), and -0.24 (-0.33, -0.14) with placebo (all $P < 0.001$). Participants chose from the following HH types: 1) feeling that shadows or objects are moving/distorting (total number of events with ON-SXB and placebo: 1693 and 2133), 2) feeling another presence in the room (1362 and 1839), 3) feeling that you are about to be attacked (655 and 1232), 4) feeling that you are flying through the air (543 and 1351), 5) feeling that you will soon fall into a hole (448 and 914), and 6) feeling caught in a fire (123 and 152). Of 12,455 HH events, 7762 (62%) were hypnagogic, and 4683 (38%) were hypnopompic.

Conclusions: There were low baseline HH rates in REST-ON, and a strong placebo effect was observed. However, these data provide insight into the HH types participants experienced. Relevant to clinician-patient discussions, approximately half the number of events where participants felt like they were about to be attacked, flying through the air, and falling in a hole were reported with ON-SXB vs placebo.

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Hypothalamic Functional Connectivity, Depressive Symptoms, and Post-Treatment SOREMPs in Narcolepsy Type 1: Links to Sleep Latency and Mediation Mechanisms

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Introduction: Narcolepsy type 1 (NT1) is characterized by sleep-onset rapid eye movement periods (SOREMPs), reflecting dysregulated rapid eye movement (REM) sleep control. Treatment response variability in SOREMP persistence remains poorly understood, particularly regarding hypothalamic functional connectivity (FC) and depressive symptoms. This study investigated clinical, polysomnographic, and neuroimaging differences between NT1 patients with low (0-1) versus high (≥ 2) post-treatment SOREMPs, and explored whether hypothalamic FC mediates the relationship between depressive symptoms and SOREMPs outcomes.

Materials and methods: One hundred ten NT1 patients were categorized into low (n=62) and high (n=48) post-treatment SOREMPs groups. Demographic, clinical variables (symptoms and questionnaires), and polysomnography (PSG)/multiple sleep latency test (MSLT) parameters were compared. Resting-state fMRI assessed hypothalamic FC with whole-brain regions. LASSO regression modeled associations between FC, sleep latency, and clinical variables, while mediation analysis tested hypothalamic pathways as mediators of depression-SOREMP relationships.

Results: High post-treatment SOREMPs patients exhibited shorter pre/post-treatment REM sleep latency, lower post-treatment wakefulness index, and higher depressive symptom prevalence compared to low SOREMPs patients. Hypothalamic FC differed significantly between groups: low SOREMPs patients showed enhanced connectivity in right medial hypothalamus-right thalamus/left precuneus, left medial hypothalamus-left inferior parietal lobule (IPL), and right lateral hypothalamus-left IPL pathways, but reduced connectivity in left lateral hypothalamus-right insula/left anterior cingulate cortex pathways ($p < 0.05$, GRF-corrected). LASSO regression identified left medial hypothalamus-left IPL FC as a significant predictor of post-treatment MSLT mean sleep latency ($\beta = 0.272$, $p = 0.001$), alongside age and pre-treatment sleep latency. Mediation analysis revealed complete mediation by two hypothalamic pathways: depressive symptoms predicted reduced right lateral hypothalamus-left IPL FC (indirect effect: 0.15-1.05), associated with fewer SOREMPs, and increased left lateral hypothalamus-right insula FC (indirect effect: 40 0.08-1.14), associated with more SOREMPs.

Conclusions: Hypothalamic-parietal/insular FC abnormalities link depressive symptoms to post-treatment SOREMP variability in NT1, with specific pathways mediating opposing effects on REM sleep regulation. These findings highlight hypothalamic connectivity as a critical neural substrate for treatment response, integrating sleep-wake and emotional processing networks. Targeting these pathways may improve personalized management for NT1 patients with comorbid depression and treatment-resistant SOREMPs.

Identification of patients with narcolepsy type 1 through automatic scoring of multiple sleep latency tests

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Introduction: Narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) are central disorders of hypersomnolence (CDH) sharing excessive daytime sleepiness (EDS) as main clinical feature. In clinical routine, multiple sleep latency test (MSLT) is performed for diagnostic purposes, but the current diagnostic criteria do not indicate MSLT-specific criteria for the identification of patients with NT1. In fact, NT1 shares the same diagnostic criterion on sleep onset rapid eye movement (REM) periods with NT2 and the same diagnostic criterion on mean sleep latency with NT2 and IH. Previous

studies indicated that other MSLT features (namely mean REM latency and mean REM duration) might be sensitive and specific for identification of patients with NT1. The first aim of this study is to confirm these findings in an independent cohort. Second, in light of recent advancements of artificial intelligence (AI) for sleep scoring, we aimed to evaluate the reliability of two AI-based sleep scoring algorithms in MSLT naps. Finally, we assessed whether the automatically derived mean REM latency and mean REM duration could reliably discriminate patients with NT1.

Materials and methods: We included 35 patients with NT1, 22 with NT2, 17 with IH and 45 participants who had subjective ESD (i.e., Epworth Sleepiness Scale score >10), but who did not have any CDH diagnosis. All participants underwent an MSLT following a full-night polysomnography according to international criteria. Sleep experts scored sleep stages in each of the five naps of the MSLT. We employed the previously validated U-Sleep and YASA AI-algorithms for scoring sleep stages in each MSLT nap. Agreement between manual and automatic scorings was calculated with Cohen's kappa. By using each scoring, we derived the mean REM latency and mean REM duration for each participant. Area under the receiver operating characteristic curves (AUC) was used to evaluate how these features discriminated patients with NT1 from all remaining participants.

Results: U-Sleep had a significantly higher agreement with manual scoring compared to YASA (0.750 [inter-quartile range, IQR: 0.646-0.813] vs 0.660 [IQR: 0.557-0.747], p-value <0.001, signed ranksum test). Mean REM sleep latency could differentiate patients with NT1 with AUC values of 0.906 [95% confidence interval, CI: 0.823-0.953], 0.887 [95% CI: 0.796-0.940], 0.696 [95% CI: 0.582-0.784] for manual, U-Sleep and YASA scoring, respectively. Mean REM duration discriminated patients with NT1 with AUC values of 0.918 [95% CI: 0.850-0.963], 0.924 [95% CI: 0.844-0.966], 0.863 [95% CI: 0.788-0.924] for manual, U-Sleep, YASA scorings, respectively.

Conclusions: Mean REM latency and mean REM duration across the MSLT naps are reliable markers for discrimination of patients with NT1. U-Sleep had higher agreement with manual scoring compared to YASA. The results indicate that U-Sleep can be reliably used for MSLT scoring and for derivation of these promising NT1 diagnostic features.

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Immunity to influenza B and cross-reactivity to Pandemrix/pH1N1 in narcolepsy

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Introduction: Narcolepsy type 1 (NT1) is caused by 85-95% hypocretin (HCRT) neuron loss due to a combination of genetic and environmental risk factors and associated with DQA1*01:02/DQB1*06:02 (DQ0602, 98%) and T cell receptor (TCR) gene AJ24/AJ28/BV4-2. Pandemic influenza A H1N1 (pH1N1) and Pandemrix vaccination in 2009-2010 induced NT1 onset. Antigen specific T cell immune response in NT1 supports adaptive (auto)immunity against HCRT and Pandemrix/pH1N1. Despite this progress, the mechanism behind HCRT neuron loss and how the flu triggers a response against HCRT are unclear.

Materials and methods: Anti-hemagglutination (HA) antibody was first measured using HA inhibition assay. Binding affinity of B/Victoria candidate peptides to DQ0602 was next tested using a competition binding assay. Antigen-DQ0602 restricted/reactive T cells were further isolated using tetramer DQ0602 and single-cell RNA sequenced with 10X. Lastly, TCR clones were transfected into Jurkat 76 for TCR activation by a certain peptide presented by DQ0602.

Results: Two independent studies of our laboratory and a Chinese group have shown a higher HAI titer against B/Brisbane/60/2008 in NT1. I compared B/Brisbane/60/2008 with Pandemrix/pH1N1 and H3N2, and found a list of candidate peptides that most likely trigger immune response. Using the competition binding to DQ0602 at a relatively low concentration, four weak binders were further investigated using tetramer DQ0602 staining pooled PBMCs from multiple NT1 patients and healthy controls. I found a large population of reactive CD4+ T cells to a B/Victoria PB1 epitope that is homologous to Pandemrix/pH1N1 PB1 segment, and there is only one amino acid difference in their binding cores. Further, single cell RNA sequencing showed that over 85% of these cells are from NT1 patients and they are effector memory T cells. More than 35 clones were expanded at least 20 times, including several clones over 500 to 1,000 times. In addition, we built a TCR repertoire a) restricted by HCRT and Pandemrix/pH1N1 at baseline peripheral blood mononuclear cells (PBMCs) (n>430) and b)

from single-cell RNA sequencing cerebrospinal fluid(CSF) samples (n>2,000), and found the identical activated TCR clones in both baseline and cultured PBMCs.

Conclusions: Our research showed influenza B plays a role in NT1 pathogenesis and potential cross-reactivity to PB1 between B/Victoria and Pandemrix/pH1N1.

Impact of Stigma Associated with Narcolepsy Type 1: Insights from a Global Qualitative Study

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Introduction: Qualitative research on the impact of stigma on individuals with narcolepsy type 1 (NT1) is lacking. The 'Stigma in Narcolepsy Interview Project' performed semi-structured interviews with individuals diagnosed with NT1 to understand their lived experiences with the disorder. The resulting key themes and insights are provided.

Materials and methods: The study period was November 2024 to February 2025. Individuals with NT1 were screened from seven countries (China, France, Germany, Italy, Japan, UK, and US) to recruit five participants per country. Recruitment was based on pre-determined quotas on age, sex, time since diagnosis, education, and employment to ensure geographic and demographic diversity. Participants were ≥18 years old with a physician-confirmed NT1 diagnosis and were comfortable discussing their experiences. Interviews were double-blinded, conducted by personnel familiar with market research and trained on the discussion guide, approximately 60 minutes long, and were conducted in participants' native languages before being translated for analysis. Interviews underwent thematic analysis via manual coding. Four identified themes were iteratively reviewed, and any discrepancies were reconciled through consensus-driven judgement.

Results: Five participants with NT1 from each country completed the study (N=35). Mean ages across the countries varied between 29–41 years old, 17 (48.6%) participants were female, and 25 (71.4%) reported being diagnosed within the last 10 years. By design, the proportion of participants with college degrees (40-80%) and full-time employment (20-100%) varied. At the start of the interview, 30 (85.7%) participants reported experiencing stigma due to NT1.

During screening, participants associated family and friends (69%), experiences at school (51%) or work (54%), and inaccurate media portrayals (31%) as main drivers of stigma. The three most reported strategies interviewees used to cope with stigma were internalization, humor, and proactive communication. Regarding societal perceptions, 63% of participants reported there was 'no understanding' of NT1 in their culture. Further, 80% reported that they were viewed as 'lazy'; other reported perceptions included being described as 'having a psychiatric condition' (40%), a 'substance abuser' (31%), or 'rude/bored' (20%).

Emerging as the first theme from interviews, stigma associated with NT1 significantly impacted participants' quality of life from an early age. Additional themes included participants feeling stigmatized by non-specialist healthcare providers. Many participants shared feelings of not being believed or trusted and worried about being misdiagnosed when discussing their symptoms, causing them to withhold details, thereby delaying diagnosis. Many interviewees hypothesized that there was a lack of NT1 education in non-specialist settings leading to inadequate treatment and care post-diagnosis. Interviewees acknowledged that stimulants and antidepressants were most stigmatized, but nearly all reported that it would not impact their willingness to try these or other treatments.

Conclusions: These findings highlight the significant impact of stigma on individuals with NT1 in this study. Fear of being misdiagnosed with a mental health condition, or judged for their symptoms, can lead some to withhold information from healthcare providers, resulting in delayed or misdiagnosis. Understanding these challenges is essential to create a more supportive environment for those living with NT1.

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Impact of Switching From High- to Low-Sodium Oxybate on Ambulatory Blood Pressure in People With Narcolepsy

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Introduction: People with narcolepsy have an increased incidence of hypertension and cardiovascular disease (CVD) risk. Excess sodium intake is strongly associated with hypertension and CVD.

Materials and methods: XYLO, an open-label, single-arm study (NCT05869773), evaluated people with narcolepsy aged 18–70 years with screening systolic blood pressure (SBP) 130–155 mmHg taking twice-nightly high-sodium oxybate (SXB; Xyrem®) 6–9 g for ≥6 weeks, switching to low-sodium oxybate (LXB; Xywav®) at the same dosage/regimen for ≈6 weeks. The primary endpoint was change in mean 24-hour ambulatory SBP from baseline to end-of-treatment (EOT). Secondary endpoints were changes in mean daytime ambulatory, office (seated resting), and nighttime ambulatory SBP.

Exploratory endpoints included changes in mean 24-hour ambulatory, daytime ambulatory, office, and nighttime ambulatory diastolic blood pressure (DBP). An interim analysis using prespecified stopping criteria (75% completers) was performed. One-sided multiplicity-adjusted P-values ("*" denotes statistical significance) for SBP least squares mean (95% CI) changes adjusted for baseline values, and two-sided nominal P-values for corresponding DBP changes, are reported.

Results: Forty-three participants with narcolepsy (mean age, 45 years; 65% female; 33% on stable antihypertensives) were evaluated. At baseline, mean (SD) office SBP and DBP were 138.0 (5.7) and 85.2 (6.6) mmHg, respectively. Mean (SD) total SXB and LXB dosages were 8.0 (1.1) and 8.1 (1.1) g/night, respectively, representing 1457 (206) and 118 (16) mg sodium (difference of ≈1339 mg of sodium). The mean (SD) 24-hour urinary sodium was 4695.9 (2831.8) mg/day at baseline and 2934.9 (1401.3) mg/day at EOT. The mean (SD) 24-hour ambulatory SBPs at baseline and EOT were 132.3 (11.6) and 128.2 (12.0) mmHg, respectively; the change from baseline was –4.1 (–6.9, –1.4; $P=0.0019^*$) mmHg, meeting prespecified study stopping criteria. Changes in daytime and nighttime ambulatory SBP were –5.1 (–7.8, –2.4; $P=0.0003^*$) and –2.0 (–5.3, 1.4; $P=0.1265$) mmHg, respectively. The change in office SBP was –9.2 (–11.9, –6.5; $P<0.0001^*$). The change in 24-hour ambulatory DBP was –2.3 (–4.1, –0.5; $P=0.0118$). Changes in daytime and nighttime ambulatory DBP were –2.8 (–4.8, –0.9; $P=0.0045$) and –1.1 (–3.6, 1.5; $P=0.3993$); the change in office DBP was –3.8 (–6.0, –1.6; $P=0.0014$). Treatment-emergent adverse events (all mild/moderate) occurred in 33% of participants.

Conclusions: Switching from SXB to LXB reduced daily treatment-related sodium intake in participants with narcolepsy and was associated with clinically meaningful BP reductions, consistent with evidence on dietary sodium effects.

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Impaired Vigilant Attention in Pediatric Narcolepsy Type 1

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Introduction: Cognitive symptoms, such as decreased attention, are common in pediatric Narcolepsy Type 1 (NT1). However, objective data assessing attention dysfunction in this population are limited, particularly regarding its relationship with sleepiness or disrupted nighttime sleep. The psychomotor vigilance task (PVT) has been used to measure attention dysfunction in adults with central disorders of hypersomnolence but is not widely used in pediatric NT1. This study compared PVT metrics between pediatric NT1 patients and healthy controls. We hypothesized that attention dysfunction would be

worse in NT1 and associated with increased self-reported momentary sleepiness and disrupted nighttime sleep.

Materials and methods: 26 pediatric NT1 participants (mean age 15.9) and 16 healthy controls (mean age 16.3) completed 3-minute PVT testing in the evening before polysomnography (PSG) and again the following morning. Before each PVT, participants rated their sleepiness. Wake/N1 indices were extracted from PSG data as a measure of disrupted nighttime sleep. PVT metrics were compared between NT1 patients and controls using linear mixed models to evaluate the effects of age, gender, time of PVT, and group-time interactions. Outcomes included lapses (RT 355 ms), mean reaction time (RT), mean 1/RT, and slowest 10% 1/RT.

Results: NT1 participants showed reduced vigilant attention across PVT metrics compared to controls as measured by lapses ($p < .001$), mean RT ($p = .016$), mean 1/RT ($p = .003$), and slowest 10% 1/RT ($p = .021$). Contrary to our hypothesis, PVT performance was unrelated to momentary self-reported sleepiness. PVT performance was significantly correlated with more parent-reported concerns about attention, suggesting inattentiveness as measured by PVT may correspond with clinically significant attention dysfunction. Finally, poor PVT performance was correlated with disrupted nighttime sleep and percentage of time in stage NREM1 sleep, indicating that sleep quality may play a role in vigilant attention dysfunction in the pediatric NT1 population.

Conclusions: This study demonstrates that pediatric NT1 patients exhibit significant attention dysfunction as measured by PVT. Notably, momentary self-reported sleepiness did not predict PVT outcomes, suggesting that objective attention impairment in NT1 may not directly correspond to subjective sleepiness. PVT performance did correlate with measures of nocturnal sleep, which warrants further exploration. The 3-minute PVT is useful and feasible for assessing attention in pediatric NT1.

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Improvement in Patient-reported Cognitive Functioning in Patients with Narcolepsy Type 1 Treated with the Orexin 2 Receptor Agonist Alixorexton (ALKS 2680)

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Introduction: Narcolepsy type 1 (NT1) is typically characterized by excessive daytime sleepiness (EDS) and cataplexy. Patients also often complain of “brain fog,” impaired attention, and persistent fatigue—symptoms that are often not adequately addressed by available therapies or reflected in outcome measures. Cognitive complaints in narcolepsy only partly correlates with EDS severity and may persist even when EDS is pharmacologically controlled. Further, cognitive difficulties may be driven by underlying orexin pathway dysfunction. Alixorexton (ALKS 2680), a highly potent, oral, selective orexin 2 receptor agonist, may enhance cognition distinctly from sleepiness by activating receptors expressed throughout cognitive circuitry. In the Vibrance-1 study, once-daily alixorexton demonstrated clinically meaningful and statistically significant improvements from baseline in wakefulness compared to placebo in patients with NT1. The study also included patient-reported outcomes instruments to assess perceived problems with concentration, memory, expressing thoughts, word finding, thinking, and problem solving.

Materials and methods: Vibrance-1 was a global, placebo-controlled, dose-ranging phase 2 study with a 6-week randomized, double-blind, parallel group treatment period followed by an open-label extension. After 2 weeks of washout from narcolepsy medications, adult patients with NT1 were randomized to receive placebo or alixorexton once daily at doses of 4, 6, or 8 mg. The study included the British Columbia Cognitive Complaints Inventory (BC-CCI) as an exploratory endpoint. The BC-CCI is a 6-item instrument to capture patients' perception of cognitive difficulties within the past week. Total scores range from 0 to 18, with higher scores reflecting a greater degree of cognitive impairment.

Categories of cognitive complaints are: 0 to 4 (none or minimal), 5 to 8 (mild), 9 to 14 (moderate), and 15 to 18 (severe). The study also included the Patient Global Impression of Severity (PGI-S) for Cognition to measure patient's perception of the severity of their cognitive dysfunction.

Results: Ninety-two patients were randomized. At baseline, most patients reported mild or moderate cognitive symptoms, with mean (SD) total scores on the BC-CCI of 10.5 (4.83) in the placebo group and 8.3 (4.32), 7.8 (4.63), and 8.4 (3.01) in the alixorexton 4, 6, and 8 mg groups, respectively. Mean BC-CCI scores improved from baseline in all alixorexton dose groups at the first post-dose timepoint (Week 2) and were sustained through Week 6 (nominal p values at Week 6 all <0.0001 versus placebo). At Week 6, patients who received alixorexton were more likely to report less severe cognitive difficulties, as measured by PGI-S Cognition, than those who received placebo (nominal p<0.01 for all groups). Improvements on these cognitive scales mirrored improvements observed on study endpoints evaluating core symptoms of narcolepsy, as reflected by sleep latency on the Maintenance of Wakefulness Test, daytime sleepiness on the Epworth Sleepiness Scale, and the Narcolepsy Severity Scale.

Conclusions: In this phase 2 study, 6 weeks of treatment with once-daily alixorexton improved patient-reported cognitive functioning compared to placebo across all doses in patients with NT1.

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Improvement in the Severity of Narcolepsy Symptoms and Fatigue in Patients with Narcolepsy Type 1 Treated with the Orexin 2 Receptor Agonist Alixorexton (ALKS 2680)

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Introduction: Excessive daytime sleepiness (EDS) and cataplexy are hallmarks of Narcolepsy type 1 (NT1); however, many patients also experience sleep paralysis, hypnagogic/hypnopompic hallucinations, and disrupted nighttime sleep. These symptoms, together with others such as fatigue and cognitive complaints, result in significant morbidity and impaired quality of life, and may be insufficiently addressed by current therapies. Orexin engages multiple neurologic pathways distributed throughout the brain, including those associated with wakefulness, fatigue, mood, and cognition. In Vibrance-1, once-daily alixorexton (ALKS 2680), a highly potent, oral, selective orexin 2 receptor agonist, produced clinically meaningful and statistically significant improvements in mean sleep latency and EDS compared to placebo in patients with NT1. Vibrance-1 also included, as exploratory endpoints, instruments to assess the severity of narcolepsy symptoms and fatigue.

Materials and methods: Vibrance-1 was a global, placebo-controlled, dose-ranging phase 2 study with a 6-week randomized, double-blind, parallel group treatment period followed by an open-label extension. After 2 weeks of washout from narcolepsy medications, adult patients with NT1 were randomized to placebo or alixorexton once daily at doses of 4, 6, or 8 mg. The Narcolepsy Severity Scale (NSS) assessed perceived severity, frequency, and consequences of the key symptoms of narcolepsy. The Clinical Global Impression of Severity (CGI-S) measured the severity of the disease from the clinician's perspective. The PROMIS-Fatigue Short-form 6a assessed patients' perceived fatigue within the past week calculated as a standardized T-score, with lower values representing less fatigue. The Patient Global Impression of Severity (PGI-S) for Fatigue measured patient-perceived severity of fatigue.

Results: Ninety-two patients were randomized. Baseline NSS scores reflected severe symptoms with mean (SD) values of 32.7 (7.36) in the placebo group and 32.5 (9.10), 29.0 (8.37), and 30.9 (9.46) in the alixorexton 4, 6, and 8 mg groups, respectively. At Week 6, mean NSS scores improved from baseline in all alixorexton dose groups (nominal p values all <0.001 versus placebo). Clinicians rated patients who received alixorexton as more likely to have less severe symptoms, as measured by CGI-S, compared to

placebo (nominal $p < 0.05$ for all groups). On PROMIS-Fatigue, most patients reported above-average fatigue at baseline, with mean (SD) T-scores of 66.17 (8.82) in the placebo group and 64.53 (7.64), 61.40 (7.97), and 63.60 (10.62) in the alixorexton 4, 6, and 8 mg groups, respectively. Mean PROMIS-Fatigue scores improved from baseline in all alixorexton dose groups at Week 6 (nominal p values all < 0.01 versus placebo). At Week 6, patients who received alixorexton were more likely to report less severe fatigue, as measured by PGI-S Fatigue, than those who received placebo (nominal $p < 0.01$ for all groups).

Conclusions: In all dose groups, 6 weeks of once-daily alixorexton led to improvement from baseline in the severity of disease symptoms and in patient-reported fatigue compared to placebo in this phase 2 study of patients with NT1.

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Improvement of Individual Excessive Daytime Sleepiness Symptoms With Once-Nightly Sodium Oxybate for Narcolepsy

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Introduction: The Epworth Sleepiness Scale (ESS) is a commonly used 8-item patient-reported outcome measure for excessive daytime sleepiness. While aggregate data are typically presented, individual domains vary in clinical significance. This post hoc analysis from the phase 3 REST-ON trial (NCT02720744) evaluated the efficacy of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) on individual ESS domains.

Materials and methods: Participants aged ≥ 16 years with narcolepsy were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2–3, 6 g; weeks 4–8, 7.5 g; weeks 9–13, 9 g) or placebo. ESS data from the modified intent-to-treat population (mITT; ≥ 1 efficacy measurement after receiving the 6-g dose) at weeks 3, 8, and 13 were analyzed.

Results: In the mITT population (ON-SXB, $n=97$; placebo, $n=93$), ON-SXB was associated with significant sleepiness improvements vs placebo for sitting and reading, watching TV, lying down to rest in the afternoon, and sitting quietly after lunch; all doses $P < 0.01$. ON-SXB was associated with significant sleepiness improvement vs placebo as a passenger in a car for an hour without a break (least squares mean difference [LSMD; 95% CI] in change from baseline: 6 g, -0.39 [-0.61 to -0.17]; 7.5 g, -0.59 [-0.85 to -0.32]; 9 g, -0.67 [-0.95 to -0.38]; all doses $P < 0.001$). Significant sleepiness improvements were observed with 7.5-g and 9-g ON-SXB when sitting inactive in public (LSMD vs placebo [95% CI]: 7.5 g, -0.34 [-0.61 to -0.07], $P=0.014$; 9 g, -0.44 [-0.71 to -0.18], $P=0.001$) and sitting and talking to someone (7.5 g, -0.29 [-0.47 to -0.11], $P=0.002$; 9 g, -0.24 [-0.44 to -0.04], $P=0.018$). Significant sleepiness improvement as a driver stopped in traffic was observed with 9-g ON-SXB (LSMD vs placebo [95% CI], -0.35 [-0.63 to -0.07]; $P=0.015$).

Conclusions: At all ON-SXB doses, participants had significant improvements vs placebo in sleepiness while completing routine activities. The greatest improvements in these activities were observed with the 9-g ON-SXB dose, including the domain for sleepiness as a driver stopped in traffic, a key safety concern. ON-SXB may be helpful in addressing safety challenges for people with narcolepsy.

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Increased FoxA1⁺ Treg Cells Proportion of Peripheral Blood in Patients with Narcolepsy Type 1

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Introduction:

Narcolepsy type 1 (NT1) is a rare sleep disorder characterized by excessive daytime sleepiness (EDS), cataplexy, hypnagogic hallucinations, and sleep paralysis. The pathological hallmark of NT1 is the selective loss of hypocretin (Hcrt) neurons in the lateral hypothalamus, leading to decreased cerebrospinal fluid (CSF) hypocretin-1 (Hcrt-1) concentrations. The global prevalence of NT1 ranges from approximately 0.02% to 0.18%. Patients often experience disrupted nocturnal sleep, comorbid obstructive sleep apnea hypopnea syndrome, and REM sleep behavior disorder, which significantly impair daily functioning and increase the risk of injury due to cataplexy. The etiology of NT1 is multifactorial, involving genetic susceptibility, immune dysregulation, and environmental triggers. Notably, the incidence of NT1 rose following the 2009 H1N1 influenza pandemic and vaccination campaigns, highlighting the role of immune mechanisms. Regulatory T (Treg) cell dysfunction has been implicated in autoimmune diseases, contributing to chronic inflammation and tissue damage. FoxA1, a transcriptional activator, regulates Treg cell differentiation and function and has been linked to central nervous system autoimmune diseases. Given these findings, this study aimed to investigate the proportion of FoxA1⁺ Treg cells in peripheral blood mononuclear cells (PBMCs) of NT1 patients and explore associations with clinical features, providing insight into potential immunopathogenic mechanisms and therapeutic targets.

Materials and methods: Twenty-one patients with NT1 and 21 healthy controls were recruited to this study. All subjects were monitored via polysomnography and multiple sleep latency test (MSLT). The Epworth sleepiness scale (ESS) was used to assess the severity of excessive daytime sleepiness. Patients with NT1 were examined human leukocyte antigen (HLA) gene and cerebrospinal fluid hypocretin-1 (Hcrt-1) concentration. Peripheral blood samples of all subjects were collected, and Ficoll method was used to separate PBMC. Flow cytometry was used to analyze the percentage of FoxA1⁺ Treg cells.

Results: The CD4⁺ T cells proportion in peripheral blood of patients with NT1 group was higher than that in control group ($52.32\% \pm 6.79\%$ vs $45.07\% \pm 7.06\%$, $P < 0.05$). The CD25⁺ FoxA1⁺ Treg cells proportion in the CD4⁺ T cell population of patients with NT1 was higher than that in the control group ($5.20\% \pm 2.23\%$ vs $2.07\% \pm 0.88\%$, $P < 0.001$). There was no significant correlation between the percentage of CD25⁺ FoxA1⁺ Treg cells and the cerebrospinal fluid Hcrt-1 concentration, age, MSLT sleep latency or disease duration ($P > 0.05$).

Conclusions: The CD4⁺ T cells proportion in peripheral blood of patients with NT1 increased. In the CD4⁺ T cell population, the CD25⁺ FoxA1⁺ Treg cells proportion increased in patients with NT1.

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Initial preclinical development of a novel dual orexin receptor agonist

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Introduction: Dual orexin receptor agonists with effectiveness after systemic administration may be of interest for the treatment of narcolepsy and other pathological conditions.

Materials and methods: We designed a novel dual orexin receptor agonist (OX-D, international patent application WO 2024/003128 A1) and performed its initial pre-clinical evaluation in vitro on murine neuroblastoma Neuro-2a cells and human HEK-293T cells and in vivo on orexin knock-out mice, a model of narcolepsy type 1.

Results: In vitro, OX-D was able to cross the plasma membrane of Neuro-2a murine neuroblastoma cells, suggesting its ability to cross the blood-brain barrier. OX-D was effective in eliciting intracellular calcium responses in murine neuroblastoma cells transfected with either human orexin receptor 1 or 2, but not in non-transfected cells, and its estimated EC₅₀ in HEK-293T cells transfected with orexin receptors was 68 nM and 11 nM on orexin receptor 1 and 2, respectively. Intracerebroventricular infusion of OX-D (160 µM, 5 µL/h, for 6 h from lights on) in freely-behaving orexin knock-out mice (N = 8 females, C57Bl6/J background, 12:12 h light-dark cycle, 24-h EEG and EMG recordings) elicited a dramatic increase in wakefulness and a corresponding decrease in non-REM sleep throughout the light period and a dramatic decrease in REM sleep persisting also in the dark period compared with vehicle

infusion. Subcutaneous bolus injection of OX-D (160 nmol in 1 mL at lights on) in freely-behaving orexin knock-out mice (N = 12 females, C57Bl6/J background, 12:12 h light-dark cycle, 24-h EEG and EMG recordings) mildly but significantly decreased REM sleep during the light and dark periods and significantly decreased cataplexy-like state during the dark period compared with vehicle injection. This decrease in cataplexy like state occurred in 10 out of 12 mice and was confirmed to implicate a decrease in bona-fide cataplexy in a subset of 4 mice with simultaneous video recordings.

Conclusions: These results suggest that OX-D is a dual orexin receptor agonist with anti-cataplectic activity after subcutaneous administration in orexin knock-out mice.

iSPHYNCS: An Update on the Internationalization and New Approaches of the Swiss Primary Hypersomnolence and Narcolepsy Cohort Study

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Introduction: The international Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS) aims to provide new data to improve diagnostics and the management of primary central disorders of hypersomnolence (CDH). The three main specific aims of iSPHYNCS are 1) discovery of new biomarkers, 2) assessment of treatment adherence, and 3) patient-related outcomes, to set the ground for personalized patient treatment.

Materials and methods: The study plans to prospectively include 500 CDH patients and 60 healthy controls (HC) by the end of 2026. Recruitment is ongoing at 10 tertiary sleep centers in Switzerland, Germany, and the Netherlands. Italy and Norway plan to start recruitment shortly. The multi-modal study approach includes questionnaires, clinical assessments, video-polysomnography, the Multiple Sleep Latency Test (MSLT), vigilance tests, actigraphy, long-term activity monitoring with Fitbit, immunological studies, quantitative hypocretin measurements, proteomics, gut microbiomics, and genetics/epigenetics. AI-powered analyses, including unsupervised clustering, are used for data-driven patient phenotyping.

Results: 303 participants, including 13 children, have been recruited. The study population comprises 75 individuals with narcolepsy type I (NT1), 185 individuals of the "narcoleptic borderland" (NBL), such as narcolepsy type 2, idiopathic hypersomnia and insufficient sleep syndrome, as well as 43 HC. Initial analyses reveal notable differences among NT1, NBL, and HC groups across various domains, including questionnaire responses, neuropsychiatric profiles, gut microbiome, polysomnographic, Fitbit and vigilance data. We demonstrate that novel approaches like long-term activity monitoring with wearable devices has the potential to give new insights into sleep-wake behavior, disease progression and therapy success. First results on unsupervised patient clustering based on questionnaires, objective sleepiness measures and vigilance data indicate that symptom severity may be more affected by psychiatric co-morbidities than by the primary sleep disorders.

Conclusions: Following an initial three-year phase in Switzerland, the internationalization of iSPHYNCS was successfully launched in 2023. Preliminary results suggest novel and promising clinical, biological, and digital markers of CDH. Proteomics and genetics/epigenetics analyses are currently being explored.

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Long-term assessment of social jetlag by Fitbit smartwatch in patients with central disorder of hypersomnolence

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Introduction: Patients with central disorders of hypersomnolence (CDH) suffer from excessive daytime sleepiness (EDS) and often have irregular or abnormal sleep-wake patterns. Social jetlag (SJL) reflects the mismatch between an individual's circadian rhythm and social schedule. SJL in CDH has rarely been studied, partly because standard questionnaires are not validated for this population. We aimed to characterize SJL in CDH using objective sleep-wake data from Fitbit smartwatch. We hypothesized that patients with CDH would show larger SJL compared to healthy controls (HC).

Materials and methods: We analyzed daily sleep-wake data measured by Fitbit smartwatches from 37 HC, 50 patients with narcolepsy type 1 (NT1), and 116 narcolepsy borderland (NBL) patients enrolled in the International Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS) between September 2020 and April 2025. Weekly SJL was calculated as the difference between average mid-sleep points on weekends and weekdays. Monthly SJL was the mean of weekly SJL per month. A linear mixed model (LMM) predicted monthly SJL by diagnosis (HC as reference), adjusting for age, BMI, gender, season, daylight saving time (DST: summer vs. winter), and monthly mean nocturnal sleep duration.

Results: NBL patients (estimated difference: 19.0 min, $p = 0.0015$) and NT1 (estimated difference: 12.3 min, $p = 0.074$) had significantly larger or a trend towards larger SJL compared to HC in the LMM, controlling for confounders. No difference was found between NT1 and NBL ($p = 0.23$). These findings were replicated under DST summer-time conditions (NBL-HC: 21.4 min, $p = 0.0039$; NT1-HC: 14.2 min, $p = 0.097$; NBL-NT1: 7.18 min, $p = 0.25$); however, in winter-time only NBL had larger SJL than HC (NBL-HC: 16.0 min, $p = 0.047$), not NT1 ($p = 0.27$). HC showed significantly larger SJL in winter-time vs. summer-time (9.67 min, $p = 0.045$), whereas no such seasonal difference was found in patients (NT1: $p = 0.22$; NBL: $p = 0.15$). SJL was unrelated to BMI or gender, but was negatively associated with nocturnal sleep duration ($p = 0.021$). Post hoc pairwise Wilcoxon tests indicated that NT1 and NBL patients had greater variance in nocturnal sleep duration during weekends (NT1: $p = 0.041$; NBL: $p = 0.038$) but not during weekdays, compared to HC.

Conclusions: Wearable technologies enable the longitudinal assessment of SJL in patients with CDH during daily life. Patients with CDH exhibit larger SJL than healthy controls, particularly during summer-time. DST may influence SJL differently in CDH and healthy individuals. The persistent SJL difference between NBL and HC across DST conditions may be a potential marker of NBL. In contrast, increased SJL in HC but not in CDH during winter-time suggests a failure of compensatory mechanisms in CDH in response to circadian disruption or greater sleep need in winter. This limited ability to compensate for sleep debt may lead to varied coping strategies on days off, explaining the greater variability in nocturnal sleep duration on weekends among CDH patients.

Long-Term Safety and Tolerability of Once-Nightly Sodium Oxybate: A Post Hoc Analysis From RESTORE

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Introduction: Once-nightly sodium oxybate (ON-SXB; LUMRYZ™) is an extended-release formulation of sodium oxybate that eliminates the second, middle-of-the-night dose required by immediate-release twice-nightly oxybate (TN-OXB) formulations. RESTORE (NCT04451668) was an open-label/switch study evaluating the long-term safety/tolerability of ON-SXB in people with narcolepsy.

Materials and methods: Participants ≥16 years of age with narcolepsy who had completed the phase 3 REST-ON trial, were on stable-dose TN-OXB (switch participants), or were oxybate-naïve were eligible for RESTORE. Switch participants' initial ON-SXB doses were equivalent/closest to their prior total nightly TN-OXB dose. After participants titrated their ON-SXB dose (±1.5 g/week; maximum, 9 g/night) with no tolerability issues for ≥3 months, participants entered the stable dosing period. Treatment-emergent adverse events (TEAEs) were recorded quarterly for switch participants in the safety population (all participants who received ≥1 dose of ON-SXB).

Results: A total of 130 switch participants were included in the safety population and received ON-SXB for a median (range) duration of 502.5 (8-1169) days during the >3-year study. Of these participants, 115 continued into the stable dosing period and were included in this analysis. Of the 115 who entered the stable dosing period, 73.9% (85/115) reported ≥1 TEAE. TEAEs reported by ≥3% of participants included COVID-19 (18.3%), nasopharyngitis (11.3%), nausea (10.4%), sinusitis (8.7%), fall (8.7%), headache (7.0%), enuresis (7.0%), cough (6.1%), upper respiratory tract infection (5.2%), urinary tract infection (5.2%), somnolence (4.3%), tremor (4.3%), vomiting (3.5%), dyspnea (3.5%), rash (3.5%), decreased appetite (3.5%), hypertension (3.5%), concussion (3.5%), and contusion (3.5%). Eight (7%) participants reported ≥1 serious TEAE (events, n=10); of these, 2 serious TEAEs were deemed related to ON-SXB (gastroesophageal reflux disease and cataplexy). Five participants (4.3%) experienced ≥1 TEAE that led to ON-SXB discontinuation (upper abdominal pain, fatigue, fall, dizziness, paresthesia, irritability, nightmare, and hypertension; n=1 [0.9%] each).

Conclusions: Reported AEs were consistent with the known AEs of oxybates. Only 4% of participants discontinued owing to a TEAE during the stable dosing period, underscoring the largely transient nature of AEs and the long-term tolerability of ON-SXB.

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Medical Education Significantly Improves Knowledge of the Role of Orexin in Narcolepsy Type 1 and the Neurocognitive Impact

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Introduction: Understanding the role of orexin in patients with and without sleep disorders provides the basis for confidence in future decision-making regarding therapies that target the orexin system. However, most clinicians are unfamiliar with the role of orexin in sleep disorders. In addition, patients with narcolepsy commonly experience impairments in cognition that are underrecognized in practice.

We sought to improve physician knowledge of the role of orexin in narcolepsy type 1 (NT1) and the impact on neurocognitive symptoms in a series of two CME activities published in June and October 2024 (available at <https://www.medscape.org/viewarticle/1001223> and <https://www.medscape.org/viewarticle/1001723>).

Materials and methods: Physicians participated in one or both video-based, online, segmented CME activities with synchronized slides. The effects of the education were assessed using a repeated pairs, pre-assessment/post-assessment study design. Differences from pre- to post-assessment were evaluated using the McNemar's test. $P \leq .05$ is the significance level.

Results: 2,368 physicians completed both pre- and post-assessment questions for one or both activities, including 546 neurologists, 1,685 psychiatrists, and 137 pulmonologists. Significant improvements were seen across pre/post assessment questions in

1. Identifying the role of orexin in maintaining wakefulness, controlling muscle tone during REM sleep and motivation/reward (Correct response at pre-assessment vs post-assessment for neurologists 58% vs 71%, $P < .001$; for psychiatrists 54% vs 68%, $P < .001$; for pulmonologists 43% vs 54%, $P < .05$)
2. Recognizing that a CSF orexin-1 level below 110 pg/mL is the most specific way to differentiate NT1 from NT2 (Correct response at pre-assessment vs post-assessment for neurologists 18% vs 34%, $P < .001$; for psychiatrists 11% vs 25%, $P < .001$; for pulmonologists 11% vs 40%, $P < .001$)
3. Identifying memory and executive function as the cognitive domains most affected in NT1 apart from attention (Correct response at pre-assessment vs post-assessment for neurologists 75% vs 84%, $P < .001$; for psychiatrists 69% vs 81%, $P < .001$; for pulmonologists 77% vs 84%, $P = \text{NS}$)
4. Recognizing the inclusion of cognitive symptoms and mood as newer endpoints in narcolepsy clinical trials (Correct response at pre-assessment vs post-assessment for neurologists 56% vs 64%, $P < .01$; for psychiatrists 52% vs 61%, $P < .001$; for pulmonologists 57% vs 61%, $P = \text{NS}$)

Conclusions: This study demonstrates the success of online, accredited, multi-faculty, video-based education in improving knowledge amongst physicians in recognizing the role of orexin and the cognitive disturbances in NT1.

This knowledge is important for understanding the rationale behind the emerging orexin receptor agonists in development for NT1 and will prepare physicians to contemplate and eventually take action in implementing these therapies once available, to enable a better quality of life for patients with NT1.

Metabolic comorbidities in narcolepsy: a systematic review and meta-analysis

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Introduction: Narcolepsy is a chronic sleep-wake disorder, but patients also suffer from an increased risk of developing endocrine or metabolic dysfunctions. However, current evidence remains less consistent regarding the prevalence of specific metabolic disorders, especially across the narcolepsy subtypes. To address the disparities and clarify the morbidity risk of metabolic comorbidities in narcolepsy, we performed a systematic review and meta-analysis to delineate the prevalence rates and risk of metabolic disorders in this population and stratified subgroups.

Materials and methods: This meta-analysis assessed the prevalence of metabolic comorbidities in narcolepsy, categorized as Metabolic syndrome (MetS) and associated disorders (i.e., obesity, diabetes, hypertension, and dyslipidemia) and other metabolic disorders (i.e., overweight, prediabetes, pubertal praecox, non-dipping blood pressure, thyroid disease, and cardiovascular disorder). We searched PubMed, Web of Science, EBSCO, and Cochrane Library up to April 8, 2025. Pooled prevalence rates and odds ratios (ORs) between strata and the control group were calculated using the random-effects model. Sensitive analyses examined narcolepsy subtype (i.e., narcolepsy subtype 1, NT1 and narcolepsy subtype 2, NT2), age (i.e., children and adults), sex, stimulants and utilization of anticataleptic agents,

and the presence of orexin deficiency or human leukocyte antigen (HLA)-DQB1*06:02 genotype. For conditions with insufficient data, we performed the systematic review.

Results: A total of 54 studies with 9,827 males and 18,298 females were included. **For the MetS and associated disorders**, obesity emerged as the predominant disorder (29%), while the prevalence of diabetes, hypertension, and dyslipidemia was below 20%. MetS was present in 30%, affecting more than half of the adult patients with NT1. ORs indicated NT1 patients using the stimulants and antiepileptic agents suffered more from hypertension than the drug-naïve ones. Sensitivity analyses showed relatively higher prevalence of obesity (28% vs. 18%) and dyslipidemia (24% vs. 14%) in NT1, and of obesity in children (37% vs. 22%). Males exhibited a predominance in diabetes, hypertension, and dyslipidemia. In patients with confirmed orexin deficiency or the HLA-DQB1*06:02 genotype, the results were similar to NT1, except for a notably high prevalence of dyslipidemia (48%) in the orexin deficiency cluster. **For the other metabolic disorders**, in NT1 patients, Prediabetes and non-dipping blood pressure affected 33% and 53%, respectively. Pubertal praecox involved 18%. Moreover, the pooled prevalence of overweight increased with age. After all, data on cardiac diseases and NT2 patients were limited. The meta-results generated from studies designed with comparison groups showed an elevated risk of metabolic disorders in narcolepsy than the general population and patients with other hypersomnia or diseases, but the findings were less significant compared to the BMI-matched population.

Conclusions: Our study revealed a wide spectrum of prevalent metabolic disturbances in narcolepsy, especially MetS and related disorders. Notably, non-dipping blood pressure and prediabetes are common in NT1, warranting extra attention to their long-term cerebrovascular and cardiovascular risks. Additionally, the trend of increasing overweight but decreasing obesity with age suggests the early disease phase is critical for metabolic deterioration. Given the inconclusive literature and insufficient research on this topic, future studies need to better characterize these disturbances, particularly risk factors and mechanisms underlying orexin dysfunction.

Multimodal Detection of Narcolepsy Type 1 Using Genetic and Nocturnal Polysomnography Data

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Introduction: Efficient screening methods with high specificity which can be applied to large sample sizes are needed to improve significantly underdiagnosed people with narcolepsy type 1 (NT1). To address this unmet need, we combined polygenic risk scores (PRS), HLA typing, and nocturnal polysomnography (PSG) data. These methods are developed and validated using a dataset significantly larger than those used in previous studies, ensuring their reliability and generalizability.

Materials and methods: People with diagnosed narcolepsy were studied across 7 different global locations, involving multiple collaborators. We developed a custom U-Sleep model for variable-resolution sleep staging using electroencephalography, electrooculography, and electromyography data from 19,381 PSG recordings from the National Sleep Research Resource and the Stanford Sleep Clinic. Sleep staging was performed across epochs from 0.25 to 3600 seconds, leveraging novel multiscale transition matrix (MTM) features to capture NT1-specific transitions and overlapping sleep stages. Next, a Gaussian processes classifier was trained on features from 21,846 PSGs across 14 cohorts (NT1: n=327; controls: n=21,519) and tested on 634 separate PSGs (NT1: n=317; controls: n=317). An ensemble model combined multiple time resolutions, weighted by prediction accuracy. Classifier performance was evaluated using 5-fold cross-validation. We developed a multi-information model integrating new PRS scores with HLA DQB1*06:02 typing, where HLA- and PRS+ conditions map to control and NT1 prediction, respectively, with PSG used when neither applies.

Results: Adding PRS to HLA increased the specificity from 81.9% to 100.0%, with a sensitivity of 42.6%, enabling potential screening of NT1 using genetics alone. PSG alone yielded 90.9% sensitivity at 99.5% specificity, surpassing State-of-the-Art (SOTA). When combining PSG with HLA, our approach increased to 91.2% sensitivity at the same high specificity. Adding PRS further rescued HLA+ cases missed based off PSG, and increased sensitivity to 95.0% while maintaining 99.5% specificity. MTM

features meaningfully boosted classification performance (approximately 1% gain) compared to SOTA features, which themselves significantly outperformed standard clinical PSG measures. Ensemble models showed that combining multiple resolutions improved performance, notably specificity. Additionally, post-hoc analyses showed that genetic information noticeably improved model robustness.

Conclusions: These findings suggest that the proposed multimodal model is a robust framework for NT1 classification, providing more specific and sensitive screening methods.

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Narcolepsy as a potential risk factor for Schizophrenia

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Introduction: Narcolepsy is a severe sleep disorder with characteristics of fatigue, fragmented sleep, cataplexy and hypnagogic hallucinations. Earlier clinical studies have reported the onset of schizophrenia after narcolepsy but the causality behind narcolepsy and schizophrenia is unknown. Our goal was to understand the causality between narcolepsy and schizophrenia.

Materials and methods: To estimate the comorbidity between narcolepsy and schizophrenia, we employed data from the FinRegistry that contains data for the total population of Finland in total 7.2 million individuals (N = 1664 individuals with narcolepsy and 55,372 with schizophrenia). We then used Mendelian randomization and previously published genome-wide association data to test the causality between narcolepsy and schizophrenia.

Results: We observed a robust causal association from narcolepsy to schizophrenia using the HLA-independent lead variants ($P\text{-value} = 6.0 \times 10^{-4}$), which was accentuated when including the HLA locus ($P\text{-value} = 4.48 \times 10^{-7}$). Furthermore, we observed a modest bidirectional causality from schizophrenia to narcolepsy ($P\text{-value} = 0.015$). There was no evidence of pleiotropy.

Conclusions: Our findings indicate a causal relationship where narcolepsy may increase the risk for schizophrenia, and a bidirectional causality from schizophrenia to narcolepsy. Additionally, our results clarify the psychiatric burden in narcolepsy.

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Narcolepsy is associated with an increased risk of HLA-related autoimmune diseases: Evidence from a nationwide healthcare system data in South Korea

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Introduction: To determine the incidence rate of narcolepsy in South Korea and closely examine the relationship between narcolepsy, which is believed to be an autoimmune response, and other systemic autoimmune diseases.

Materials and methods: We examined data from the South Korean nationwide health insurance claims database from 2010 to 2019. Our study included patients with narcolepsy as well as age- and sex-matched controls without narcolepsy. We estimated the incidence of narcolepsy and the odds ratio of narcolepsy and associated autoimmune comorbidities in South Korea.

Results: We identified 8710 patients with narcolepsy (59.8% men and 40.2% women). The incidence of narcolepsy was 0.05%. Patients with narcolepsy were at a significantly high risk of ankylosing spondylitis, rheumatoid arthritis, and Sjögren's syndrome, which diseases are known to be related to human leukocyte antigen (HLA) genes.

Conclusions: Narcolepsy is closely related to systemic autoimmune diseases, particularly those related to HLA genes.

Narcolepsy Revolution: Interpretable machine learning for automated sleep stage classification in narcolepsy and hypersomnia

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Introduction: Narcolepsy is a rare neurological disorder with the occurrence of rapid eye movement sleep after sleep onset as a typical symptom. Current diagnostic protocols rely on manual assessments of sleep neurophysiology, including overnight polysomnography followed by the Multiple Sleep Latency Test (MSLT) by clinically trained personnel. These procedures are resource-intensive and operationally demanding, contributing to prolonged diagnostic delays in many healthcare systems due to limited clinical capacity. Machine learning offers significant promise for improving the diagnosis of narcolepsy and other sleep disorders by enabling automated, data-driven analysis of sleep neurophysiology.

Materials and methods: We used an open-source, annotated polysomnography dataset (MNC, [sleepdata.org](#)) and implemented a data analysis and sleep stage classification pipeline aimed at supporting diagnostic decision-making in clinical practice. We extracted features from a single frontal EEG trace, which included time-domain features, frequency-domain features, cross-frequency coupling metrics, and features derived from empirical mode decomposition. We then trained machine learning models including XGBoost and Random Forest (RF) to predict sleep stages in healthy control, narcolepsy, and hypersomnia datasets.

Results: The RF classifier demonstrated the best performance for sleep stage classification, achieving up to 82% accuracy, 82% specificity, and 92% sensitivity when trained on combined feature sets. Features with the highest importance for sleep stage classification included permutation entropy, the mean frequency of the EMD derived intrinsic-mode-function 1, and low frequency power of the autocorrelation. A subsequent Vision-informed Transformer (ViT base, patch 32) trained on the images of hypnograms achieved 100% accuracy on 6 test samples comparing narcolepsy to healthy controls.

Conclusions: By leveraging features extracted from a single lead sleep EEG, machine learning can identify diagnostically relevant features with high accuracy and consistency. This approach can be directly translated to the use of wearable devices that employ dry-electrode EEG recordings during sleep, and has the potential to streamline diagnostic workflows, reduce clinician workload, and shorten time to diagnosis, particularly in resource-constrained settings.

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Narcolepsy's Sustained Attention Deficits: Unveiled by Dysfunctional Brain Dynamics

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Introduction: Narcolepsy Type 1 (NT1) has significant sustained attention deficits, which is a rare chronic neurological disorder caused by orexin neuron loss or dysfunction. sustained attention is a fundamental component of human cognition, these deficits directly impact NT1 patients' daily functioning and work capacity, leading to them as a potential diagnostic criterion. Yet the underlying neural mechanisms remain unclear. Here, we hypothesized that both **low arousal levels** and **attentional misallocation** contribute to these deficits.

Materials and methods: In total, 40 NT1 patients were recruited from the Department of Neurology of Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, China. Another 41 healthy controls matched for age, sex were recruited from the school or community by advertisement. We employed resting-state EEG microstate analysis combined with behavioral measures to investigate the neural correlates of attention impairments in NT1 (n = 40) and Controls (n = 41). Sustained attention

deficits were assessed using the Sustained Attention to Response Task (SART). Participants' resting-state EEG was recorded using a 64-electrode cap, followed by microstate analysis to investigate abnormal brain network dynamics in NT1. Source localization analysis was employed to identify the neural generators of the observed microstates. Correlation analyses were conducted to test our two potential hypotheses regarding low arousal and attentional misallocation.

Results: Behavioral results showed significantly sustained attention deficits in NT1 patients, with higher omission errors (33.33 ± 33.70 vs. 7.95 ± 12.27 , $P < 0.001$), slower reaction times (373.13 ± 71.88 vs. 321.36 ± 45.97 ms, $P < 0.001$), and larger response time variability (115.06 ± 60.86 vs. 66.89 ± 18.12 ms, $P < 0.001$). Distinct patterns of microstate were altered in NT1 patients, including reduced properties in microstate C and D and increased characteristics in microstate A and F. Crucially, we found that a lower occurrence of microstate C ($r = -0.47$, $P = 0.003$), microstate D ($r = -0.57$, $P < 0.001$), and a longer duration of microstate F ($r = 0.60$, $P < 0.001$) indicated lower attentional performance in NT1 patients. Source localization results supported our hypotheses: microstate D sources overlapped with the attention control network; microstate C showed major activity in the default mode and limbic networks; and microstate F sources corresponded to the anterior default mode network.

Conclusions: Our study provides evidence that sustained attention deficits in narcolepsy type 1 are linked to dysfunctional brain dynamics. The distinct patterns of microstate alterations, combined with specific brain-behavior correlations, support our dual-process hypothesis of attention impairments in NT1. Clinically, the identification of specific microstate patterns associated with sustained attention deficits could serve as potential biomarkers for diagnosis and treatment monitoring.

Nocturnal Fragmentation and Dream Enactment behaviors in Narcolepsy: Diagnostic Biomarkers Associated with Hypocretin-1 Deficiency

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Introduction: Narcolepsy, a rare chronic neurological disorder, is characterized by excessive daytime sleepiness (EDS) and disrupted nocturnal sleep patterns, substantially compromising patients' quality of life. While EDS and cataplexy are hallmark features, nocturnal manifestations remain undercharacterized. This study investigates distinctive sleep phenotypes in narcolepsy, particularly nocturnal frequent awakenings (at least ≥ 5 times) and REM sleep-related dream enactment behaviors (RBD-like symptoms), aiming to establish clinically relevant biomarkers for early diagnosis and mechanistic exploration.

Materials and methods: In this retrospective cross-sectional study, we analyzed 126 patients with EDS from Xuanwu Hospital from 2023 to 2025, stratified into three groups: type 1 narcolepsy (NT1, $n=78$), type 2 narcolepsy (NT2, $n=21$), and clinical controls (CC, $n=27$; suspected central hypersomnia with normal cerebrospinal fluid hypocretin-1 [hcrt-1] levels and negative multiple sleep latency test [MSLT] results). Data collection included standardized questionnaires assessing 35 sleep symptoms and polysomnography (PSG) metrics. Comparative analyses employed χ^2 tests, ANOVA, and ROC curve modeling to identify narcolepsy-specific signatures.

Results: Narcolepsy patients exhibited near-universal EDS (97.4%), with high rates of cataplexy (NT1: 85.7%), hypnagogic hallucinations (38.4%), and sleep paralysis (42.3%). Notably, nocturnal disturbances significantly distinguished narcolepsy from controls: frequent awakenings (89.7% vs. 59.2%; $\chi^2=9.437$, $P=0.002$) and dream enactment behaviors (50.0% vs. 25.9%; $\chi^2=4.022$, $P=0.045$). PSG revealed narcolepsy-specific pathophysiology, including elevated periodic limb movement indices (13.5 ± 28.1 vs. 4.8 ± 19.9 /h; $P=0.002$) and arousal indices (24.6 ± 11.4 vs. 17.7 ± 9.0 /night; $P=0.014$). In NT1, arousal indices inversely correlated with CSF hcrt-1 levels ($r=-0.257$, $P=0.016$). ROC analysis identified three discriminators: cataplexy (AUC=0.798, sensitivity 88.9%, specificity 70.7%), frequent awakenings (AUC=0.633, sensitivity 85.9%, specificity 40.7%), and dream enactment (AUC=0.608, sensitivity 47.5%, specificity 74.1%).

Conclusions: Nocturnal fragmentation (frequent awakenings) and REM-related motor dysregulation (dream enactment) emerge as clinically significant features of narcolepsy, serving as accessible diagnostic red flags. These phenotypes facilitate early differentiation from other sleep disorders, potentially minimizing diagnostic delays. The inverse relationship between hcrt-1 deficiency and nocturnal hyperarousal in NT1 suggests hypocretinergic modulation of sleep stability, providing novel

mechanistic insights. These findings underscore the importance of comprehensive nocturnal evaluation in narcolepsy workups and lay groundwork for targeted biomarker development.

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Once-Nightly Sodium Oxybate Improves Narcolepsy Symptoms in People With Narcolepsy: Interim Results From the Real-World REFRESH Study

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Introduction: Once-nightly sodium oxybate (ON-SXB; LUMRYZ™) is approved to treat excessive daytime sleepiness (EDS) or cataplexy in patients 7 years of age and older with narcolepsy. Interim results from REFRESH (NCT06792708), a multicenter, observational, real-world study assessing clinical effectiveness, patient satisfaction, and safety of ON-SXB for treatment of narcolepsy, are reported.

Materials and methods: REFRESH enrolled adults aged ≥18 years with narcolepsy type 1 (NT1) or 2 (NT2) who switched from current twice-nightly oxybates (TN-OXB; switch participants), previously used TN-OXB, or were oxybate-naïve. Prior/current treatment with ON-SXB was exclusionary. ON-SXB dosing followed product labeling (eg, titration in 1.5-g increments weekly or more gradual, based on efficacy and tolerability, up to 9 g). Participants completed the Epworth Sleepiness Scale (ESS) weekly (weeks 1-6) and then every other week (weeks 8-16). The Narcolepsy Severity Scale (NSS) and Sheehan Disability Scale (SDS) were completed over 4 monthly clinic visits. Patient Global Impression of Change (PGI-C) and Clinical Global Impression of Change (CGI-C) surveys were completed at the end-of-study visit. Safety data are reported as adverse drug reactions (ADRs; ie, adverse events related to study drug).

Results: As of April 4, 2025, 86 participants were screened and 67 initiated ON-SXB treatment (NT1, n=24 [35.8%]; NT2, n=43 [64.2%]; mean [SD] age, 38.0 [13.4] years); month 4 data were available for 20 participants. Twenty-five (37.3%) participants were currently taking TN-OXB, 9 (13.4%) had prior TN-OXB experience, and 33 (49.3%) were oxybate-naïve. Respective mean (SD) ESS scores for switch and non-switch participants were 10.4 (5.4) and 14.5 (4.5) at baseline and 7.1 (4.6) and 8.8 (4.4) at week 16; mean (SD) change from baseline (CFB) was -3.2 (3.4) and -5.6 (5.7). Respective mean (SD) NSS total scores for switch and non-switch participants were 16.0 (8.1) and 23.4 (9.5) at baseline and 11.4 (11.1) and 14.1 (8.6) at month 4; mean (SD) CFB was -5.0 (5.3) and -7.3 (5.6). Respective mean (SD) SDS scores for work/school, social life, and family life/home domains for all participants were 5.3 (2.9), 5.8 (2.7), and 5.9 (2.8) at baseline and 3.1 (2.5), 3.5 (2.8), and 3.7 (2.9) at month 4 (mean [SD] CFB: -1.9 [2.0], -0.8 [2.1], and -1.8 [2.6]). On the PGI-C (n=26) and CGI-C (n=24), 76.9% and 79.2% of participants, respectively, were “much” or “very much” improved. ADRs were reported by 22/67 (32.8%) participants; common ADRs (≥10% of participants) were nausea (28.4%), vomiting (14.9%), dizziness (11.9%), and headache (10.4%). Most (86.1%) events were mild or moderate; severe events included nausea (n=4), vomiting (n=3), dizziness (n=2), and enuresis (n=1). ON-SXB treatment was discontinued by 3/67 (4.5%) participants owing to tolerance concerns.

Conclusions: After switching from current TN-OXB use to ON-SXB, participants experienced clinically meaningful improvements in ESS scores to within the normal range; narcolepsy disease severity on the NSS improved from moderate at baseline to mild by end of study. Similar results were observed for participants who had prior TN-OXB use or were oxybate-naïve. ON-SXB was well tolerated; ADRs were consistent with known oxybate safety profiles.

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Optogenetic activation of the histaminergic system in the amygdala of narcoleptic mice reduces the occurrence of cataplexy

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Introduction: Cataplexy, the pathognomonic symptom of narcolepsy type 1 (NT1), is characterized by a loss of muscle tone during wakefulness and triggered by a strong positive emotion. A large body of evidence have demonstrated that activation of GABAergic neurons of the amygdala, a structure of the limbic system that processes emotions, plays a key role in triggering cataplexy mouse models of NT1 (Sardar et al, 2023). Of interest, Pitolisant®, used as one treatment option for NT1, greatly reduces cataplexy (Szakacs et al., 2017; Davis et al, 2021), but mechanisms involved are poorly understood. Through its antagonism/inverse agonism on H3R autoreceptors, Pitolisant® enhances the release of histamine (HIS) into the extracellular space (Ligneau et al., 2007). We thus hypothesized that Pitolisant® might suppress cataplexy by acting on the limbic system, particularly the amygdala. To test this hypothesis, we first tested whether Pitolisant® suppressed cataplexy in NT1 mice; second, we encovered which portion of the amygdala was activated during cataplexy by using the neuronal marker of activation c-fos, and finally, we optogenetically stimulated HIS axonal fibers locally in the amygdala and investigated the effect on cataplexy in a newly developed mouse model of narcolepsy, the Historex mice (a cross breeding of orexin-deficient mice with mice expressing the enzyme CRE-recombinase exclusively in HIS neurons).

Materials and methods: (1) Pitolisant® was dose-dependently administered i.p. in orexin-deficient mice (orex-KO) mice;

(2) Four orex-KO and 4 wild-type mice were given chocolate at 7pm and sacrificed 6hrs later. Brains were collected and processed with c-Fos immunohistochemistry. Number of c-fos neurons were counted in all subdivision of the amygdala. (3) Historex mice were stereotactic bilaterally injected with AAV-EF1-DIO-ChR2-EYFP (n=7) or AAV-EF1-DIO-EYFP control (n=4) viruses. All mice were implanted for polysomnography (EEG/EMG). HIS axonal fibers were optoactivated locally in the amygdala (10Hz, 5mW/mm², for 6h from light-off, n=11). Experiments were performed in triplicates.

Results: Pitolisant successfully suppressed cataplexy in orex-KO mice. We also found and increased c-Fos activated neurons throughout the rostrocaudal extent of the amygdala in orex-KO mice compared to wild-type mice. We found that 24-30% penetrance of the cre-transgene in HIS neurons only. Nevertheless, chronic photoactivation of histaminergic fibers overlying the amygdala induced a significant 20% and 27% reduction in the total amount and number of episodes of cataplexy, respectively. Optogenetic photoactivation induced no change in Historex control group, which does not express the ChR2 photoreceptor. Finally, chronic photoactivation of histaminergic fibers had no effect on the total amount or fragmentation of vigilance states.

Conclusions: Our findings indicate that optoactivation of HIS in the amygdala reduces the amount and number of cataplexy without altering vigilance states. Interestingly, recent data show that optoactivation of HIS axons in the amygdala of healthy mice significantly suppresses glutamatergic transmission in the central amygdala via H3 receptors (Zhang et al, 2024). Altogether, these data suggest that Pitolisant® may suppress cataplexy by dampening the amygdala response to positive emotions. We provide here the first mechanistic insights into the potential mode of action of Pitolisant® in cataplexy.

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Oveporexton (TAK-861) Improves Wakefulness in People with NT1: Assessment of At-home Napping and In-clinic Microsleeps

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Introduction: Excessive daytime sleepiness (EDS) in narcolepsy profoundly impacts daily life. In clinical trials, EDS is commonly assessed using the Maintenance of Wakefulness Test (MWT), which measures

the ability to stay awake in soporific conditions. However, sleep onset latency (SOL), the primary endpoint in MWT studies, does not capture the quality of wakefulness prior to falling asleep, nor provide information on EDS in an uncontrolled real-world environment. Here, we explore two EDS measures that are complementary to MWT SOL. We use wrist-worn accelerometry to assess at-home napping and characterize EDS during MWT by measuring microsleeps (3-15 sec periods of sleep prior to sleep onset). In a phase 2 randomized, placebo-controlled trial (NCT05687903), naps and microsleeps are evaluated as biomarkers for EDS following treatment with oreporexton (TAK-861), an oral orexin receptor 2-selective agonist, in narcolepsy type 1 (NT1).

Materials and methods: Participants with NT1 were randomized to receive oreporexton (first dose at 8AM; 0.5mg twice 3 hours apart; 2mg twice 3 hours apart; 2mg then 5mg 3 hours later; or 7mg once daily) or placebo. Wrist-worn accelerometry data were collected continuously during baseline and treatment periods, and naps were estimated using a previously described algorithm. Derived nap endpoints included the proportion of nap-free days, total minutes of daytime sleep on days with ≥ 1 nap, and nap count. MWTs were in-clinic 40 minute wake trials (10AM/12PM/2PM/4PM) conducted at baseline and after 28 and 56 days of treatment. Microsleeps were scored manually following AASM standards, and annotated events were used to compute microsleep rate (number of microsleep divided by SOL) and time-to-first microsleep. Nap endpoints were analyzed with generalized linear mixed-effects models. Microsleep rate was analyzed via a zero-inflated negative binomial mixed-effects model, with SOL as an offset. Time-to-first microsleep was assessed using a mixed effects Cox proportional hazard model, which included treatment, visit, and time, and their interactions as fixed effects, and random intercept per subject.

Results: Data were collected for 112 participants with NT1 (placebo: n=22, 0.5mg/0.5mg: n=23, 2mg/2mg: n=21, 2mg/5mg: n=23, 7mg: n=23). All oreporexton-treated groups experienced increases in nap-free days over 4 weeks and slept less time per day (all $p < 0.001$) after placebo-correction and baseline adjustment, except the 0.5mg/0.5mg group for the latter endpoint. Microsleep rates decreased by Weeks 4 and 8 across oreporexton-treated groups versus baseline (from ~6 microsleeps per 10 minutes to < 2 per 10 minutes, all $p < 0.001$). Placebo-corrected change from baseline revealed reductions in microsleep rates across oreporexton-treated groups at Weeks 4 and 8 (all $p < 0.05$). Time-to-first microsleep increased at Weeks 4 and 8 across oreporexton-treated groups versus baseline (all $p < 0.001$). Hazard ratios for all treatment groups versus placebo at Weeks 4 and 8 were < 0.2 (all $p < 0.002$). No significant effects were observed in the placebo group.

Conclusions: Oreporexton reduced multiple aspects of EDS, including at-home napping and in-clinic microsleeps. These reductions observed in both an unconstrained, natural home environment and in controlled clinical settings demonstrate oreporexton's potential as an effective treatment for EDS in participants with NT1.

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Oxybate Awareness, Usage, and Experience Among People With Narcolepsy: A MyNarcolepsyTeam Survey Analysis

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness (EDS) and can occur with or without cataplexy. Oxybates are FDA-approved to treat EDS or cataplexy in people with narcolepsy. Immediate-release twice-nightly sodium oxybate (TN-SXB) and calcium, magnesium, potassium, and sodium oxybates (mixed-salt oxybates) are administered at bedtime and 2.5-4 hours later, whereas extended-release once-nightly SXB (ON-SXB; FT218) is administered once at bedtime. This study assessed oxybate awareness, usage, and experience among people with narcolepsy (PWN).

Materials and methods: The MyNarcolepsyTeam survey was an anonymous, voluntary survey conducted from April 10 to May 9, 2024. Eligible participants were age ≥ 21 years, United States residents, and reported a narcolepsy diagnosis. The 36-item survey assessed respondents' demographics, symptom management, and relationships with healthcare providers (HCPs).

Results: Of 88 respondents, 77% were female, 75% were ≥ 50 years of age, and 39% and 50% had narcolepsy type (NT) 1 and NT2, respectively. Respondent brand awareness of oxybates was high (70%), with highest awareness for TN-SXB (55%), followed by mixed-salt oxybates (43%) and ON-SXB (23%). Of 82 respondents seeing an HCP, only 39% had discussed oxybates with their HCP. Current oxybate use was reported by 13% of respondents (15% of NT1 respondents; 7% of NT2 respondents), 82% of whom experienced symptom improvement within 2 weeks of starting oxybate treatment. Benefits of oxybate use included getting a better night's sleep (64%) and waking up refreshed (64%). Of 77 respondents not currently taking oxybates, 36% reported they did not know enough about oxybates. Of respondents who had previously taken an oxybate, 28% discontinued within 1 month of initiating treatment. The most commonly reported reason for discontinuing oxybate treatment was side effects (40% [age ≥ 60 years, 47%; age < 60 years, 27%]).

Conclusions: These results demonstrate that while respondents were moderately aware of oxybates, over one-third reported lacking enough information to consider starting oxybate treatment. Despite TN-SXB approval by the FDA in 2002, only 1:8 respondents were currently receiving oxybates. As narcolepsy medication regimens can be daunting, clinicians have the opportunity to counsel PWN about oxybate treatment options, including the potential for early symptom improvement and proactive side effect management to reduce discontinuation.

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Pan-Cancer Prognostic Modeling Using Narcolepsy-Associated Genes: A Transcriptomic Framework Bridging Sleep Regulation and Tumor Biology

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Introduction: Narcolepsy is a chronic neurological sleep disorder involving dysregulation of REM sleep and immune function. Emerging evidence indicates that genes implicated in narcolepsy may also contribute to oncogenic processes such as epithelial mesenchymal transition (EMT), immune escape, and cell proliferation. However, the potential application of narcolepsy-associated genes as prognostic markers in cancer has not been systematically investigated.

Materials and methods: A curated set of narcolepsy-related genes was identified through literature and neuroimmunology databases. Using transcriptomic profiles from The Cancer Genome Atlas (TCGA), we applied LASSO Cox regression to construct a 12-gene prognostic signature. The derived narcolepsy risk score stratified patients into high- and low-risk groups, and its predictive performance for overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) was assessed across 33 cancer types. Validation was performed using independent cohorts from CGGA and GEO.

Results: The narcolepsy-based prognostic model exhibited strong predictive value in multiple cancers, especially lower-grade glioma, clear cell renal carcinoma, and colorectal carcinoma. High-risk groups showed upregulation of EMT-related genes, mitotic activity, and extracellular matrix remodeling, along with reduced immune infiltration. Functional enrichment analysis confirmed that risk-associated genes were involved in immune evasion and tumor-promoting inflammation. Immunohistochemistry (IHC) on tumor tissues further supported the differential expression of selected signature genes.

Conclusions: We present a novel pan-cancer prognostic signature derived from narcolepsy-associated neuroimmune genes. This model reveals a potential mechanistic link between sleep regulation pathways and tumor progression, and offers a clinically relevant tool for risk stratification. The findings support further exploration of sleep-immune-tumor crosstalk as a novel axis in oncology.

Patient Experience of Oveporexton (TAK-861) for Narcolepsy Type 1 in a Phase 2 Clinical Trial

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Introduction: Oveporexton (TAK-861) is a novel oral orexin receptor 2 agonist developed for the treatment of narcolepsy type 1 (NT1). The safety and efficacy of oveporexton was investigated in an 8-week randomized, double-blind, placebo-controlled, dose-ranging Phase 2 trial (NCT05687903) in patients with NT1. While clinical trials provide information on the efficacy and safety of new treatments, qualitative feedback from patients on their treatment experience, in addition to standard patient questionnaires, offers a more comprehensive understanding of a treatment's impact on patients' lives. This cross-sectional, qualitative analysis explored patient perceptions of treatment and overall experiences of participation in the NT1 Phase 2 oveporexton trial.

Materials and methods: Participants aged 18-70 years, with an Epworth Sleepiness Scale (ESS) total score >12, and ≥4 partial/complete episodes of cataplexy/week were randomized to twice daily oral oveporexton or placebo (0.5mg/0.5mg, 2mg/2mg, 2mg/5mg, 7mg/placebo, or placebo/placebo). Participants who completed the final Week 8 visit were given the option to complete an exit interview. Semi-structured interviews were conducted by a third party vendor within 3 weeks of the final visit. Interviewees provided separate informed consent prior to interviews. Questions focused on participants' experience of the trial and treatment impact on narcolepsy symptoms and daily life. Transcripts were analyzed using content analysis (ATLAS.ti) to identify recurring themes and concepts. Responses were summarized using descriptive statistics.

Results: Twenty-five participants (oveporexton n=21, placebo n=4; 52% female; mean age 30.4 [SD 11.2] years, mean 10.2 [8.7] years since diagnosis) completed an exit interview. Eleven (44%) reported the reason for joining the trial was to have better symptom control, and 9 (36%) wanted to try a new treatment. Twenty-three interviewees (92%) indicated they were dissatisfied with their previous treatment(s); 15 (65%) reported low effectiveness and 7 (30%) reported side effects as their rationale. Twenty-one indicated that the trial team satisfactorily managed their expectations regarding dosing, administration, side effects, and outcomes. Oveporexton-treated participants reported noticeable improvements in the symptoms they rated as being most important to improve: excessive daytime sleepiness (18/18 [100%]), cataplexy (19/19 [100%]), cognitive symptoms (9/9 [100%]), and disturbed nighttime sleep (7/9 [78%]), versus 1/3 (33%), 0/1 (0%), 1/4 (25%) and 0/3 (0%), respectively, of participants on placebo. Improvements in these same top symptoms were meaningful for 67-100% of oveporexton-treated participants versus only 1 (25%) participant on placebo. Most (83-100%) oveporexton-treated participants noted improvements in work impacts, social and leisure activities, independence/self-care, physical activities, daily activities, activities avoided due to cataplexy, family time, and mood/emotions versus no reported improvement in impacts with placebo. Eighteen of 19 (95%) of responding oveporexton-treated participants indicated they would recommend it to someone else with narcolepsy.

Conclusions: Participants with NT1 reported a favorable impact on their symptoms and quality of life with oveporexton treatment, with good overall treatment perception. Qualitative patient perception findings can serve to support efficacy and treatment satisfaction data of newer treatments for regulatory assessments and subsequently for treatment decision-making.

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Phenotypic clusters of narcolepsy type 1: Insights from age of onset, weight gain, sleep patterns, and impulsivity

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Introduction: This study aimed to discern the underlying relationships between clinical manifestations and neuroimaging phenotypes among patients with narcolepsy type 1 (NT1).

Materials and methods: Demographic characteristics, clinical manifestations, polysomnography parameters, and comorbidities were collected in 158 NT1 patients. Using R software, we applied k-means cluster analysis to create homogeneous NT1 patient clusters. Subsequently, we identified

clinical and neuroimaging features within each cluster and examined associations between neuroimaging and clinical phenotypes across different subgroups.

Results: Four clusters were found: patients with the youngest onset-age exhibit more severe objective sleepiness. However, it is easily ignored or not reported due to mild subjective sleepiness, which may be responsible for the long delay between disease onset and diagnosis in this group of patients. Patients with teenage onset and greater weight gain showed shorter sleep latency, more obvious disturbed nocturnal sleep (DNS), the highest proportion of hallucination and sleep paralysis, as well as the highest motor impulsivity score, but minimum volumes in the left para-hippocampal gyrus (PHG) and right precuneus. Patients with teenage onset and less weight gain showed the longest sleep latency and maximum volumes in the right frontal region and left posterior cingulate cortex (PCC). Adult-onset patients reported the highest Epworth Sleepiness Scale (ESS) scores, more obvious impulsivity behavior and more sleep apnea comorbidity. Volumes in left PHG and left PCC were associated with mean sleep latency, respectively.

Conclusions: Narcolepsy patients with teenage onset and greater weight gain exhibit severe sleepiness, severe DNS and high motor impulsivity. Results from this research will provide a new reference for the pathogenesis, diagnosis, and management of narcolepsy.

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Precision medicine approach in Brazilian patients with primary hypersomnias using hypocretin and high-resolution HLA sequencing : insights from an admixture population

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Introduction: The major genetic risk factor for narcolepsy is HLA-DQB1*06:02, which is closely associated with low cerebrospinal fluid (CSF) hypocretin, a characteristic of narcolepsy type 1 (NT1), although it's also associated with narcolepsy type 2 (NT2) to a lesser degree. Genetic factors underlying idiopathic hypersomnia (IH) remain unclear. Brazil boasts a large and diverse population, with a genetic background often underrepresented in population studies with a low prevalence of HLA-DQB1*06:02 (around 60-70%) among NT1 patients compared to other countries (nearly 90-95% in Chinese, Korean, most of Europe, and North Americans). However, these low prevalence of HLA-DQB1*06:02 came from studies that were conducted without hypocretin measurement. Recent data shows that when CSF hypocretin levels are measured and documented to be low the association with NT1 of HLA-DQB1*06:02 rises to 98-100%.

Materials and methods: Patients suspected of having primary hypersomnias underwent a comprehensive investigation at the Hypersomnia Research Center in Pedro Ernesto University Hospital, which included polysomnography, multiple sleep latency tests, genetic testing, and CSF hypocretin measurement via radioimmunoassay at the Stanford Narcolepsy Centre in the USA. This study included 68 patients diagnosed with narcolepsy or IH according to ICSD-3 criteria from November 2021 to January de 2024: 24 NT1, 27 NT2, and 17 IH. Genetic data from 340 healthy individuals of the Brazilian Bone Marrow Donor Registry (REDOME) was used for comparison, considered the third largest biobank in the world. High-resolution HLA sequencing was performed using the Next Generation Sequencing (NGS) Holotype HLA kit from Omixon, Inc., Budapest, Hungary, and allele frequencies were compared between the case and control groups, matched by sex, ethnicity, and geographic location, using a 1:5 case-to-control ratio. The risk of susceptibility or protection was determined by comparing the diagnostic groups and their controls by calculating the odds ratio (OR), using the chi-square test or Fisher's exact test and corrected by the Bonferroni factor, using Epi Info©. A 95% confidence interval and p-value<0.05 were determined.

Results: All NT1 patients (100%) carried the HLA-DQB1*06:02 allele, significantly higher than controls (25%), patients with NT2 (18.52%), or IH (23.53%) (p < 0.001). The allele DRB1*15:03, linked to African

heritage, emerged as the second most prevalent allele among NT1, forming a haplotype DRB1*15:03~DQB1*06:02 with an odds ratio of 39.0 (95% CI: 9.6–157.8, $p < 0.001$) in comparison with controls; however NT1 subgroup didn't present black people as the majority. No risk allele was observed comparing NT2 and IH with their controls ($p > 0.05$). Risk alleles already described in the literature for narcolepsy were found among 67/68 patients of all types of hypersomnias (NT1, NT2, and IH).

Conclusions: HLA-DQB1*06:02 was the main risk factor for NT1, but not for NT2 and IH, with a high frequency (100%), similar to what is seen in other ethnicities. The second risk allele for NT1 was DRB1*15:03 instead of DRB1*15:01, which suggests a higher influence of African heritage in the population studied.

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Prevalence and Incidence of Comorbidities in Individuals With Narcolepsy or Idiopathic Hypersomnia: A Systematic Literature Review

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Introduction: Narcolepsy and idiopathic hypersomnia (IH) are hypersomnolence disorders primarily characterised by excessive daytime sleepiness. Previous studies have observed an increased prevalence and risk of developing cardiovascular (CV) and cardiometabolic (CM) diseases among individuals with narcolepsy. However, prevalence and incidence estimates vary across studies due to differing populations, study designs, time periods, and outcome definitions. This systematic literature review (SLR) aimed to identify studies evaluating the prevalence and incidence of comorbidities in individuals with narcolepsy or IH.

Materials and methods: This gold-standard SLR was conducted following PRISMA guidelines to identify relevant studies. Electronic database searches, supplemented by review of conference proceedings and trial registries, were conducted through 10 December 2024 based on prespecified *Population, Intervention, Comparison, Outcomes, and Study Design* criteria. Screening and data extraction were conducted by two independent reviewers; discrepancies were resolved by a third reviewer. Quality assessment was conducted using relevant *Critical Appraisal Skills Programme* checklist domains.

Results: Of 3130 records screened, 127 publications were included in the SLR; most were cohort or cross-sectional studies ($n=106$; 83.5%) and were primarily among people with narcolepsy ($n=118$; 93.0%). For narcolepsy, data were available for narcolepsy overall ($n=45$), narcolepsy subtypes 1 and 2 (NT1; NT2; $n=34$), NT1 only ($n=36$), and NT2 only ($n=2$). Fifty-five (43.3%) narcolepsy publications also reported data for a relevant comparative population. Prevalence data were reported in almost all narcolepsy publications ($n=114$; 98.3%) for 310 different comorbidities as frequency measures (percentages) or measures of association (odds ratios [OR]). Prevalence estimates of CV/CM conditions were most commonly reported as frequencies, including hypertension ($n=26$), cardiovascular disease (CVD; $n=22$), diabetes ($n=29$), dyslipidaemia ($n=18$), obesity ($n=44$), and overweight ($n=14$). Within the 27 publications reporting association data, the prevalence of comorbidities was generally higher in people with narcolepsy; higher prevalence of hypertension (7/8 studies), CVD (7/8), diabetes (6/10), obesity (7/7), and dyslipidaemia (5/6) was reported in individuals with narcolepsy compared to those without. Five studies reported incidence of comorbidities as measures of frequency, and 8 reported incidence as a measure of association (eg, OR) using a comparison group. The data for IH were more limited. Prevalence of comorbidities in people with IH was reported in 23 publications for 90 different comorbidities. The most commonly reported CV/CM comorbidity frequency estimates were for hypertension ($n=4$ studies), diabetes ($n=4$), and CVD ($n=3$). Measures of association were reported in 8 publications; 7 studies compared individuals with and without IH and found a higher prevalence of hypertension ($n=3/3$), CVD ($n=4/4$), and stroke ($n=3/3$) in the IH cohort; 1 study found a lower prevalence of type 1 diabetes ($n=1/1$).

Conclusions: This SLR found a growing literature base evaluating the prevalence and incidence of CV/CM comorbidities in individuals with narcolepsy and IH, though evidence is more scarce for IH.

Most studies found higher prevalence of CV (eg, hypertension, CVD) and CM (eg, obesity) comorbidities among individuals with narcolepsy or IH versus those without, with varying prevalence estimates reported. Incidence data were limited in narcolepsy, and even more limited in IH. Meta-analyses will be conducted to empirically synthesize findings from this SLR.

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Psychiatric and Sleep Disturbances in Narcolepsy Patients and Their Families: An Epidemiological Study

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Introduction: Narcolepsy has a known genetic component, with first-degree relatives of patients having a 20-40 times increased risk of developing the disorder. This study aimed to investigate the prevalence of psychiatric problems and sleep disturbances in families of narcolepsy patients, considering the potential genetic influence and their psychiatric burden.

Materials and methods: We conducted a cross-sectional study by enrolling narcolepsy patients aged 12 and older (including children) who have been diagnosed with narcolepsy at St. Vincent's Hospital Sleep Clinic and other medical institutions and family members. As of now, 132 narcolepsy patients and 113 family members (1st degree) are involved. Participants completed validated questionnaires by internet based survey including the Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory II (BDI-II), Epworth Sleepiness Scale (ESS), and Adult ADHD Self-Report Scale (ASRS) to assess sleep quality, depression, daytime sleepiness, quality of life, and ADHD symptoms, respectively.

Results: Narcolepsy patients showed significantly poorer sleep quality (PSQI mean $\pm$ SD : 12.88 $\pm$ 2.82) compared to their family members (PSQI mean $\pm$ SD: 10.17 $\pm$ 3.05), both groups with higher PSQI scores compared to the general population norm, indicating poorer sleep quality. Patients exhibited higher excessive daytime sleepiness (ESS mean $\pm$ SD : 16.93 $\pm$ 4.26) compared to family members (ESS mean $\pm$ SD : 6.03 $\pm$ 5.13). Patients also demonstrated more severe depressive symptoms (BDI-II mean $\pm$ SD: 43.2 $\pm$ 14.84) than their families (BDI-II mean $\pm$ SD: 26.98 $\pm$ 9.16). Significantly, 54 participants (47.7%) in family group showed moderate depression, while 40 participants (35.3%) showed severe depression. Moreover, ADHD symptoms were more prevalent in patients (ASRS mean $\pm$ SD: 11.5 $\pm$ 5.87) compared to family members (ASRS mean $\pm$ SD: 4.27 $\pm$ 4.29).

Conclusions: This study reveals a substantial burden of psychiatric problems and sleep disturbances in both narcolepsy patients and their family members, with patients showing significantly more severe symptoms across all measures. The findings highlight the need for comprehensive care approaches that address not only the patients' needs but also the mental health and sleep quality of their family members. Further genetic studies are warranted to elucidate the specific mechanisms underlying these familial patterns and to develop targeted interventions for this population

Real-World Experience of Once-Nightly Sodium Oxybate Treatment in People With Narcolepsy: Interim Results From REFRESH

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Introduction: Oxybate treatment improves quality of life (QOL) for people with narcolepsy; however, the middle-of-the-night dosing required by twice-nightly oxybate (TN-OXB) can be burdensome. Once-

nightly sodium oxybate (ON-SXB; LUMRYZ™) is approved to treat excessive daytime sleepiness (EDS) or cataplexy in patients 7 years of age and older with narcolepsy. Interim survey data from REFRESH (NCT06792708), a prospective, real-world study assessing clinical effectiveness, patient satisfaction, and safety of ON-SXB for narcolepsy treatment, are reported.

Materials and methods: REFRESH enrolled adults aged ≥18 years with narcolepsy type 1 or 2 who switched from current TN-OXB use (switch participants), had prior TN-OXB use, or were oxybate-naïve. Exclusion criteria included prior/current treatment with ON-SXB and any condition deemed exclusionary by the study clinician or contraindicated by product labeling. ON-SXB dosing followed product labeling (eg, titration in 1.5-g increments weekly or more gradual, based on efficacy and tolerability, up to 9 g). At baseline and end of study (EOS), all participants completed a 7-question survey about their QOL and narcolepsy symptoms (eg, fatigue). Switch participants completed a baseline survey about their experience with TN-OXB treatment (switch survey). All participants completed an EOS questionnaire about their experience with ON-SXB treatment.

Results: As of April 4, 2025, 67 participants initiated ON-SXB treatment; 25 (37.3%) were switch participants, 9 (13.4%) had prior TN-OXB use, and 33 (49.3%) were oxybate-naïve. Mean (SD) QOL on a scale of 0=“worst possible” to 10=“best possible” was 5.6 (1.42) at baseline (n=67) and 7.1 (1.41) at EOS (n=26). Mean (SD) fatigue on a scale of 0=“never fatigued” to 10=“extremely fatigued” was 7.3 (1.81) at baseline (n=67) and 4.6 (2.06) at EOS (n=26). All 25 switch participants completed the switch survey; 76% split 2 TN-OXB doses equally and 24% took a higher first dose. The second TN-OXB dose was moderately-to-extremely burdensome for 80% of switch participants; 80% missed the second dose during the 3 months prior to study entry, of whom 55% missed the second dose at least once a week. Missed doses resulted in worsening fatigue and sleepiness for 85% and 80% of participants, respectively. EOS questionnaires were completed by 26 participants (switch=11); participants reported their narcolepsy was “somewhat better” or “much better” with ON-SXB (switch=73%, overall=89%). With ON-SXB treatment, participants reported benefits: being better able to not fall asleep during the day (switch=55%; overall=69%), being better able to sleep through the night (switch=64%; overall=81%), getting more done at work/school (switch=46%; overall=58%), being better able to socialize (switch=46%; overall=62%), and experiencing less drowsy driving (switch=27%; overall=42%). In total, 91% of switch participants preferred ON-SXB, 9% had no oxybate preference, and no participant preferred TN-OXB; 73% reported better adherence to a once-nightly dosing schedule.

Conclusions: Participants in REFRESH experienced meaningful symptom improvement with ON-SXB, including improved QOL, reduced drowsy driving, and improved nocturnal sleep. Prior to study entry, switch participants found twice-nightly dosing of TN-OXB burdensome and often missed doses; >90% of switch participants preferred ON-SXB to TN-OXB.

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Real-World Risk of Sodium-Associated Negative Clinical Outcomes Among Individuals With Narcolepsy in the United States

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Introduction: Narcolepsy is associated with an elevated prevalence of comorbid cardiovascular, cardiometabolic, and renal diseases, with risk potentially exacerbated by excess sodium intake. This study aimed to compare the risk of sodium-associated negative clinical outcomes (NCOs) between individuals with and without narcolepsy and to quantify the risk of NCOs among individuals with narcolepsy, comparing those with and without prior risk factors.

Materials and methods: Komodo Research Data (01/01/2016–31/01/2024) were used to identify US individuals diagnosed with narcolepsy (*index*: first observed narcolepsy diagnosis) and individuals without narcolepsy (*index*: randomly selected date within ≥48 months of continuous healthcare plan eligibility), using a 1:5 ratio of individuals with and without narcolepsy. All individuals were required to have ≥12 months of continuous enrolment in both the pre- and post-index periods. Entropy balancing was used to balance demographic characteristics (index year, age, sex, race/ethnicity, US region of

residence, and health plan type at index) between cohorts. The narcolepsy cohort was stratified into two subgroups: higher-risk (≥ 1 sodium-associated risk factor during the 12-month pre-index period) and lower-risk (no risk factors in the pre-index period). Based on pragmatic literature review and clinical expert discussion, sodium-associated NCOs were defined as cardiovascular (hypertension, stroke, transient ischaemic attack, heart failure, major adverse cardiovascular event [MACE; ie, heart failure, stroke, myocardial infarction, unstable angina, or coronary revascularisation procedures]), cardiometabolic (oedema), and renal (kidney failure, chronic kidney disease, proteinuria) conditions. Development of incident NCOs or progression of NCOs were identified during the post-index period. Risk was compared between the narcolepsy and non-narcolepsy cohorts and between the higher-risk and lower-risk narcolepsy subgroups using weighted and unweighted Cox proportional hazards models. **Results:** Among 29,317 and 146,585 individuals in the narcolepsy and non-narcolepsy cohorts, respectively, demographics were similar after balancing. Mean (standard deviation) age was 41.4 (17.0) and 41.5 (17.3) years, respectively, and 62.1% were female in both cohorts. The narcolepsy cohort had a higher risk (hazard ratio [HR; 95% confidence interval (CI)]) of any NCO (1.79 [1.75–1.83]), hypertension (1.72 [1.67–1.76]), MACE (1.90 [1.76–2.05]), oedema (2.12 [2.00–2.25]), and renal NCOs (1.77 [1.67–1.87]), compared with the non-narcolepsy cohort. Within the narcolepsy cohort, 58.8% ($n=17,227$) of individuals were identified as higher-risk. Risk of any NCO (HR [95% CI]) was elevated among higher-risk versus lower-risk individuals (2.06 [1.97–2.15]). Higher-risk individuals had an increased risk (HR [95% CI]) of hypertension (1.59 [1.52–1.67]), MACE (10.08 [7.87–12.92]), oedema (7.66 [6.51–9.02]), and renal NCOs (6.82 [5.86–7.95]) compared with lower-risk individuals. **Conclusions:** In this real-world study, individuals with narcolepsy had an elevated risk of development or progression of cardiovascular, cardiometabolic, and renal NCOs relative to those without narcolepsy. More than half of individuals with narcolepsy had prior sodium-associated risk factors; these individuals had an increased risk of NCOs relative to those without pre-existing comorbidities. These results emphasise the need to reduce sodium intake and mitigate the risk of NCOs among individuals with narcolepsy. Lowering sodium intake may help to reduce the clinical burden of short- and longer-term sodium-associated NCOs in individuals with narcolepsy. **Acknowledgments:** Funded by Jazz Pharmaceuticals.

Rising Pressure to Understand the Risks of Hypertension in Children with Narcolepsy Type 1

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Introduction: Most children/adolescents with Narcolepsy Type 1 (NT1) are treated with stimulants or modafinil, yet the cardiovascular effects of these medications have not been investigated in this population. We compared vital signs in youth with NT1 before and after exposure to stimulants/modafinil to test the hypotheses that these medications increase rates of elevated blood pressure (BP) and hypertension (HTN) and that body mass index (BMI) influences these outcomes. We also explored whether there was a relationship between baseline HTN risk and features of nocturnal sleep, including percentage of rapid eye movement (REM) sleep and wake/N1(NREM1) index, which is an objective measure of disrupted nighttime sleep (DNS).

Materials and methods: In this retrospective study, we collected electronic medical data including vital signs and polysomnography/multiple sleep latency test (PSG/MSLT) results from 39 youth with NT1 aged 7-18 at three points over 20-month period: baseline (drug-naïve/weaned), after initiating treatment, and after treatment optimization. We performed stepwise regression to determine predictors of baseline elevated BP/HTN. We used McNemar's test and generalized estimating equations to assess the effects of stimulant/modafinil exposure on vital signs.

Results: The prevalence of elevated BP/HTN at baseline was 51% in our cohort and increased 21% from baseline to the final visit ($p = .03$). Systolic BP increased significantly with stimulant/modafinil exposure ($p < 0.05$), while diastolic BP and heart rate (HR) showed non-significant increases. BMI was associated with increased systolic BP and HR across the three time points but not at baseline. We did not find any relationship between sleep features and risk of elevated BP/HTN at baseline.

Conclusions: Youth with NT1 are at risk for elevated BP/HTN, particularly after stimulant/modafinil treatment. We recommend revising clinical guidelines to address this risk and advocate for controlled

studies to better understand the cardiovascular risks and implications of these treatments in pediatric NT1.

Risk of Developing Tolerance During Treatment for Excessive Daytime Sleepiness in Patients with Narcolepsy

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Introduction: Treating excessive daytime sleepiness (EDS) with psychostimulants can potentially lead to tolerance, resulting in a loss of efficacy and the need to continuously increase the medication dosage. However, data comparing the risk of tolerance between different psychostimulants and wake promoters are not currently available. We conducted a long-term observational study to compare the risk of tolerance among three first-line medications approved for treating excessive daytime sleepiness in patients with narcolepsy.

Materials and methods: The prospective observational study included drug-naïve patients with narcolepsy types I and II who received their first monotherapy with modafinil, pitolisant, or solriamfetol for EDS. The study had a long-term follow-up period of seven years. All cases of tolerance were documented, and the incidence of tolerance and changes in medication dosage were compared. The EDS was measured by Epworth Sleepiness Scale (ESS).

Results: Of the 351 study participants, 131 (37.3%) received modafinil, 112 (31.9%) received pitolisant, and 108 (30.8%) received solriamfetol. There were no significant differences in age, gender, or initial ESS scores between the treatment groups. During the study period, 35.9% of patients on modafinil, 14.8% on solriamfetol, and 2.7% on pitolisant developed tolerance ($p < 0.05$). The majority of patients on pitolisant or solriamfetol (94.8%) developed tolerance within the first two years of treatment. Among patients taking modafinil, two patterns of tolerance development were observed. 46.8% percent of tolerance cases occurred within the first two years of therapy, and 44.7% of cases were observed after five years. The following increases in the daily dose were observed among patients who developed tolerance: 184% for modafinil, 116% for solriamfetol, and 78% for pitolisant ($p < 0.05$). No cases of cross-tolerance were observed among patients who switched medications, including those who switched to modafinil, solriamfetol, pitolisant, sodium oxybate, or methylphenidate.

Conclusions: In this study, we found that modafinil was associated with the highest risk of tolerance development in patients treated for narcolepsy with cataplexy (EDS), whereas pitolisant was the most favorable in terms of the risk of tolerance. Additionally, two major patterns of modafinil tolerance development were observed: „early“ tolerance, which occurred within the first two years of treatment, and „late“ tolerance, which develops after five years of therapy. In contrast, solriamfetol and pitolisant mainly had cases of early tolerance. Late tolerance was not typical for these medications.

Risk of New-onset Cardiovascular and Cardiometabolic Conditions in Narcolepsy: An Analysis of the All of Us Research Program

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Introduction: Narcolepsy is a central disorder of hypersomnolence characterised by excessive daytime sleepiness and disrupted nighttime sleep. The prevalence of cardiovascular and cardiometabolic conditions is higher among individuals with versus without narcolepsy; however, literature on potential differences in new onset of cardiovascular or cardiometabolic conditions between people with and without narcolepsy is limited. This study aimed to evaluate the incidence of hypertension, obesity,

hyperlipidaemia, and coronary arteriosclerosis (CA) among US participants in the *All of Us* Research Program, comparing those with versus without narcolepsy.

Materials and methods: A retrospective, observational cohort study was conducted using electronic health record (EHR) and survey data from *All of Us*, a nationwide initiative aimed at comprehensively characterizing the health of the diverse US population. Participants with narcolepsy were selected using Systematized Nomenclature of Medicine (SNOMED) codes (1/1/2009–31/1/2022). Non-narcolepsy participants were matched 3:1 to those with narcolepsy at index (earliest narcolepsy diagnosis) date on age, sex, earliest EHR, time in EHR, and social determinants of health survey completion. Hypertension, hyperlipidaemia, obesity, and CA were defined using SNOMED codes, in addition to antihypertensive medication use for hypertension. For the total follow-up period, as well as 1-, 3-, and 5-year periods after index, crude incidence rates (IRs) per 100 person-years (PY) were calculated; adjusted hazard ratios (HRs) were estimated using Cox proportional hazards models.

Results: This study included 694 participants with narcolepsy (mean [standard deviation; SD] age: 48.0 [16.8] years; 71.5% female; mean [SD] follow-up: 5.2 [3.5] years) and 2072 without narcolepsy (mean [SD] age: 49.2 [16.4] years; 69.9% female; mean [SD] follow-up: 5.2 [3.5] years). Over the total follow-up, participants with versus without narcolepsy had higher IRs (95% confidence interval [CI]) per 100 PY of hypertension (6.74 [5.91, 7.57] vs 4.00 [3.16, 4.85]), hyperlipidaemia (5.93 [5.08, 6.77] vs 3.57 [2.72, 4.42]), obesity (5.02 [4.19, 5.85] vs 2.53 [1.69, 3.37]), and CA (1.92 [1.07, 2.77] vs 1.07 [0.21, 1.93]). Among participants with narcolepsy, the highest rate of hypertension was in the 1-year follow-up period (16.82 [14.86, 18.78]), followed by the 3-year (10.18 [9.05, 11.31]) and 5-year (7.05 [6.17, 7.92]) follow-up periods. Similar trends were observed for obesity, hyperlipidaemia, and CA. In adjusted models, participants with versus without narcolepsy had significantly higher risk of developing hypertension (HR [95% CI]: 2.02 [1.53, 2.67]), hyperlipidaemia (1.96 [1.52, 2.54]), obesity (2.42 [1.93, 3.05]), and CA (1.75 [1.27, 2.42]) over total follow-up. Those with versus without narcolepsy had a greater risk of developing hypertension at 1-year follow-up (3.84 [2.37, 6.22]); HR (95% CI) was 2.67 (1.89, 3.77) and 2.25 (1.66, 3.06) at the 3- and 5-year follow-up periods, respectively. Similar trends were observed for obesity, hyperlipidaemia, and CA.

Conclusions: Participants with narcolepsy had a higher risk of developing hypertension, hyperlipidaemia, obesity, and CA versus those without narcolepsy. Cardiovascular and cardiometabolic risk should be considered when managing narcolepsy.

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Safety and Tolerability of Once-Nightly Sodium Oxybate: A Post Hoc Analysis From the Long-Term RESTORE Study

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Introduction: In the phase 3 REST-ON clinical trial, extended-release, once-nightly sodium oxybate (ON-SXB) demonstrated a safety profile consistent with the known oxybate safety profile, with adverse drug reactions (ADRs) primarily related to tolerability. The long-term safety and tolerability of ON-SXB were investigated in the open-label/switch study RESTORE (NCT04451668).

Materials and methods: Participants in RESTORE were ≥16 years of age with narcolepsy type 1 or 2 who had completed the REST-ON trial (without starting another oxybate), were on immediate-release twice-nightly SXB (TN-SXB) for ≥1 month, or were oxybate naive. For participants who completed REST-ON but had not initiated TN-SXB or who were oxybate naive, ON-SXB was initiated at 4.5 g/night and increased weekly by 1.5 g/night as needed up to 9 g/night during a 1- to 2-month titration period. Participants then received ON-SXB until they could be transitioned to commercial therapy. This analysis included data from participants who completed REST-ON (without starting another oxybate) or who were oxybate naive and received ≥1 dose of ON-SXB (safety population). Safety data are reported

as treatment-emergent adverse events (TEAEs; ie, any AE that occurs during treatment) and ADRs (ie, TEAEs considered drug-related).

Results: Of the 50 participants (mean age, 33 years; female, 60%; white, 80%; mean [range] ON-SXB treatment, 408.1 [8–1098] days) who were from REST-ON (n=15) or were oxybate naïve (n=35), 76% (38/50) reported ≥ 1 TEAE; most were mild (n=18; 36%) or moderate (n=18; 36%) in severity. TEAEs occurring in $\geq 10\%$ of participants included nausea (26%), COVID-19 (12%), somnolence (12%), dizziness (10%), vomiting (10%), sinusitis (10%), and tremor (10%). One (2%) participant reported ≥ 1 serious AE considered related to ON-SXB treatment (anxiety, delusional thoughts) that led to ON-SXB discontinuation. ADRs were reported by 56% (28/50) of participants. ADRs occurring in $\geq 10\%$ of participants included nausea (24%), somnolence (12%), and dizziness (10%). Seven (14%) participants experienced ≥ 1 ADR that led to ON-SXB discontinuation; only nausea led to discontinuation in >1 participant (n=2).

Conclusions: These data from RESTORE demonstrate that REST-ON and oxybate-naïve participants tolerated ON-SXB well, as TEAEs were primarily mild/moderate in severity. ADRs were aligned with the known safety profile of TN-SXB.

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Samelisant, a potent and selective histamine H3 receptor inverse agonist: safety, tolerability and pharmacokinetics following single and multiple ascending doses in healthy subjects

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Introduction: Samelisant is a potent and selective histamine H3 receptor inverse agonist currently under development for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy. By antagonizing the H3 receptor, Samelisant increases the release of key wake-promoting neurotransmitters, histamine, dopamine, and norepinephrine, in the cortex of rats.

Electroencephalogram (EEG) studies conducted in various rodent models have demonstrated Samelisant's ability to promote wakefulness. These preclinical findings strongly support the therapeutic potential of Samelisant for the management of sleep-related disorders such as narcolepsy.

Materials and methods: In a Phase-1 clinical trial (NCT02342041), safety, tolerability, and pharmacokinetics of Samelisant was evaluated in a single-center, multi-faceted study after single and multiple ascending doses in healthy adult male subjects. In single ascending dose studies, subjects were dosed with Samelisant immediate release tablets in the dose range between 0.1 mg to 20 mg. In multiple ascending dose study, once daily doses of 1 mg to 6 mg Samelisant immediate release tablets were administered for 14 days to healthy adult male subjects. Effect of food, gender and age on Samelisant pharmacokinetics was evaluated in healthy volunteers at the dose of 6 mg (NCT02881294). Samelisant was quantified in plasma and urine using a validated LC-MS/MS method. Safety and tolerability was assessed throughout the study by adverse events, physical examination, vital signs, ECG, clinical laboratory tests, and suicidal ideation/behavior evaluation by Columbia Suicidal Severity Rating Scale (C-SSRS).

Results: Absorption of Samelisant was rapid and exposures (C_{max} and AUC) were dose proportional at the tested doses between 0.1 mg to 20 mg following single oral dose. Samelisant exhibited a 2.2-fold accumulation following multiple dosing in healthy adult subjects. Steady state was achieved on day 6 after multiple dosing. Renal excretion of unchanged drug was the major route of elimination for Samelisant. Food, gender and age had no effect on the Samelisant pharmacokinetics. Samelisant was well tolerated up to the highest tested dose of 20 mg single dose or 6 mg repeated dose in healthy adult subjects. There were no clinically relevant or serious adverse events reported by any subject.

Conclusions: Samelisant has favourable safety and pharmacokinetic profile after single and multiple dose administration for 14 days in healthy adult subjects. Following single or multiple oral administrations, Samelisant exposures were approximately dose proportional at the tested doses. Samelisant was well tolerated in humans with adequate plasma exposure for efficacy and favorable pharmacokinetics suitable for once a day oral administration.

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Samelisant (SUVN-G3031) Alleviates Excessive Daytime Sleepiness in Narcolepsy Patients: Results from a Phase-2 Study

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Introduction: Narcolepsy is a chronic sleep disorder characterized by excessive daytime sleepiness (EDS), uncontrollable sleep attacks, cataplexy, hypnagogic hallucinations, and sleep paralysis. Current treatments for narcolepsy often come with significant limitations, such as side effects, limited efficacy, or the necessity of combining multiple therapies. Samelisant is a selective inverse agonist of histamine 3 receptors, showing promising potential as a monotherapy treatment for this condition. In preclinical studies involving orexin knockout mice, Samelisant demonstrated wake-promoting effects and reduced cataplexy, underscoring its therapeutic potential. Samelisant safety/tolerability has been established in healthy subjects. The objective the study was to assess the efficacy and safety of Samelisant in treating EDS in patients with narcolepsy.

Materials and methods: Samelisant was evaluated as a monotherapy in a Phase 2 proof-of-concept study conducted across the United States and Canada for the treatment of excessive EDS in patients with narcolepsy (NCT04072380). The study enrolled adult patients aged 18 to 65 years, diagnosed with narcolepsy according to ICSD-3 criteria. Eligible participants had an Epworth Sleepiness Scale (ESS) score of ≥ 12 and a mean sleep latency of < 12 minutes on the Maintenance of Wakefulness Test (MWT). A total of 190 patients were randomized in a 1:1:1 ratio to receive either placebo, Samelisant 2 mg, or Samelisant 4 mg once daily for 14 days. The primary efficacy endpoint was the change in ESS score from baseline to Day 14. Secondary and exploratory endpoints included changes from baseline in Clinical Global Impression–Severity (CGI-S), MWT, and Patient Global Impression–Change (PGI-C) scores. Safety assessments included adverse events, physical examination, vital signs, ECG, clinical laboratory tests, and suicidal ideation/behavior evaluation by Columbia Suicidal Severity Rating Scale (C-SSRS).

Results: Samelisant achieved primary efficacy endpoint demonstrating a statistically significant ($p < 0.024$) and clinically meaningful reduction (-2.1 point) in ESS total score compared to placebo. Treatment with Samelisant resulted in a significant improvement in EDS on scales assessed by both clinicians and patients.

Samelisant was generally safe and well tolerated in narcolepsy patients and there were no serious events or death reported.

Conclusions: Samelisant holds promise as a monotherapy for the treatment of EDS in narcolepsy, and a global Phase-3 study will be initiated in H2 2025 to evaluate its efficacy in narcoleptic patients.

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Single-cell RNA and TCR sequencing of cerebrospinal fluid cells from patients with recent-onset type 1 narcolepsy

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Introduction: Narcolepsy type 1 (NT1) is caused by hypocretin (HCRT) neuron loss in the brain, and highly (98%) associated with human leukocyte antigen (HLA) DQA1*01:02/DQB1*06:02 (DQ0602) allele and T cell receptor (TCR). The strong HLA and TCR association and increased frequencies of CD4⁺ T cells reactive to HCRT in the peripheral blood suggest autoimmunity targeting HCRT. Further, patients with NT1 usually experience cataplexy and have significantly decreased levels of hypocretin-1 (orexin-A) in the cerebrospinal fluid (CSF). The pathogenesis of NT1 is still not completely understood. In this study, we are aiming to explore the autoimmune mechanism of NT1 with single-cell RNA and TCR sequencing of CSF cells.

Materials and methods: In this study, we selected CSF cells from 25 NT1 (duration of the disease < 1.0 year, $n = 15$). As a control, we used CSF cells from 15 patients with rhythm disorders or emotional problems. These cells were thawed and incubated with DNA-barcoded dextramers (dCODE

dextramers) DQ0602 loaded with 16 peptides, including the autoantigen (HCRT) and pandemic 2009 H1N1 (pH1N1) antigen (pHA and NP) peptides that caused a strong immune response in CD4⁺ T cells of patients with NT1 as reported in previous studies. Single-cell RNA sequencing for TCR and whole transcriptome was performed with 10x platform and analyzed with Scanpy.

Results: The frequency of CD4⁺ T cells in NT1 increased significantly compared with the healthy controls. We identified 1421 significant differentially expressed genes (DEGs) in NT1 compared to healthy controls. The most strongly upregulated genes in NT1 as compared to controls were coding for ITK, BRD2, TAGAP, KLF6, EEF2, and CD44. ITK and TAGAP play an important role in various autoimmune diseases, including rheumatoid arthritis, by regulating the proliferation and differentiation of T cells. BRD2 and EEF2 have been studied in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. KLF6 and CD44 have respectively been reported to be related to the regulation of sleep duration and cognitive impairment in sleep deprivation.

Conclusions: We confirmed the crucial role of CD4⁺ T cells in the pathogenesis of narcolepsy and suggest that genes related to immunological or neurological diseases likely contribute significantly. These findings provide further insights into narcolepsy mechanisms and identify potential therapeutic targets.

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Sleep Architecture With Low-Sodium Oxybate Treatment in Narcolepsy: Results From the DUET Study

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Introduction: Jazz DUET (Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment) was a phase 4, prospective, multicentre, single-arm, multiple-cohort, open-label study (NCT05875974) evaluating effectiveness of low-sodium oxybate (LXB, Xywav[®]) on daytime and nighttime-related signs and symptoms, including polysomnography (PSG)-based sleep architecture and disrupted nighttime sleep (DNS), in participants with narcolepsy (type 1 [NT1] or 2 [NT2]) or idiopathic hypersomnia. This abstract includes results from the narcolepsy cohort.

Materials and methods: DUET included a screening period (2-week washout for current oxybate users), 8-day baseline period (BL; with overnight PSG and assessments on day 8), 2- to 8-week LXB titration period (LXB initiation with individualised dosing adjustments to achieve optimal dosage), 2-week stable-dose period (SDP), 8-day end-of-treatment period (EOT; with overnight PSG and assessments on day 8), and 2-week safety follow-up. Nocturnal PSGs (*ad libitum* protocol) were scheduled to allow ≥10 hours in bed, unless the participant naturally awakened earlier; bedtime was per habitual bedtime. PSG recordings were centrally scored. Data were analysed in the completer set; least squares mean (LSM) changes were adjusted for baseline values. Total number of shifts from deeper to lighter sleep/wake stages was defined as N1/N2/N3/REM to wake and N2/N3/REM to N1. Key secondary endpoints (total stage shifts, N3 duration) were controlled for multiplicity with sequential testing; *P* values for other comparisons were not controlled for multiplicity.

Results: Fifty-five participants with narcolepsy enrolled and took ≥1 LXB dosage (safety set; NT1, n=26; NT2, n=29); 13 transferred to a different study cohort and 34 completed the study (completer set; NT1, n=16; NT2, n=18). Most participants in the safety set were female (73%) and White (80%) (mean [SD] age, 33.4 [12.9] years). Mean (SE) total sleep time (TST) at BL was 453.2 (13.7) and at EOT was 452.4 (12.0) minutes (LSM change [95% CI]: -0.78 [-23.7, 22.1]; *P*=0.9451). Mean (SE) total number of shifts from deeper to lighter sleep/wake stages at BL was 54.6 (4.8) and at EOT was 41.6 (4.4) (LSM [95% CI]: -13.1 [-19.0, -7.1]; *P*<0.0001). Mean (SE) time spent in N1 sleep at BL was 45.3 (4.9) and at EOT was 37.2 (4.3) minutes (LSM [95% CI]: -8.1 [-14.9, -1.4]; *P*=0.0196), percentage of

sleep stage per TST was 10.4% and 8.2% ($P=0.0037$); in N2 sleep, 241.8 (10.5) and 243.3 (13.0) minutes (LSM [95% CI]: 1.5 [-23.6, 26.6]; $P=0.9040$), 53.1% and 53.2% ($P=0.9869$); in N3 sleep, 61.1 (6.0) and 106.1 (11.9) minutes (LSM [95% CI]: 45.0 [27.0, 63.0]; $P<0.0001$), 13.7% and 24.0% ($P<0.0001$); and in REM, 105.0 (7.3) and 65.8 (5.7) minutes (LSM [95% CI]: -39.2 [-50.8, -27.5]; $P<0.0001$), 22.8% and 14.7% ($P<0.0001$).

Conclusions: Participants with narcolepsy taking open-label LXB experienced changes in duration and percentage of individual sleep stages, including increased N3 sleep and decreased N1 and REM, consistent with previous oxybate studies. Changes in N2 sleep and TST were negligible. Fewer shifts from deeper to lighter stages of sleep/wake were observed, suggesting improvement in DNS. These findings represent the first evaluation of LXB on PSG sleep architecture in individuals with narcolepsy.

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Successful Transition From Twice-Nightly Oxybates to Once-Nightly Sodium Oxybate: A Post Hoc Analysis From RESTORE

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Introduction: Extended-release, once-nightly sodium oxybate (ON-SXB; LUMRYZ™) eliminates the middle-of-the-night dosing required with immediate-release, twice-nightly oxybates (TN-OXBs). RESTORE (NCT04451668) was an open-label/switch study that assessed the safety and tolerability of ON-SXB in people with narcolepsy.

Materials and methods: Participants with narcolepsy aged ≥ 16 years who had completed the phase 3 REST-ON trial, were on stable-dose TN-OXB (switch participants), or were oxybate-naïve were eligible. For switch participants, initial ON-SXB doses were equivalent or closest to their prior total nightly TN-OXB dose. Doses could be titrated at ± 1.5 g/week until stable dosing was achieved (minimum, 4.5g/night; maximum, 9g/night). Treatment-emergent adverse events (TEAEs) during the 8-week dose titration period were recorded weekly for switch participants in the safety population (ie, received ≥ 1 ON-SXB dose) who completed a nocturnal AE questionnaire.

Results: Safety data were collected for 99.2% (129/130) of switch participants. All TEAEs reported by $\geq 3\%$ of switch participants occurred during weeks 1-3; no TEAEs $\geq 3\%$ were reported during weeks 4-8. At week 1, TEAEs $\geq 3\%$ included nausea (3.2%), vomiting (3.2%), decreased appetite (3.2%), and urinary retention (3.2%) with the 6-g dose, and headache (7.0%) and somnolence (4.7%) with 9g. At week 2, TEAEs $\geq 3\%$ included nausea (3.2%), upper respiratory infection (3.2%), dizziness (3.2%), and hypertension (3.2%) with 6g. At week 3, TEAEs $\geq 3\%$ included vomiting (3.2%), enuresis (3.2%), insomnia (3.2%), and somnambulism (3.2%) with 6g. No TEAEs $\geq 3\%$ were reported with 4.5g during weeks 1-3, or with 7.5g or 9g during weeks 2-3. Most TEAEs were mild or moderate in severity. The only reported severe TEAE was dyskinesia (1.2%) with the 7.5-g dose. During the ≥ 3 -year RESTORE study, only 5.4% of switch participants discontinued ON-SXB due to a TEAE.

Conclusions: For participants switching from stable-dose TN-OXB, ON-SXB was well tolerated during the 8-week titration period, with most TEAEs being of mild to moderate severity and consistent with the oxybate safety profile. By week 4, no TEAEs were reported by $\geq 3\%$ of participants, suggesting resolution of many TEAEs during titration. Participants successfully switched to ON-SXB from their nearest or equivalent prior total nightly TN-OXB dose.

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Symptom Severity in Central Disorders of Hypersomnolence is Associated with Cerebrospinal Fluid Hypocretin-1 Concentration

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Introduction: Central disorders of hypersomnolence (CDH) are neurological conditions characterized by excessive daytime sleepiness and/or increased sleep duration. Narcolepsy type 1 is distinguished by hypothalamic hypocretin-1 deficiency. The aim of this study was to identify key symptoms in addition to cataplexy that indicate hypocretin-1 deficiency, and to investigate the relationship between CDH symptom presentation and varying CSF hypocretin-1 levels.

Materials and methods: This study was based on data from the European Narcolepsy Network (EU-NN) database. 302 CDH patients from the EU-NN database were included, with 257 individuals exhibiting low hypocretin-1 (<200 pg/mL), including 163 individuals < 40 pg/mL, 59 between 41-110 pg/mL and 35 between 110-200 pg/mL. 45 individuals had hypocretin-1 levels >200 pg/mL. A machine learning approach using stochastic gradient boosting (SGB) was employed to explore non-linear associations and identify symptoms predictive of hypocretin-1 deficiency. Using logistic regression and quantile regression models we analyzed the association between absolute hypocretin-1 levels (independent variable) and 26 variables on demographics, subjective symptom severity, objective polysomnography and MSLT measures (dependent variables) while adjusting for age, sex and BMI. Cataplexy features were only analyzed in individuals with low hypocretin-1 <200 pg/mL. All CSF hypocretin-1 measurements were performed using standardized radioimmunoassay (RIA) protocols harmonized across EU-NN centers.

Results: Using machine learning, we identified previously underappreciated predictors of hypocretin-1 levels, including PSG sleep latency and REM sleep latency. Regression analyses further confirmed that lower hypocretin-1 levels were associated with shorter REM sleep latency and sleep latency in both MSLT and PSG, more SOREMPs, higher Epworth Sleepiness Scale scores, increased PLMI, and more frequent reports of disturbed nocturnal sleep. Among individuals with cataplexy and hypocretin-1 levels below 200 pg/mL, lower levels were further linked to earlier excessive daytime sleepiness onset, younger age at diagnosis, and greater diagnostic certainty of hypnagogic hallucinations and sleep paralysis. Moreover, lower hypocretin-1 levels were significantly associated with more frequent and complete cataplexy episodes. Interestingly, sleep drunkenness was more prevalent among individuals with higher hypocretin-1 levels and was associated with longer reported daytime sleep duration.

Conclusions: Lower hypocretin-1 levels were associated with more severe symptoms, both across the overall CDH population and within the subgroup of cataplexy patients with hypocretin deficiency (<200 pg/mL). Even within the deficient range, variation in hypocretin-1 levels contributed to individual differences in symptom presence and severity. These findings suggest that hypocretin-1 plays a greater role in shaping the clinical heterogeneity of CDH than previously appreciated.

The diagnostic value of EEG-MSLT in narcolepsy type 1

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Introduction: The diagnosis of narcolepsy type 1 (NT1) currently requires polysomnography-multiple sleep latency tests (PSG-MSLT). However, PSG-MSLT are inaccessible in most of the Chinese hospitals. This study aimed to evaluate the diagnostic value of electroencephalogram multiple sleep latency tests (EEG-MSLT) for NT1 and explore its potential as an alternative to PSG-MSLT.

Materials and methods: Patients included were children (<18 years old) presented with EDS and admitted to the Department of Sleep Medicine, Peking University People's Hospital, between October 2019 and October 2024. They all underwent EEG-MSLT and PSG-MSLT. HLA-DOB1*06:02 genotyping and cerebrospinal fluid (CSF) hypocretin-1 testing were measured if feasible. Kappa statistic was used for consistency analysis.

Results: 49 patients (28 males, 21 females; age: 9.61 ± 3.27 years) were included. All patients presented with excessive daytime sleepiness (EDS), alongside clinical manifestations including cataplexy (n = 45, 91.8%), sleep paralysis (n = 13, 26.5%), and hallucinations (n = 25, 51.0%). CSF hypocretin-1 testing in 29 patients revealed 27 (93.1%) had levels ≤ 110 pg/ml, while HLA-DQB1*06:02 genotyping was positive in 41 of 48 cases (83.7%).

EEG-MSLT yielded a mean sleep latency (mSL) of 4.53 ± 3.26 minutes, with 22 patients showing ≥ 2 sleep-onset rapid eye movement periods (SOREMPs). In comparison, PSG-MSLT demonstrated a significantly shorter mSL (3.14 ± 3.24 minutes, $P < 0.05$) and more frequent SOREMPs ($P < 0.001$), with 45 patients having ≥ 2 SOREMPs. These results indicate EEG-MSLT underestimates NT1 diagnostic markers.

EEG-MSLT showed limited diagnostic performance for children NT1, with a sensitivity of 42.86% and specificity of 57.14%, reflecting poor discriminative capacity. A Kappa consistency test ($\kappa = 0.065$, $P = 0.482$) revealed no significant agreement between EEG-MSLT and PSG-MSLT.

Conclusions: In real-world clinical settings, EEG-MSLT demonstrates insufficient sensitivity and specificity for NT1 diagnosis in children compared to PSG-MSLT. Further optimization or combination with other methods is needed.

The Effect of Pitolisant on Sleep-Promoting Neurons

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Introduction: Pitolisant is an H3 receptor antagonist/inverse agonist indicated for the treatment of excessive daytime sleepiness in people with narcolepsy. It is currently believed to promote wakefulness by directly activating the cortex and other brain regions through release of histamine (HIS), norepinephrine (NE), and other neurotransmitters. However, wakefulness requires both the activation of arousal-promoting neurons and the inhibition of sleep-promoting neurons, including those in the ventrolateral preoptic (VLPO) nucleus. Sleep-active, sleep-promoting neurons in the VLPO express GABA and the neuropeptide galanin (VLPO^{Gal}), and these VLPO^{Gal} neurons are both necessary and sufficient for normal sleep. In this study, we tested the hypothesis that pitolisant may also promote wakefulness by inhibiting VLPO^{Gal} sleep-promoting neurons.

Materials and methods: We used the GPCR activation-based (GRAB) sensor for norepinephrine (GRAB_{NE}) to measure changes in NE levels in the VLPO after intraperitoneal (ip) injection of pitolisant in mice. We expressed GRAB_{NE} in the VLPO region, and implanted a fiberoptic cannula above the VLPO

to measure changes in NE levels via fiber photometry. In a second set of experiments, we investigated the effects of pitolisant on VLPO^{Gal} neurons in mouse brain slices using whole-cell patch-clamp recordings.

Results: We found that ip injection of pitolisant (5, 10 and 20 mg/Kg) increased wakefulness and elevated NE concentrations in the VLPO in a dose-dependent manner. In brain slices, pitolisant inhibited the firing of VLPO^{Gal} neurons, but this effect was indirect. Consistent with this, we found that VLPO^{Gal} neurons do not express H3 receptors. Instead, pitolisant indirectly inhibits VLPO^{Gal} neurons by activating local GABAergic interneurons, which in turn suppress VLPO^{Gal} neuronal activity. These interneurons express H3 receptors and inhibit VLPO^{Gal} neurons through local axonal collaterals. Additionally, pitolisant locally increases NE, which directly inhibits VLPO^{Gal} neurons via $\alpha 2$ -adrenergic receptors and indirectly via $\alpha 1$ -adrenergic receptors by activating the same GABAergic interneurons targeted by pitolisant.

Conclusions: These results suggest that, in addition to direct activation of wake-promoting brain regions, pitolisant also promotes arousal by inhibiting sleep-promoting neurons in the VLPO. Pitolisant's actions in the VLPO involve activation of a local GABAergic circuit via H3 receptors plus the release of NE, both of which contribute to the inhibition of VLPO^{Gal} neurons.

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The First Light: Efficacy and Safety of a Multi-Dose Study of Oveporexton (TAK-861), an Oral Orexin Receptor 2 Agonist for the Treatment of Narcolepsy Type 1

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Introduction: Narcolepsy type 1 (NT1) is a neurologic disorder characterized by excessive daytime sleepiness, sudden muscle weakness triggered by emotions (cataplexy), disrupted nighttime sleep, sleep paralysis, hypnagogic/hypnopompic hallucinations, and cognitive symptoms. NT1 is caused by loss of orexin producing neurons in the hypothalamus, which regulate wakefulness, sleep and cognition. Re-establishing orexin transmission with orexin receptor agonists is a promising therapeutic approach for NT1. In phase 2 studies, oveporexton (TAK-861), an investigational oral orexin receptor 2 (OX2R)-selective agonist, was generally well tolerated and delivered sustained improvements across the spectrum of NT1 symptoms, assessed by both objective and patient-reported measures. Here, we report results from a phase 3 study that evaluated the efficacy, safety and impact on functioning, quality of life and cognition of oveporexton in participants with NT1.

Materials and methods: This randomized, double-blind, placebo-controlled study (TAK-861-3001) included adults aged 16–70 years across Europe, Japan, and North America with an International Classification of Sleep Disorders, Third Edition (ICSD-3) or ICSD-3-text revision diagnosis of NT1 supported by sleep tests or orexin CSF concentrations ≤ 110 pg/mL; Epworth Sleepiness Scale (ESS) score ≥ 11 ; and ≥ 4 partial/complete episodes of cataplexy/week without treatment. Participants were randomized 3:3:2 to twice-daily oral oveporexton 1 mg, oveporexton 2 mg, or placebo at least 3 hours apart for 12 weeks, after which participants either completed 4 weeks follow-up or entered the long-term extension study. The primary endpoint was change from baseline in mean sleep latency on the

Maintenance of Wakefulness Test (MWT) at week 12. Secondary endpoints included change from baseline in ESS total score at week 12, weekly cataplexy rate (WCR) at week 12, and occurrence of treatment-emergent adverse events (TEAEs).

Results: Overall, 168 participants (98 [58.3%] female) were randomized to ovesporexton 1mg/1mg (n=61), ovesporexton 2mg/2mg (n=66), or placebo (n=41). At baseline, mean age was 31.4 years and, mean ESS score was 18.5, mean MWT sleep latency was 5.0 minutes and median WCR was 26.0 attacks/week. At week 12, statistically significant least square (LS) mean (95% CI) changes from baseline were achieved with ovesporexton 1mg/1mg and 2mg/2mg vs placebo in MWT sleep latency (13.83 [10.23, 17.44] and 17.20 [13.66, 20.73] minutes vs placebo, respectively; both $P < 0.001$), and ESS total score (-8.00 [-9.87, -6.13] and -9.75 [-11.59, -7.90] vs placebo, respectively; both $P < 0.001$). Incidence rate ratios of WCR at week 12 for ovesporexton vs placebo were 0.34 (1mg/1mg) and 0.38 (2mg/2mg) (both $P < 0.001$ vs placebo). Overall, 88.1% of ovesporexton-treated participants (111/126) experienced ≥ 1 TEAEs versus 53.7% (22/41) with placebo. The most common TEAEs were pollakiuria and insomnia; there were no treatment-related serious TEAEs. 157 (93.5%) participants completed the study, of which 150 (95.5%) enrolled into the long-term extension study.

Conclusions: In this phase 3 study ovesporexton showed significant improvements versus placebo on subjective and objective measures of wakefulness, sleepiness and cataplexy frequency and was generally well tolerated.

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The prevalence and treatment of narcolepsy in New Zealand

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Introduction: No previous New Zealand-research on the epidemiology of narcolepsy or its medical management have been reported.

This study aimed to:

1. Estimate the incidence and prevalence of narcolepsy.
2. Describe trends in the medication types and demographics of prescriptions.

Materials and methods: National case numbers in 2021-2023 were collated from all sleep centres providing testing for narcolepsy and used to estimate incidence and prevalence. Concurrently, all narcolepsy-related special authority (SA) prescription approvals from Pharmac New Zealand in 2021-2023 were analysed by medication type and demographics.

Results: Between 2021-2023, 348 MSLT tests for narcolepsy revealed 56 cases, giving an incidence of 0.36 per 100,000 person-years and a prevalence of 21.9 cases per 100,000 people. During this period Pharmac approved 762 requests for narcolepsy-medications, of which 263 were new (i.e. not repeats or renewals). Between 2021 and 2023, a total of 223 new and 762 overall (including repeats and renewals) Special Authority (SA) applications were submitted to Pharmac, all of which were approved. The annual average of new SA applications was 74.3 per year, which was 3.9 times higher than the average sleep laboratory diagnosed annual cases narcolepsy (19 cases per year). For new and overall applications For both new and overall applications, MPHIC was slightly preferred over MF, accounting for 53.8% and 57.9% of applications, respectively. Methylphenidate accounted for 53.8% new and total 57.9% applications; Modafinil for 46.2% new and total 42.6% respectively. There was variation in prescribing for regions, age, gender, and ethnicity were observed .

Conclusions: This study provided the first New Zealand-based estimates of incidence and prevalence for narcolepsy . The number of new Special Authority (SA) applications for narcolepsy medications was significantly higher than the new narcolepsy cases objectively diagnosed. Potential reasons include: disparity / difficulty accessing sleep labs; being treated with multiple medications and patients with Idiopathic Hypersomnolence (IH) being treated under narcolepsy-related SA category. We recommend Pharmac develop & fund separate criteria for the treatment of Idiopathic Hypersomnolence and the New Zealand Ministry of Health fund services to improve access for objective sleep laboratory testing and education/ implementation support for professional bodies.

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The Radiant Light: Efficacy and Safety of Oveporexton (TAK-861), an Oral Orexin Receptor 2 Agonist for the Treatment of Narcolepsy Type 1

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Introduction: Narcolepsy type 1 (NT1) is a chronic, rare, neurologic disorder of hypersomnolence caused by loss of orexin-producing neurons in the hypothalamus, which regulate wakefulness, sleep, and attention through activation of orexin receptors. NT1 results in a range of symptoms including excessive daytime sleepiness, sudden muscle weakness (cataplexy), disrupted nighttime sleep, sleep paralysis, hypnagogic/hypnopompic hallucinations, and cognitive symptoms. Orexin receptor agonists are promising treatments for NT1 as currently available therapies do not target orexin deficiency. Oveporexton (TAK-861) is an investigational oral orexin receptor 2 (OX2R)-selective agonist that stimulates OX2R to restore signaling and address the underlying orexin deficiency. In a previous phase 2b study, oveporexton delivered improvements across the spectrum of NT1 symptoms, assessed by both objective and patient-reported measures, and was generally well tolerated. Here, we report first results from a phase 3 study that evaluated the efficacy, safety and impact on functioning, quality of life and cognition of oveporexton in participants with NT1.

Materials and methods: In this double-blind, placebo-controlled, phase 3 study (TAK-861-3002) participants were randomized 2:1 to oral oveporexton 2 mg or placebo twice daily at least 3 hours apart for 12 weeks. At the end of treatment, participants either entered the long-term extension or completed 4 weeks of follow up. Key inclusion criteria included: age 16–70 years; International Classification of Sleep Disorders, Third Edition (ICSD-3) or ICSD-3-text revision diagnosis of NT1 supported by polysomnography, multiple sleep latency testing (MSLT) or orexin cerebrospinal fluid (CSF) concentrations ≤ 110 pg/mL; Epworth Sleepiness Scale (ESS) score ≥ 11 ; and ≥ 4 partial/complete episodes of cataplexy/week. The primary endpoint was change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT) at week 12. Secondary endpoints included change from baseline in ESS total score at week 12, weekly cataplexy rate (WCR) at week 12, and occurrence of treatment-emergent adverse events (TEAE).

Results: Overall, 105 participants (50 [47.6%] female) were enrolled across Asia, Australia, and Europe; 70 were randomized to oveporexton 2 mg/2 mg and 35 to placebo. At baseline, mean age was 30.7 years, mean ESS score was 17.5, mean MWT sleep latency was 4.5 minutes and median WCR was 23.5 attacks/week. At week 12, significant least square (LS) mean (95% CI) changes from baseline were achieved with oveporexton 2mg/2mg vs placebo in MWT sleep latency (20.09 [16.57, 23.61] minutes, $P < 0.001$ vs placebo). Significant changes vs placebo were also achieved at week 12 for ESS total score (LS mean [95% CI] change from baseline: -9.53 [-11.10, -7.97], $P < 0.001$) and WCR (Incidence rate ratio [95% CI] vs placebo: 0.25 [0.15, 0.42], $P < 0.001$). Sixty (85.7%) oveporexton-treated participants experienced ≥ 1 TEAEs vs 15 (42.9%) placebo-treated participants; there were no serious TEAEs. The most common TEAEs with oveporexton were pollakiuria (43 [61.4%]) and insomnia (40 [57.1%]). 101 (96.2%) completed study treatment, of which 100 (99.0%) enrolled into the long-term extension.

Conclusions: In this phase 3 study, oreporexton treatment resulted in significant improvements on measures of wakefulness, sleepiness and cataplexy frequency with oreporexton versus placebo, and was generally well tolerated.

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Treatment Considerations in Co-morbid Schizophrenia and Narcolepsy: A Case Report

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Introduction: Narcolepsy affects 1 in 2000 people and causes disabling sleepiness. Schizophrenia, a common psychotic disorder, affects 1 in 133 people and confers significant impairments across domains. Rates of co-occurrence is not exactly known. One cohort study observed 8.1% of persons with narcolepsy (PWN) as having a psychosis comorbidity and a 4-fold greater risk for psychosis in PWN. Some alertness promoting medications used in narcolepsy treatment, such as modafinil, methylphenidate and amphetamine, may exacerbate psychosis by increasing dopamine activity. There are case reports of sodium oxybate exacerbating psychosis

Materials and methods: A 21-year-old man with was admitted for auditory hallucinations and bizarre behaviour. He put his cell phone in his microwave to prevent his conversations from being overheard. He was diagnosed with schizophrenia.

The patient had a PSG + MSLT confirmed diagnosis of narcolepsy with cataplexy that predated this by 9 years.

His methylphenidate extended-release 20mg was discontinued for concerns that it was precipitating psychosis. He was previously intolerant to modafinil (emotional numbing) and Concerta (appetite suppression) as per chart review.

Paliperidone was effective for psychosis but worsened sleepiness, which was disabling. The patient would fall asleep during in-patient assessments. A retrial of modafinil worsened auditory hallucinations and delusions of persecution, and discontinued. He was discharged on paliperidone IM with well-controlled psychosis but sleepiness remained.

Results: As an outpatient, caffeine 100mg up to 4x per day PRN was trialed but insufficient in promoting meaningful improvements to wakefulness. A new pitolisant was initiated to treat sleepiness and cataplexy, and was successful to a material degree without exacerbation of psychosis. Unfortunately, after 8 weeks of treatment, the patient lost access to pitolisant for one month due to insurance coverage issues, during which his irresistible sleepiness and cataplexy returned. The pitolisant was restarted upon insurance approval, and his wakefulness and cataplexy again improved. He remains stable on pitolisant 40mg and paliperidone 75mg IM q4 weekly. He has residual but non-disabling sleepiness. We have asked him to use PRN caffeine judiciously to buttress wakefulness.

Conclusions: In conclusion, some traditional stimulants may worsen psychosis in PWN. Pitolisant, an inverse H3 agonist, which does not theoretically affect dopamine pathways, may be a suitable treatment for sleepiness and cataplexy in comorbid psychosis.

Understanding Path to Diagnosis, HCP Relationships, and Treatment Regimens Among People Living With Narcolepsy

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Introduction: Narcolepsy is a chronic, disabling hypersomnolence disorder requiring lifelong management. People with narcolepsy (PWN) often experience diagnostic delays and difficulties with

quality care, including healthcare provider (HCP)- and treatment-related challenges. This survey assessed the path to diagnosis, HCP relationships, and treatment regimens among PWN from MyNarcolepsyTeam, a social network of >11,000 members.

Materials and methods: MyNarcolepsyTeam members were invited to participate in a 36-question online survey fielded between April 10 and May 9, 2024. Eligible participants had a narcolepsy diagnosis, were age ≥ 21 years, and resided in the United States. Data were analyzed descriptively.

Results: Of 88 total respondents (female, 77%; age ≥ 50 years, 74%), 39% had narcolepsy type 1, 50% had narcolepsy type 2, and 11% were unsure. Most (81%) respondents saw ≥ 2 clinicians to receive a diagnosis; 36% visited ≥ 5 clinicians. 98% had undergone ≥ 1 sleep study, which was the most common diagnosis method (83%). Following diagnosis, 68% of respondents visited multiple HCPs to address narcolepsy symptoms. Of 82 respondents currently seeing an HCP, 56% were extremely/very satisfied with their clinician. Satisfaction was higher among respondents seeing sleep specialists vs non-sleep specialists (70% vs 38%). More respondents seeing sleep specialists vs non-sleep specialists reported discussions that address mental health (48% vs 31%) and long-term planning (38% vs 15%). Fifty percent of respondents currently seeing an HCP discussed the advantages and disadvantages of treatments with their HCP. Seventy-nine (90%) respondents were taking ≥ 1 medication to treat their symptoms; 67% took ≥ 2 medications. Current medications for narcolepsy most commonly included traditional stimulants (56%; [Adderall®, Ritalin®, etc.]) and antidepressants (38%). Nearly half of respondents (44%) found their treatment regimen extremely/very/somewhat challenging, of whom 83% were taking multiple medications. Reported treatment challenges included loss of efficacy, side effects, access barriers, and the complexity of medication regimens.

Conclusions: These findings highlight the challenges PWN face, emphasizing the need for expedited diagnosis and access to specialized healthcare. Despite greater satisfaction with care from sleep medicine specialists, there is a shortage in this field. This gap underscores the necessity for improved treatment regimens and enhanced discussions between PWN and HCPs to address mental health support and long-term planning.

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Validation of Waveband for Evaluation of Sleep in Hypersomnia Disorders

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Introduction: Narcolepsy type 1 (NT1) is a rare neurologic disorder linked to orexin deficiency and characterized by excessive daytime sleepiness, cataplexy, hallucinations, sleep paralysis, and disrupted nighttime sleep. NT1 diagnosis and clinical trials evaluating NT1 therapies currently rely on in-clinic polysomnography (PSG) and Multiple Sleep Latency Test, which are time-consuming, burdensome, uncomfortable for patients, and require trained personnel. Unfortunately, PSG is unable to readily capture sleep variability across nights and may not reflect a natural sleep environment. NCT06531876 is a prospective clinical validation study to evaluate Waveband (formerly referred to as Dreem 3S), an FDA-cleared at-home dry-electrode encephalography device, in individuals with suspected hypersomnia disorders and those with confirmed NT1 to understand wear compliance, data quality, and sleep staging accuracy.

Materials and methods: Data from 68 participants were analyzed, including 17 with suspected disorders of primary hypersomnia (Arm A) and 51 with investigator-confirmed NT1 diagnoses (Arm B). Participants recorded six nights of sleep and one 24-hour monitoring period with Waveband at home, followed by one (Arm A) or two (Arm B) nights of in-clinic PSG with concurrent Waveband. At-home wear compliance was measured by algorithmically detected “on-head” device wear time and data quality was assessed using the Waveband “scorability” algorithm. PSG was scored by three Registered Polysomnography Technologists (RPSGTs). In-clinic Waveband data were automatically scored using a

proprietary sleep-staging algorithm and algorithmic results were adjudicated by three RPSGTs.

Perceived usability of Waveband and PSG was assessed using the System Usability Scale (SUS).

Results: At-home wear compliance and data quality benchmarks were met: 100% of participants had four or more overnight recordings (mean $\pm$ SD; Arm A: 5.9 $\pm$ 0.2; Arm B: 5.5 $\pm$ 0.7) with at least four hours of wear time and 85% of that being "scorable" data. For the 24-hour period, 100% of Arm A participants and 90% of Arm B participants had at least 17 hours of wear time (Arm A: 22.8 $\pm$ 1.6; Arm B: 22.1 $\pm$ 3.0) with at least 85% of that being "scorable" data. SUS scores for Waveband (Arm A: 76.2 $\pm$ 11.8; Arm B: 77.6 $\pm$ 13.6) were higher than for PSG (Arm A: 52.8 $\pm$ 18.3; Arm B: 49.9 $\pm$ 19.7). Agreement of adjudicated Waveband and PSG was high across sleep stages, with mean Cohen's Kappa of 84.1 % (Arm A) and 77.7% (Arm B). By stage, overall/positive/negative agreement was 97.8/86.4/99.3% (wake), 96.1/46.7/98.9% (NREM1), 91.0/87.9/92.9% (NREM2), 95.4/93.8/95.3% (NREM3) and 97.9/95.6/98.4% (REM) for Arm A participants and 95.6/84.4/97.2% (wake), 94.8/44.4/98.5% (NREM1), 89.3/85.1/92.2% (NREM2), 96.0/88.5/96.5% (NREM3) and 94.0/86.6/95.6% (REM) for Arm B participants. Unadjudicated Waveband and PSG agreement was similarly high.

Conclusions: These results provide validation and feasibility data that support using Waveband to collect high-quality sleep data and quantify sleep stages in a hypersomnia population. Waveband could provide insight into diagnosis, treatment response and disease progression. Further, Waveband has potential to be used as an alternative to PSG for monitoring sleep longitudinally in a patient's home, thereby improving data quality and collection with multiple measurements at a lower burden and cost.

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Vibrance-1: A Randomized Phase 2 Study Evaluating Safety and Efficacy of the Orexin 2 Receptor Agonist Alloxorexton (ALKS 2680) in Patients with Narcolepsy Type 1

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Introduction: Narcolepsy type 1 (NT1) is a central disorder of hypersomnolence characterized by excessive daytime sleepiness, cataplexy, and hypocretin/orexin deficiency. Alloxorexton (ALKS 2680) is a highly potent, oral, and selective orexin 2 receptor agonist. In a phase 1b study, single doses of alloxorexton were evaluated in patients with NT1, narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH). Focusing on NT1, alloxorexton was well-tolerated and demonstrated dose-dependent improvements in mean sleep latency on the Maintenance of Wakefulness Test (MWT). These findings guided dose selection for the phase 2 Vibrance-1 study. Here we present results obtained during the randomized double-blind treatment period of the Vibrance-1 study.

Materials and methods: Vibrance-1 is a placebo-controlled, dose-ranging phase 2 study with a randomized double-blind parallel group treatment period and an open-label extension period. After 2 weeks of washout, patients with NT1 are randomized 1:1:1:1 to receive placebo or alloxorexton once daily at 4, 6, or 8 mg for 6 weeks. Eligible patients are 18-70 years old with NT1, body mass index (BMI) ≥ 18 and ≤ 40 kg/m², no comorbid sleep-related illness that may influence sleep/wake, no significant cardiovascular or psychiatric conditions, and no activities that interfere with nighttime sleep. The primary endpoint is change from baseline to week 6 in mean sleep latency on the MWT over 4 sessions at 2, 4, 6, and 8 hours post dose. Key secondary endpoints include Epworth Sleepiness Scale (ESS) and weekly cataplexy rate (WCR). Safety is being evaluated by treatment-emergent adverse events, laboratory assessments, vital signs, electrocardiograms, and the Columbia-Suicide Severity Rating Scale.

Results: Ninety-two patients were randomized to placebo or alloxorexton and received ≥ 1 dose of study drug. Patients were enrolled in Europe (n=61 [66%]), the United States (n=23 [25%]), and Australia (n=8 [9%]). At baseline, patients' mean (standard deviation [SD]) age was 33.5 (12.1) years. The majority

were female (n=57 [62%]). Pretreatment symptom severity was demonstrated by mean sleep latency on the MWT (mean [SD], 3.1 [3.1] minutes), ESS (mean [SD], 18.5 [3.1]), and WCR (mean [SD], 26.1 [32.6]). Study results from the full patient cohort in the randomized double-blinded treatment period will be presented.

Conclusions: The baseline characteristics from patients randomized in the ongoing Vibrance-1 study indicate severe NT1 symptoms. The findings from this study will inform the further clinical development of alixorexton as a treatment for narcolepsy.

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Weight loss response to GLP-1 RA in adults with narcolepsy cataplexy

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Introduction: Patient with narcolepsy cataplexy (NC) often has weight gain and obesity, probably due to orexin/hypocretin deficiency, which makes the diet more difficult in NC. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have been demonstrated effective for weight loss in obesity with diabetes or non-diabetes, obstructive sleep apnea, knee osteoarthritis and so on, while their effects on obesity in NC remain unclear. This study explores the weight loss effects of one GLP-1 RAs (semaglutide) in adults with NC.

Materials and methods: This study was conducted between July 2024 and Mar 2025 at the Division of Sleep Medicine, Peking University People's Hospital. Weight loss effects of 12 adults with NC and obesity receiving semaglutide plus lifestyle interventions (Group A) and 24 sex-, age-, and BMI-matched adults with non-NC (Group B), as well as 12 adults with NC and obesity receiving lifestyle interventions alone (Group C). Weight and side effects were measured weekly, while clinical examinations, biological measurements, and questionnaires conducted at baseline and Week 12.

Results: Overall, the average age of the three groups is 29.69 ± 7.63 years, and the vast majority (70.83%) were male in Group A and C (24 adults with NC and obesity). At baseline, the BMIs were 34.09 ± 2.08 for Group A, 33.44 ± 2.38 for Group B and 32.20 ± 4.49 for Group C, with no statistical difference. Both Groups A and B completed 12 weeks on injectable semaglutide with losing $7.72\% \pm 4.47\%$ and $7.73\% \pm 3.20\%$ bodyweight respectively, while Group C lost $2.41\% \pm 2.68\%$ bodyweight. And the weight loss from the baseline was 4.12%, 5.97%, 7.72% for Group A, and 2.56%, 5.43%, 7.73% for Group B, and 1.46%, 1.79%, 2.41% for Group C at Weeks 4, 8, 12, respectively. Additionally, in Group A, 8(66.7%) patients lost $\geq 5\%$ weight, 5(41.67%) patients lost $\geq 10\%$ weight; in Group B, 20(83.3%) patients lost $\geq 5\%$ weight, 6(25%) patients lost $\geq 10\%$ weight; and in Group C, 2(16.67%) lost $\geq 5\%$ weight, with no patients achieving $\geq 10\%$. The reported adverse events in patients using semaglutide were mainly nausea, vomiting, constipation, and diarrhea.

Conclusions: In adults with NC and obesity, injectable semaglutide resulted in weight loss similar to that observed in matched patients with simple obesity and had a similar side effect profile, while better than lifestyle intervention alone. Although patients with NC have a deficiency in orexin/hypocretin, they can still successfully lose weight with the GLP-1 RAs.

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When Those Supposed to Save You from Suicide Kill You: Sleep-Disrupting Psychiatric Containment of Undiagnosed Type 1 Narcolepsy Turned Insomnia

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Introduction: Type 1 narcolepsy (T1N) is a rare neurological condition characterized by orexin-A deficiency, disrupted sleep-wake regulation, and altered REM architecture. In some patients, this includes enhanced dream awareness and volitional dream construction, which may underpin identity,

cognition, and vocation. During acute severe insomnia, these patients may present with suicidal ideation secondary to existential distress and sleep deprivation, not primary psychiatric pathology. This autoethnographic case explores how psychiatric crisis protocols, devoid of sleep medicine integration, can cause irreversible neurologic and existential injury and loss of systemic trust.

Materials and methods: This is a first-person case analysis by the author, a 22-year-old woman at the time of admission and aspiring filmmaker whose sense of self was built around lifelong dream-directing abilities. After months of inverted circadian rhythm, she developed acute severe insomnia (sleeping ~1 hour per 24 hours at 8 AM) for weeks. In December 2020, during COVID-19 and the holiday period, she sought help for irreparable insomnia and existential fear. She expected a calm, monitored setting for sleep restoration and support. Instead, she was subjected to psychiatric containment with 40+ patients for five nights, without sleep-focused evaluation. CSF orexin-A was confirmed years later to be < 50 pg/mL.

Results: Pre-admission: The patient already noticed a reduction in dream vividness, contributing to existential terror. Without T1N official diagnosis, she could not communicate her condition represented catastrophic override of hypersomnolence, not psychiatric illness.

Containment: In a shared psychiatric ward with 40+ patients, her fragile 1-hour morning sleep was eliminated entirely by noise and overstimulation, resulting in complete sleep loss.

Post-containment: For months, she could only sleep 3-4 hours /day. Dream remained grayscale devoid of narrative.

Five-year follow-up: Dream vividness and control have partially returned but remain impaired, suggesting likely irreversible neurological change.

Collateral consequences: Voluntary disclosure of the psychiatric admission led to immediate on-campus housing revocation, later overturned via an external psychologist's letter. She experienced months of homelessness in between. Upon readmission, she was forced to sign acknowledgment accepting the institution's prior decision. The compounding trauma of misdiagnosis, containment-induced neurologic injury, housing discrimination, and institutional betrayal resulted in lasting erosion of trust in national systems and enduring existential injury.

Conclusions: This case reveals the consequences of failing to recognize sleep disorders during psychiatric crisis intake. For T1N patients, loss of REM vividness may constitute psychological death. When sleep-driven crises are misclassified and institutional containment erases rare, fragile sleep, the result may be permanent vocational, functional, and existential loss. Suicide prevention systems must incorporate sleep triage, especially for rare neurological disorders.

Sleep-informed crisis care, rare condition diagnostic access, and anti-discrimination are not optional—they are essential protections against identity erasure and systemic traumatization and retraumatization.

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Neurological Disorders Affecting Sleep

A longitudinal exploration of posture changes and effects on sleep in motor neurone disease

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Introduction: Sleep disruption is highly prevalent in individuals with motor neurone disease (MND), particularly amyotrophic lateral sclerosis (ALS), and significantly contributes to disease burden. Degeneration of motor neurons and resultant muscle weakness and immobility is frequently associated with spasticity, cramps, restless legs syndrome and impaired mobility, that can all negatively impact sleep. Upper airway dysfunction, particularly with bulbar involvement, can also lead to sleep-disordered breathing, sialorrhea, choking, and aspiration, which can also impair sleep. Discomfort and psychological factors including distress and depression may also impair sleep through insomnia. Despite the awareness of disturbed sleep and multiple potential causes in MND, the mechanisms underlying poor sleep in MND remain poorly examined and understood. Given that declining mobility over time in MND could importantly influence sleep quality through discomfort and postural influences on sleep and sleep disordered breathing, this study sought to test for potential movement decline and postural influences on sleep with MND progression.

Materials and methods: Polysomnography (PSG) data were examined from a prospective longitudinal observational study conducted between December 2015 to January 2018 through a multidisciplinary MND clinic in South Australia (BreatheMND-1 study), which enrolled 37 patients with a confirmed diagnosis of MND, based on the El Escorial criteria. Where possible, participants completed laboratory or home PSG assessments at baseline, three, six, and 12 months. Sleep posture changes and sleep efficiency in each posture were examined using linear mixed-effects model analyses to test for posture effects and changes from baseline to last available follow-up.

Results: Baseline and repeat follow-up PSG data were available and analysed from 22 patients (median follow-up time 6 months). The total time available for sleep (mean [95%CI] 8.2 [7.7 to 8.8] h) was not different between baseline and follow-up visits. However, sleep efficiency was very poor at baseline (42.9 [32.9 to 53.1]%) and significantly further reduced at last available follow-up (30.8 [20.7 to 40.9]%, $p=0.018$). Sleep efficiency was poorest in prone compared to left and right lateral positions (22.2 [10.1 to 34.3] vs 43.0 [32.7 to 53.4] and 45.1 [34.7 to 55.3]% respectively, $p=0.001$), although there was very little prone sleep positioning (0.2 [0 to 0.9] h vs left 3.2 [2.5 to 3.9], right 1.9 [1.2 to 2.7] and supine 2.8 [2.0 to 3.5] h, $p<0.002$). The number of posture shifts from each body position increased from baseline (4.7 [2.8 to 6.5]) to last available follow-up (7.2 [5.4 to 9.1] /posture/night, $p=0.011$), but with no significant differences in the average time spent in each posture other than shorter prone versus left lateral positioning (27.8 [0 to 62.6] vs 72.9 [43.1 to 102.7] min, $p=0.025$).

Conclusions: These findings highlight the very poor and declining nature of sleep in MND, and that progressive loss of motor strength, control and mobility likely contribute to sleep loss through discomfort and potentially posture-dependent sleep disturbance effects. Further work is clearly warranted to better understand the mechanisms underpinning poor sleep in MND, and the potential utility of overnight movement and sleep changes over time as markers of disease progression and treatment efficacy.

An exploration of the factors influencing the uptake of non-invasive ventilation by people with motor neurone disease in Australia: a qualitative study of patient and health professional perspectives

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Introduction: Motor neurone disease (MND, also known as Amyotrophic Lateral Sclerosis) is an incurable condition, with treatment primarily focusing on management of symptoms and maintaining quality of life. Non-invasive ventilation (NIV) has been shown to improve quality of life and extend survival in people with MND however the uptake of NIV is low in Australia. This aim of this study was to understand the factors that influence the uptake of NIV by people with MND (pwMND) in Australia.

Materials and methods: A qualitative study, informed by the COM-B (Capability, Opportunity, Motivation = Behaviour) framework and Theoretical Domains Framework. Semi-structured interviews were conducted with pwMND, carers of pwMND, and healthcare professionals involved in the care of

pwMND. Interviews were transcribed verbatim and analysed using a two-stage approach; a deductive Framework Analysis was conducted to ascertain the factors that influence NIV uptake and the stage in the patient journey to NIV uptake that these factors occur, followed by an inductive thematic analysis to derive greater meaning from the influencing factors.

Results: Interviews were conducted with 39 participants, eight pwMND, four carers of pwMND, and 27 healthcare professionals (nine neurologists, eight sleep/respiratory physicians, five nurses, three physiotherapists, one palliative care physician, and one MND advisor). A total of 29 key influencing factors to NIV uptake were identified, of which 17 were barriers, 10 were facilitators, and 2 were a barrier or facilitator. Thirteen factors related to the decision to trial NIV by pwMND, and included their motivations to trial NIV, their capacity to use the device, and their attitudes towards NIV. Nine factors related to the skills, knowledge and attitudes towards NIV and MND of health professionals, which were found to influence their responsiveness and willingness to recommend NIV to pwMND. Seven factors related to the design and accessibility of NIV services in the Australian healthcare system. Inconsistent and inadequate NIV service delivery models were found to limit access to NIV for pwMND, even for those who were interested in trialing NIV.

Conclusions: This study identified many important factors influencing the uptake of NIV among pwMND in Australia. This study demonstrates that health system design and knowledge and attitudes towards NIV of both people with lived experience of MND and health care professionals can impact access and uptake of NIV.

These findings will be used to inform the development of targeted interventions that address the barriers to NIV uptake, with the overall goal to increase uptake of NIV, reduce health care inequity, and optimise quality of life for people living with MND.

Association Between Long Sleep Duration and Dementia Risk Among Elderly Farmers: A Cross-Sectional Analysis

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Introduction: Dementia represents a significant public health concern among older adults worldwide. Growing evidence suggests that sleep duration may serve as an important modifiable risk factor for cognitive decline, warranting investigation in vulnerable populations. The agricultural workforce is experiencing rapid demographic aging, heightening the need for dementia prevention and early detection strategies in farming communities. Elderly farmers face unique challenges including physically demanding work, higher prevalence of chronic diseases, and limited healthcare access, making them particularly susceptible to cognitive impairment. This study examined the relationship between sleep duration and cognitive function in elderly Korean farmers.

Materials and methods: We performed a cross-sectional analysis of 710 Korean farmers aged 60 years and older. Cognitive impairment was assessed using the Mini-Mental State Examination for Dementia Screening (MMSE-DS) with age-, sex-, and education-adjusted cutoff scores. Participants reported their typical daily sleep duration, which was categorized as short (<6 hours), normal (6-8 hours, reference group), or long (>8 hours). Multivariable logistic regression models were constructed to examine associations while controlling for demographic characteristics, medical comorbidities, depression, lifestyle factors, pesticide exposure, agricultural work type, and physical activity levels.

Results: Compared to farmers sleeping 6-8 hours nightly, those with prolonged sleep duration (>8 hours) demonstrated nearly three-fold increased odds of cognitive impairment (OR = 2.96, p = 0.007). Conversely, short sleep duration (<6 hours) was not significantly associated with dementia risk (OR = 0.71, p = 0.302).

Conclusions: Our findings align with international research demonstrating associations between extended sleep duration and cognitive decline. The results suggest that prolonged sleep among elderly farmers may serve as an early indicator of dementia risk. Given the occupational hazards and healthcare barriers faced by agricultural workers, integrating sleep assessment into rural health surveillance programs could enhance early detection of cognitive impairment. Future longitudinal research is needed to determine whether extended sleep duration precedes cognitive decline or represents a consequence of underlying neurodegenerative processes.

Association of functional variants in core circadian genes with intensity of neuropathic pain in post-surgical patients with breast cancer

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Introduction: Increasing evidence suggests that genetic variants in core circadian genes are associated with sleep disorders, which are a frequent comorbidity of neuropathic pain (NP). In current study, we explored the potential association between the circadian single nucleotide polymorphisms (SNPs) with intensity of chronic post-surgical NP in the patients treated for breast cancer. Currently it is not known why only some patients develop chronic post-surgical NP, while others do not, after the same type of nerve injury during surgical procedure.

Materials and methods: The association of SNPs in circadian core genes (CLOCK; BMAL1, PER1/2/3, CRY1/2) to NP was examined in the BrePainGen cohort (N=1000, Finland) of female patients who underwent surgery for breast cancer during 2006-2010, with a follow-up of up to 5.5 years. Genomic DNA was extracted from 10 ml of peripheral blood prior to the surgery and genome-wide genotyping was performed using Illumina OmniExpress SNP microarray. Information regarding pain intensity at the operated area and intensity of other types of chronic pain were collected from the patients. The genotype distribution and allele frequencies of circadian SNPs were extracted from the genome-wide data and tested for association to post-surgical NP by Pearson X2 test and odds ratio with 95% confidence interval.

Results: As a result, we found that the frequency of recessive allele of circadian PER1 polymorphism rs2585405 was three times higher in patients with moderate to severe NP compared to patients with mild NP at the 3 years follow-up. Patients with and without post-surgical NP displayed a significant difference in distribution of rs2585405 genotypes ($p=0.001$, $X^2=14.39$) and allele frequencies ($p=0.007$, $X^2=10.13$).

Conclusions: These findings show that a functional variant of circadian PER1 is associated with the intensity of post-surgical NP in cancer patients which might open the new therapeutic avenues for personalised treatments of cancer pain by taking into account the inter-individual differences in biological clocks.

Association of Polysomnographic Sleep Alterations and Cognition in Lewy Body Diseases

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Introduction: Lewy body diseases, including Parkinson's disease (PD) and dementia with Lewy bodies (DLB), are the second most common neurodegenerative disorders in older adults. Sleep disturbances are an early and prominent feature of PD and DLB, with their presence closely linked to the development of core non-motor symptoms, including dementia, visual hallucinations and cognitive fluctuations. In healthy individuals, poor sleep is associated with cognitive dysfunction; however, few studies have comprehensively examined the relationship between objectively measured sleep alterations and cognition across the Lewy body disease spectrum. This study aimed to characterise alterations in sleep macroarchitecture in PD and DLB, and to explore associations between objective sleep parameters and cognitive functioning across neuropsychological domains.

Materials and methods: This study involved: 34 participants with DLB, 58 with PD, and 58 controls without objective cognitive impairment. All participants underwent overnight in-laboratory polysomnography (PSG), including EEG (10–20 system), EOG, submental EMG, ECG, respiratory monitoring (nasal pressure, thoracic and abdominal belts), pulse oximetry, body position, and anterior tibialis EMG. Sleep staging was scored in 30-second epochs according to AASM criteria. Cognitive assessments included global cognition (MMSE) and six neuropsychological domains: executive function

(TMT-B), switching and cognitive flexibility (D-KEFS CWIT 4), inhibition (D-KEFS CWIT 3), visuospatial function (Clock Drawing Test), attention and working memory (Digit Span Backward), learning and memory (RAVLT), and language (COWAT). Group differences in sleep architecture were analysed using general linear models with permutation testing. Linear regressions examined associations between cognitive domains and PSG variables across PD and DLB. All analyses controlled for age and sex, with FDR corrections applied.

Results: Alterations in sleep macroarchitecture were shared across Lewy body diseases. Compared to controls, PD and DLB showed significantly reduced sleep latency (PD: $pFDR < 0.001$, DLB: $pFDR = 0.04$), increased REM latency (PD: $pFDR = 0.028$, DLB: $pFDR = 0.024$), and reduced REM sleep percentage of total sleep time (PD: $pFDR < 0.001$, DLB: $pFDR < 0.001$). Respiratory disturbance index (RDI) during REM sleep was also significantly lower in PD and DLB (PD: $pFDR < 0.001$, DLB: $pFDR < 0.001$). While no sleep parameters were significantly associated with global cognition (MMSE), reduced REM sleep proportion was associated with poorer performance in executive function ($\beta = -0.038$, $p = 0.006$), and cognitive flexibility ($\beta = -0.079$, $p = 0.013$) across Lewy body diseases.

Conclusions: This study highlights objective sleep alterations are prominent in PD and DLB and REM sleep proportion is associated with deficits in executive function and cognitive flexibility. The observed association between these neuropsychological subdomains and reduced REM sleep proportion suggests that REM sleep disruption may serve as an indirect marker of domain-specific cognitive vulnerability in Lewy body diseases.

Association of Sleep Fragmentation with Inflammatory Markers in Children Experiencing Febrile Seizures

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Introduction: Febrile seizures are the most common type of convulsions in children under five years old and are typically triggered by fever without evidence of intracranial infection. While generally considered benign, various environmental and physiological factors, including sleep disturbances, may influence febrile seizures. Sleep plays a crucial role in modulating immune function, and poor sleep hygiene has been linked to elevated levels of pro-inflammatory cytokines in both adults and children. This study aims to assess the association between sleep habits and serum cytokine levels in pediatric patients with febrile seizures, investigating whether poor sleep hygiene correlates with altered inflammatory profiles.

Materials and methods: From December 2023 to December 2024, blood tests were conducted on patients who visited the pediatric emergency room at Ilan CHA Hospital with febrile seizures as their chief complaint. Among the tests, inflammatory markers, including cytokines, were analysed. Sleep-related data were collected through a self-administered questionnaire on sleep hygiene completed by the patient's guardians. Statistical analysis was performed using SAS software, applying the chi-square, T, Fisher's exact, and Mann-Whitney U tests.

Results: A total of 37 patients with febrile seizures participated in the study, among whom 13 guardians agreed to complete the questionnaire. Among all participants, 24 were male and 13 were female, with an average age of 2.27. All patients had the simple type of febrile seizure, and the average seizure duration was 2.34 minutes. A history of febrile seizures was present in 13 out of 37 patients (35.1%), and a family history of febrile seizures was identified in 9 patients (24.3%). According to the sleep questionnaire, six patients under 6 months experienced sleep fragmentation, while seven did not. In the group with sleep fragmentation, there was no sex difference, while in the group without sleep fragmentation, males were predominant. In the group without sleep fragmentation, none had family members with sleep disorders, and there was no statistically significant relationship between sleep fragmentation and breastfeeding. Most children who participated in the survey had no significant difficulties with weaning soft diet intake, and differences in feeding volume were not statistically significant. Eyeball deviation during seizures was more commonly observed in the sleep-fragmented group, but this was not statistically significant. No significant differences in respiratory or gastrointestinal symptoms were found between the two groups. In the analysis of inflammatory cytokines, IL-4 and IFN-gamma showed no significant differences between the two groups. IL-6 levels were more than twice as high in the group with sleep fragmentation and were statistically significant. IL-10 was also observed to double in the sleep-fragmented group. Although C-reactive protein (CRP)

levels were more than four times higher in the sleep-fragmented group, this finding was not statistically significant.

Conclusions: In this study, patients with febrile seizures who exhibited sleep fragmentation showed significantly elevated levels of IL-6, suggesting a possible link between disrupted sleep and increased inflammatory response. Although other markers such as IL-10 and CRP were also elevated, they did not reach statistical significance. These findings indicate that sleep quality may play a role in modulating inflammation in febrile seizures.

Association of the “Weekend Warrior” and Other Leisure-Time Physical Activity Patterns with epilepsy, migraines, and sleep disorders

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Introduction: The weekend warrior (WW) exercise pattern, where individuals accumulate the recommended 150-minute moderate-to-vigorous physical activity (MVPA) over 1–2 days, has become a popular alternative to daily physical activity routines. This study investigates the association of WW and other leisure-time physical activity patterns with the risk of neurological diseases, specifically epilepsy, migraines, and sleep disorders.

Materials and methods: This study includes data from 93,684 participants, obtained from the UK Biobank. MVPA patterns were categorized into inactive, regularly active, and WW groups. Cox proportional hazards models, restricted cubic splines (RCS) and, Kaplan-Meier curves were used to assess the impact of exercise patterns on the risk of neurological diseases.

Results: Both the WW and regularly active groups exhibited significantly lower risks for epilepsy, migraines, and sleep disorders than the inactive group. The results of RCS curves for these disorders further supported these findings.

Conclusions: The WW pattern offers similar benefits to daily exercise in reducing the risk of neurological disorders, particularly epilepsy, migraines, and sleep disturbances. This finding suggests that WW activity may be a practical and flexible approach to disease prevention in modern societies.

At-home wearable EEG monitoring reveals reduced rapid eye movement sleep in mild cognitive impairment

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Introduction: Early biomarkers of Alzheimer’s disease (AD) are essential for developing effective secondary prevention. Sleep disturbances—particularly in slow wave sleep (SWS) and rapid eye movement (REM) sleep—have been closely linked to AD pathology, including amyloid accumulation and basal forebrain degeneration, both of which can precede dementia diagnosis by several years. Polysomnography (PSG) reveals deficits in SWS and REM sleep in early AD, at the mild cognitive impairment (MCI) stage. However, PSG’s high cost, limited accessibility, and low patient tolerance limit its widespread use in research and clinical settings. In contrast, wearable electroencephalography (EEG) devices offer a more practical and scalable solution for home-based sleep monitoring. Here, we use a wearable EEG device to examine SWS and REM sleep in individuals with MCI and investigate their relationship with cognitive function to test the hypothesis that declines in REM and SWS are associated with cognitive impairment and can differentiate individuals with MCI from cognitively healthy controls.

Materials and methods: Here, we present an interim analysis on 14 participants with MCI due to probable AD (mean $\pm$ SD; 68.9 $\pm$ 8.7 years, 9 female) and 23 cognitively healthy, age-matched controls (mean $\pm$ SD; 70.1 $\pm$ 7.6 years, 12 female) who underwent at-home sleep monitoring for up to six consecutive nights using the Sleep Profiler, a single-channel frontal EEG headband. Sleep stages were automatically scored using U-Sleep, a deep learning algorithm validated against technician-scored PSG data. Cognitive performance was assessed using the Montreal Cognitive Assessment (MoCA) and a

neuropsychological battery covering memory (Optimised Mnemonic Similarity Task), executive function (Digit Span, Digit Symbol Substitution Task, Trail Making Test Part B), and processing speed (Trail Making Test Part A). We compared sleep architecture between groups and examined associations between sleep parameters and cognitive scores, adjusting for age and cognitive status.

Results: Participants with MCI spent a significantly smaller proportion of total sleep time in REM sleep ($p = 0.035$, Cohen's $d = 0.75$) and a greater proportion in light (N1) sleep ($p = 0.033$, $d = 0.76$) compared to controls. No significant group differences were observed for other sleep stages (e.g., SWS; $p = 0.114$, $d = 0.550$). Reduced REM sleep was associated with poorer recognition memory ($b = 0.014$, 95% CI [0.002, 0.026], $p = 0.024$) and slower processing speed ($b = -2.90$, 95% CI [-5.22, -0.57], $p = 0.016$). No significant associations were found between SWS and any cognitive variables (e.g., recognition memory; $b = 0.008$, 95% CI [-0.003, 0.019], $p = 0.142$).

Conclusions: Wearable EEG provides a practical method for detecting sleep alterations in MCI. REM, rather than SWS, was reduced in MCI. These changes may reflect early AD-related neurodegeneration, supporting REM sleep as a promising biomarker for AD risk and highlighting the potential of home-based, non-invasive sleep monitoring as a tool for early AD detection.

BETWEEN SLEEP AND SORROWS: CASE REPORT ON NARCOLEPSY

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Introduction: Narcolepsy is a chronic neurological sleep disorder that often manifests during adolescence or early adulthood, but its subtle and overlapping symptoms can lead to delayed or missed diagnoses—particularly in patients also presenting with psychiatric symptoms. In clinical practice, excessive daytime sleepiness, cataplexy, vivid dreams, and sleep-related hallucinations are frequently misattributed to mood disorders, especially depression. This diagnostic overlap poses a significant challenge for clinicians and may result in inadequate treatment. In this case report, we present the complex clinical trajectory of Mikan, a 20-year-old Filipino college student, whose longstanding depressive symptoms masked an underlying diagnosis of narcolepsy.

Objectives: To explore the clinical presentation, diagnosis, and treatment of a 20-year-old female with overlapping depressive symptoms and excessive daytime sleepiness, cataplexy, fragmented sleep, vivid dreams and sleep-related hallucinations.

Materials and methods: This case study follows Mikan, a Filipino first-year college student, who first sought consultation in June 2023 at the Adult Outpatient Section. Detailed history taking was conducted. Polysomnography (PSG), test of wakefulness and mean sleep latency tests (MSLT) were done revealing Narcolepsy due to the presence of sleep onset REM periods (SOREMP) and short mean sleep latency of about 5 minutes². Other tests include the HLA-DQB1*06:02 genetic marker testing and the cerebrospinal fluid levels of Hypocretin which are not available in the country². She was started on Methylphenidate 10 mg/tablet 1 tablet and Fluoxetine 20 mg/capsule 1 capsule in the morning. Her repeat post-treatment sleep studies showed resolution of SOREMP but still with MSLT of about 5 minutes showing improvement. She was taught sleep hygiene and sleep diary.

Results: The patient's depressive symptoms such as persistent sadness, poor concentration and appetite, anhedonia, fatigue and suicidal ideations, began at age 11. Social withdrawal and academic decline were evident. By age 13, excessive daytime sleepiness became prominent, with involuntary sleep episodes, cataplexy, vivid dreams, hypnagogic and hypnopompic hallucinations, and fragmented nighttime sleep. Despite extended sleep durations and frequent naps, fatigue persisted. Depressive symptoms remitted partially over time, but the unresolved sleep issues significantly impaired functioning. Two sleep studies were done to confirm the diagnosis of Narcolepsy. With the medications prescribed, she was able to resume functioning and experience relief of symptoms. Sleep diary showed improvement in quality of sleep and mood.

Conclusions: Mikan's case underscores the interplay between psychiatric and sleep disorders, demonstrating how untreated sleep conditions can exacerbate or mimic mental health issues.

Psychiatric disorders are commonly overlapping with symptoms of narcolepsy including the timeline of symptoms which makes diagnosis challenging. Analysis of other studies regarding Narcolepsy

revealed association with psychiatric illnesses¹. Early multidisciplinary evaluation, including sleep studies and psychiatric assessment, is essential for accurate diagnosis and treatment. This case emphasizes the need for increased education about sleep disorders to prevent long-term psychosocial and functional impairment.

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Bridging Cognitive Assessment and Sleep Research: A Validated CDR-SB–MoCA Crosswalk for Alzheimer's Disease and Related Dementia

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Introduction: Sleep disturbances—particularly insomnia—are common in older adults and frequently co-occur with cognitive impairment and Alzheimer's disease (AD). Broadly defined sleep disorders affect 14% to 69% of individuals with Alzheimer's disease (AD), with a pooled prevalence of 39% (95% CI: 30–46%). Despite their high prevalence and clinical relevance, sleep disturbances remain underrepresented in dementia research, in part due to difficulties in harmonizing cognitive assessments across clinical and research settings. Research studies often use the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB), while clinical care relies more on tools like the Montreal Cognitive Assessment (MoCA). This misalignment limits opportunities to study sleep–cognition interactions in aging populations. The National Alzheimer's Coordinating Center (NACC) Uniform Data Set provides a valuable platform to address this issue, offering standardized cognitive assessments alongside clinician-reported sleep variables, including the presence or absence of hypsomnia or insomnia, available since 2015. In this study, we developed and validated bidirectional score conversion tables between CDR-SB and MoCA to enable harmonized interpretation of cognitive severity and to support future research on the relationship between sleep disturbances and cognitive decline.

Materials and methods: We conducted a retrospective, cross-sectional analysis using data from the NACC Uniform Data Set, which includes standardized assessments from 35 U.S.-based Alzheimer's Disease Research Centers. Participants were included if they had at least one visit between January 2015 and September 2024 where both CDR-SB and MoCA were administered on the same day. The final cohort included 23,717 individuals (59,871 visits) spanning normal cognition, mild cognitive impairment (MCI), and dementia. Bidirectional crosswalk tables were created using equipercntile equating with log-linear smoothing. Optimal parameters were selected using mean squared error, Akaike Information Criterion, and Bayesian Information Criterion. Score concordance was assessed via Spearman's rank correlation and Bland-Altman plots. Subgroup analyses were performed in individuals with a primary diagnosis of AD.

Results: CDR-SB and MoCA scores showed a strong inverse correlation (Spearman's $\rho = -0.68$; $p < 0.001$). The crosswalks allowed accurate, bidirectional translation between the instruments, preserving individual rank order, and accounting for non-linearities, as well as floor and ceiling effects, across the full spectrum of cognitive severity. Agreement between observed and converted scores was confirmed by Bland-Altman analysis, showing minimal bias and acceptable limits of agreement. Subgroup results in the AD cohort were consistent with findings from the full sample, supporting generalizability of the conversion framework.

Conclusions: This study provides the first validated, bidirectional crosswalk between CDR-SB and MoCA, addressing a major barrier to cognitive data harmonization across clinical and research settings. The resulting framework enables longitudinal tracking, pooled analyses, and consistent staging across heterogeneous data sources. Future studies will leverage this crosswalk alongside NACC sleep variables to identify and characterize individuals with co-occurring cognitive impairment and sleep disturbances. This integration will facilitate research on the interplay between sleep and cognition in aging and AD, advancing precision in diagnosis, prognosis, and targeted interventions across both cognitive and sleep medicine.

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Characterizing older patients with Obstructive Sleep Apnea at heightened risk of prospective cognitive decline and/or Alzheimer's Disease stage transition

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Introduction: Obstructive Sleep Apnea (OSA) is associated with increased Alzheimer's Disease (AD) risk, with studies showing altered levels of both established and novel biofluid AD biomarkers in cross-sectional and longitudinal analyses. OSA's heterogeneity may explain why not all OSA patients develop cognitive decline. Identifying OSA individuals at heightened risk to develop AD is critical for OSA-AD prevention trials. In 5 separate studies, we investigated the relationships between OSA a) severity measures [study 1 & 2], b) interactive effects with AD biomarkers (amyloid (A), tau (T), neurodegeneration (N) brain markers [study 3 & 4], c) interactive effects with co-occurring vascular risk [study 5], on prospective cognitive decline and AD stage transition

Materials and methods: Studies 1, 2 & 3 included 218, 135 and 143 NL community-dwelling older adults participating in ongoing studies of sleep, aging and memory at NYU, respectively. Study 4 included 1043 participants grouped by biomarker profile, as described by the A/T/N scheme, where "A" refers to aggregated A β , "T" aggregated tau and "N" to neurodegeneration, included 258 NL (OSA+ [A+TN+ n=10, A+/TN- n=6, A-/TN+ n=10, A-/TN- n=6 and OSA- [A+TN+ n=84, A+/TN- n=11, A-/TN+ n=96, A-/TN- n=36]) and 785 MCI (OSA+ [A+TN+ n=35, A+/TN- n=15, A-/TN+ n=25, A-/TN- n=16 and OSA- [A+TN+ n=388, A+/TN- n=28, A-/TN+ n=164, A-/TN- n=114]) **older-adults from Alzheimer's Disease Neuroimaging Initiative cohort.** Study 5 included 98 NL participants characterized by joint OSA and HTN status (OSA+/HTN+; OSA-/HTN+; OSA+/HTN- & OSA-/HTN-). OSA severity measures included characterizations with the apnea hypopnea index (AHI4%) and other novel metrics such as Hypoxic burden (HB), defined as the sum of individual areas under the oxygen desaturation curve, and Ventilatory burden (VB), defined as event-specific area under ventilation signal (mean normalized, area under the mean). Outcome measures included annual rate-of-change in cerebrospinal fluid (CSF) A β 42 levels and global cognition (i.e. episodic memory, language and executive function). AD-stage transition was defined as change from Global Deterioration Scale (GDS) 1 or 2 [NL] at baseline to ≥ 3 [$\geq$ MCI] during follow-up.

Results: Findings from studies 1 and 2 showed all OSA-severity measures associated with cognitive decline and/or longitudinal decreases in CSF A β 42. Strengths of the effects were such that HB>AHI4%>VB. Findings from studies 3 & 4 showed that independent of TN-status (NL and MCI), OSA+/A β + participants were approximately two to four times more likely to progress to MCI/AD ($p<.001$) and progressed six to eighteen months earlier ($p<.001$), compared to other participants combined (i.e. OSA+/A β -, OSA-/A β + and OSA-/A β -). Mixed effects models demonstrated OSA synergism with A β (NL and MCI [$\beta=1.13$, 95%CI, 0.74 to 1.52, and $\beta = 1.18$, 95%CI, 0.82 to 1.54]) respectively, and with tau ([MCI ($\beta = 1.31$, 95%CI, 0.87 to 1.47)], $p< 0.001$ for all. Study 5 showed that the co-occurrence of OSA and hypertension interact synergistically to promote β -Amyloid burden, and global cognitive decline.

Conclusions: In older adults with OSA, the risk and rate of prospective cognitive decline and/or AD stage transition are differentially influenced by the interplay of OSA disease severity, co-occurring AD pathology and vascular risk factors.

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Clinical evidence of Traditional Chinese Medicine for post-stroke sleep disorders

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Introduction: Sleep disorders are prevalent complications among stroke survivors. Current clinical guidelines and expert consensus indicated a limited repertoire of effective interventions, underscoring the urgent need for further research to advance clinical practice. Previous studies have reviewed the literature on Traditional Chinese Medicine (TCM) interventions, specifically Chinese herbal medicine (CHM) and acupuncture, for post-stroke sleep disorders, demonstrating a substantial volume of research and suggesting several potentially beneficial therapeutic approaches. However, a comprehensive review of the overall clinical evidence remains lacking. This study employs an evidence-based approach to systematically collate and appraise modern clinical research on TCM interventions for post-stroke sleep disorders, aiming to establish a robust clinical evidence framework. The findings are intended to inform clinical decision-making and guide future research priorities.

Materials and methods: A comprehensive computerized search was conducted across multiple databases including PubMed, Embase, the Cochrane Library, and Chinese databases (CNKI, Wanfang, VIP, and CBM), to identify clinical studies investigating TCM for post-stroke sleep disorders. Two independent researchers performed literature screening and data extraction. Quantitative analysis (meta-analysis) was applied to randomized controlled trials (RCTs), while qualitative analysis was used for non-randomized studies. The methodological quality of included systematic reviews was assessed using A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2), reporting quality was evaluated using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020, and the risk of bias for RCTs was analyzed using the Cochrane Risk of Bias tool (RoB 1.0).

Results: The final analysis included 13 systematic reviews, 137 RCTs, 13 non-randomized controlled trials, 9 case series, 1 case-control study, and 1 case report. For systematic reviews, AMSTAR 2.0 and PRISMA assessments revealed low overall methodological and reporting quality. The results suggested that TCM showed efficacy in improving subjective sleep quality. Among the RCTs, for post-stroke insomnia, high-quality evidence suggested that acupuncture was superior to sham acupuncture in improving subjective sleep quality. Moderate-to-low quality evidence supported the advantages of CHM and acupuncture, either used alone or in combination with hypnotic, in improving subjective sleep outcomes. Additionally, low-quality evidence suggested that combining CHM with cognitive behavioral therapy for insomnia (CBT-i) yielded better subjective sleep improvements compared to CBT-i alone. For post-stroke sleep apnea, moderate-to-low quality evidence demonstrated that combining CHM or acupuncture with continuous positive airway pressure (CPAP) therapy was more effective than CPAP alone in improving the AHI and blood oxygen saturation. Regarding other post-stroke sleep disorders, low-quality evidence highlighted the potential benefits of acupuncture in improvement of subjective sleep quality and daytime sleepiness.

Conclusions: The review of clinical evidence suggested that TCM interventions (CHM and acupuncture) may improve subjective sleep quality, objective sleep parameters, and reduce daytime sleepiness in patients with post-stroke sleep disorders. However, the overall quality of the available evidence was limited. Future research should prioritize large-scale, high-quality RCTs to strengthen the clinical recommendations of TCM for post-stroke sleep disorders.

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Daytime Sleepiness Screening in Demyelinating Diseases: Utility of the Epworth Sleepiness Scale in MS and NMO

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Introduction: Excessive daytime sleepiness (EDS) is a frequent but underexplored symptom in demyelinating diseases such as multiple sclerosis (MS) and neuromyelitis optica (NMO). It is often mistaken for fatigue but may result from lesions in the diencephalon or brainstem, or from secondary sleep disorders. The Epworth Sleepiness Scale (ESS) is a brief and validated tool that enables practical identification of EDS.

Materials and methods: An observational, cross-sectional, and descriptive study was conducted in MS and NMO patients registered in an institutional database. The ESS was applied via telephone to

patients over 18 years old with a confirmed diagnosis. Those with cognitive impairment, decompensated psychiatric disorders, or no phone contact after three attempts were excluded.

Results: Out of 31 patients (18 with MS, 13 with NMO), 20 (64.5%) were successfully contacted. Of these, 6 (30%) scored ≤ 6 (no EDS). The remaining 14 (70%) showed abnormal sleepiness: 6 (30%) had an ESS >15 (severe sleepiness, referred for polysomnography) and 8 (40%) scored between 7–15 (mild to moderate sleepiness, advised on lifestyle changes). Severe EDS was more frequent among patients with NMO.

Conclusions:

Conclusion

Excessive daytime sleepiness is common in patients with MS and NMO, particularly in the NMO group. The ESS, applied by telephone, is a useful and accessible tool for detecting this symptom and guiding timely clinical interventions. It is low-cost and can be easily integrated into routine evaluations.

Diagnostic Potential of Sleep Spindles in drug-naïve Schizophrenia Using Standard PSG Data: A Retrospective Pilot Study

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Introduction: In 2007, Ferrarelli et al. reported significant reductions in the number, amplitude, and duration of sleep spindles during non-REM stage 2 sleep in patients with schizophrenia. These abnormalities were not observed in non-schizophrenic populations. Further studies have found similar spindle abnormalities in early-onset, drug-naïve patients and even in first-degree relatives. Based on these findings, abnormalities in sleep spindles among drug-naïve patients with schizophrenia have drawn attention as potential diagnostic markers.

In this study, we conducted a pilot analysis using polysomnography (PSG) data obtained with a standard clinical montage from previously recorded drug-naïve Japanese patients with schizophrenia at Kurume University Hospital, aiming to evaluate the diagnostic utility of sleep spindle activity in schizophrenia.

Materials and methods: We analyzed PSG data collected at Kurume University Hospital between January 2001 and December 2025 from seven drug-naïve schizophrenia patients (diagnosed according to DSM-IV and never previously treated with antipsychotic medication) and seven healthy controls. Various spindle parameters—frequency, detection time, duration, and amplitude—were analyzed using spindle detection software and compared across four electrode sites (C3, C4, O1, and O2). Additionally, the effects of an initial administration of 2 mg of risperidone were evaluated.

Results: As a result, the drug-naïve schizophrenia group exhibited significantly lower spindle frequency and detection time, particularly at the C3 electrode site, compared to healthy controls. In particular, the frequency and detection time of fast spindles (12–15 Hz) were markedly reduced in drug-naïve schizophrenia patients (Frequency: Sc = 35.69, HC = 98.25, $p < 0.01$; Detection time: Sc = 242.5, HC = 708.9, $p < 0.01$).

Only slight decreases in these values were observed after risperidone administration.

In drug-naïve patients, ROC curve analyses revealed high diagnostic accuracy, with an AUC of 0.94 for both frequency and detection time of fast spindles. Both specificity values were 1.000. Similarly, the AUC for detection time of total spindles (9–15 Hz) was also 0.94, with a sensitivity of 1.000.

In patients administered risperidone, the AUCs for detection time of total and fast spindles still exceeded 0.7.

Conclusions: This study demonstrated that drug-naïve Japanese patients with schizophrenia exhibit reduced sleep spindle activity, particularly at the C3 electrode site, based on standard PSG data. Fast spindle frequency and detection time demonstrated excellent diagnostic performance, while total spindle detection time contributed to disease exclusion, suggesting their complementary diagnostic utility. The minimal changes observed after risperidone administration support the potential role of sleep spindles as trait markers.

These findings highlight the feasibility of using standard PSG data as a non-invasive tool for the early

detection of schizophrenia. To further validate these results, prospective studies with larger sample sizes using PSG data obtained with standard electrode montages are warranted.

Differential Effects of Pregabalin and Morphine on the Sleep-Wake Cycle and Circadian Rhythms in Mice with Neuropathic Pain

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Introduction: Neuropathic pain is commonly associated with disturbances in sleep architecture and circadian rhythms, leading to fragmented sleep, body temperature fluctuations, and altered locomotion. While pregabalin and morphine are frequently prescribed for neuropathic pain management, their effects on sleep and circadian regulation are poorly understood.

Materials and methods: To identify the effects of spared nerve injury on sleep architecture and circadian rhythms, wireless transmitters were implanted in male and female C57BL/6J mice before nerve injury. Pregabalin (11 mg/kg/day) and morphine (6 mg/kg/day) were continuously administered to male mice via intraperitoneally implanted osmotic minipumps following the injury. At baseline and on post-surgical days 3, 7, and 14, mechanical allodynia was assessed with von Frey filaments and dynamic allodynia with a brush test. Wireless transmitters simultaneously recorded electroencephalogram (EEG), electromyogram (EMG), locomotion, and body temperature at baseline and on post-surgical days 7 and 14.

Results: Nerve injury disrupted the sleep-wake cycle by reducing rapid eye movement (REM) sleep duration during the light phase (the habitual sleeping phase for mice) in both sexes and increasing wakefulness in female mice, without significantly affecting non-REM sleep. Additionally, nerve injury impaired the circadian rhythmicity of locomotion and body temperature. Pregabalin, but not morphine, restored REM sleep to pre-surgical levels and was more effective in restoring rhythmicity of locomotor activity and body temperature than morphine. Furthermore, pregabalin increased sleep spindle occurrence during sleep stage transitions and enhanced the power spectra within the 3.5-5.5 Hz range during REM sleep. Continuous morphine administration did not alter either sleep architecture or microstructure.

Conclusions: Administration of pregabalin, but not morphine, effectively restores REM sleep and circadian rhythms of locomotion and body temperature in a mouse model of neuropathic pain suggesting that pregabalin enhances sleep stability. This renders further support for the preference of pregabalin over morphine in managing neuropathic pain.

Differential Effects of Suvorexant on p-Tau and A β Levels in Human CSF and Plasma

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the deposition of amyloid- β (A β) extracellular plaque and intraneuronal accumulation of phosphorylated tau (p-tau) into neurofibrillary tau tangles. This leads to neuronal loss, cognitive dysfunction, and dementia. Orexin is a neuropeptide involved in regulating sleep-wake cycles that may also play a role in AD pathology. We previously reported that suvorexant (a dual orexin receptor antagonist) acutely decreased tau phosphorylation at threonine-181 (pT181) and A β levels in human cerebrospinal fluid (CSF), but the effect on plasma A β and p-tau was unknown. In this study, we tested the acute effect of suvorexant 20 mg on plasma AD biomarkers and compared to the changes we previously reported in CSF.

Materials and methods: Twenty-five participants aged 45 to 65 years were randomized to placebo (N=13) or suvorexant 20 mg (N=12). Participants had an intrathecal lumbar catheter placed with collection of samples started at 20:00. CSF and plasma were collected every 2 hours for 36 hours. Participants received their first dose of placebo or suvorexant 20 mg at 21:00 (hour 1) and second dose at 21:00 (hour 25) on the second night. The lumbar catheter was removed on day 3 at 08:00.

Results: Suvorexant 20 mg increased the ratio of plasma levels of pT181 to unphosphorylated tau-181 (T181) while having no significant effect on plasma A β levels. Plasma pT181/T181 was ~10–20%

higher in the suvorexant 20 mg group compared to placebo between hours 12–20 (08:00–16:00) when normalized to hour 0. During the period of 08:00–16:00, the area under the curve (AUC) for percent change from hour 0 between plasma pT181/T181 and CSF pT181/T181 showed a significant inverse relationship ($r=0.4246$, $p=0.039$).

Conclusions: Suvorexant acutely decreased CSF pT181/T181 and A β levels, but increased plasma pT181/T181 while plasma A β levels remained unchanged. These results were made in the setting of no significant group differences in multiple sleep measures, suggesting that suvorexant's effect on CNS and plasma p-tau and A β may be due to mechanisms involving orexin signaling pathways that affect tau phosphorylation and clearance mechanisms.

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Exploring the Association Between Heart Rate and Sleep Difficulties Across Postural Changes Following Concussion: Preliminary Observations of an Orthostatic Challenge

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Introduction: Autonomic dysregulation is common in individuals with concussion, often leading to abnormal orthostatic responses. For instance, recently concussed individuals exhibit elevated heart rate (HR) during postural changes, suggesting a shift towards sympathetic overactivation. Furthermore, evidence from non-concussed populations suggests that orthostatic dysregulation increased with age and is more pronounced in females than males. Sleep difficulties, such as longer sleep onset latency, greater variation in sleep time and sleep fragmentation, and overall poorer sleep quality, are also prevalent following concussion. Disrupted sleep has been found to negatively affect autonomic functioning, including orthostatic response with higher effects in older individuals. In turn, autonomic dysregulation may exacerbate sleep problems, potentially creating a bidirectional relationship. This study aims to investigate the association between HR measured across various postural conditions and difficulty falling asleep following concussion, while further exploring potential variations based on age and sex.

Materials and methods: Adults (18–81 years old) with a physician-diagnosed concussion were recruited from a network of interdisciplinary concussion care clinics. During the initial visit, sleep difficulties were documented based on the “trouble falling asleep” item of the Sport Concussion Assessment Tool 6 (SCAT6) Symptom Evaluation (Likert scale: 0 [none] to 6 [severe]). HR was measured during a 70° tilt-table test under two postural conditions at five time points: initial lying (after a 2-minute rest), immediate standing (~15 seconds), and at 1, 2 and 3 minutes after standing. A linear mixed-effects model was conducted to examine how HR was associated with postural conditions, sleep difficulties, age, sex, time since injury and their interactions.

Results: 265 adults (median [IQR]: 34 [26–46] years; 68% female) were included in the analysis. Time since injury (median [IQR]: 23 [16–42] days) was not significantly associated with HR (*all* $p>.050$). HR progressively increased from lying (69.61 ± 12.05 bpm) to immediate standing (79.70 ± 14.77 bpm), continuing to rise at 1- (83.78 ± 14.59 bpm) and 2-minute post-standing (85.26 ± 14.83 bpm), before stabilizing at 3-minute post-standing (84.81 ± 13.66 bpm). Participants reported moderate sleep difficulty scores (median [IQR]: 3 [1–5]). In males, regardless of age, sleep difficulties were not significantly associated with HR while lying ($F(1,77)=2.74$, $p=.102$), but worse sleep difficulties were significantly associated with higher HR during all standing posture conditions (*all* $p\leq.006$). A significant interaction between sleep difficulties, sex, and age ($F(1,231)=4.27$, $p=0.040$) showed that, in females only, older age was significantly associated with lower HR for individuals with low levels of sleep difficulties (scores 0–3; $p<.050$), but this association was not significant for individuals with more severe sleep difficulties (scores 4–6).

Conclusions: These preliminary findings suggest that post-concussion sleep difficulties are associated with increased HR during an orthostatic challenge, with variations observed across sex and age. Future

research should investigate the directionality of the association and the mechanisms underlying these sex-specific effects. Establishing the potential of sleep interventions to improve autonomic regulation following adult concussion represents an important research priority and is essential for advancing clinical care.

Impact of sleep problems and central sensitization in migraine patients

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Introduction: Sleep disorders often coexist with migraine and affect quality of life of migraine patients. Central sensitization (CS) is involved in the severity and pathophysiology of migraine. We investigated the association between coexisting sleep problems, central sensitization (CS), and headache-related disability.

Materials and methods: This study included 215 patients with migraine. Insomnia was defined as a score of 6 or higher on the Pittsburgh Sleep Quality Index, probable REM sleep behavior disorder (pRBD) was defined as a score of 5 or higher on the RBD screening questionnaire, and EDS was defined as a score of 10 or higher on the Epworth Sleepiness Scale. Suspected sleep apnea (SA) was defined as snoring or sleep apnea occurring three or more days per week. RLS was diagnosed based on a questionnaire. CS was assessed using the Central Sensitization Inventory (CSI), and headache-related disability was evaluated using the Migraine Disability Assessment (MIDAS).

Results: RLS, insomnia, EDS, SA, and pRBD were observed in 25.6%, 71.6%, 34.4%, 10.2%, and 21.4% of patients, respectively. At least one sleep problem was observed in 87.0% of patients. In a multinomial logistic regression analysis with no sleep problem as a reference, the MIDAS score was significantly higher in patients with three or more sleep problems. In a mediation analysis, an increase in sleep problems had a direct effect on the MIDAS score, and the CSI score was indirectly involved in this association.

Conclusions: This study showed a significant association between sleep problems, CS, and headache-related disability in migraine patients.

Impaired Central Respiratory Regulation in Hyperacute Lateral Medullary Infarction: Insights from Polysomnographic Analysis in a Case-Matched Study

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Introduction: Acute lateral medullary infarction (LMI) can present with early respiratory failure. Obstructive sleep apnea (OSA) is common in ischemic stroke, and LMI has been linked to sleep-disordered breathing (SDB), especially central sleep apnea (CSA). This study examined polysomnographic abnormalities associated with respiratory distress in hyperacute LMI, comparing findings to matched OSA and central sleep apnea (CSA) patients.

Materials and methods: We analyzed 19 patients with hyperacute LMI (<5 days from onset) confirmed by MRI. After high-likelihood OSA screening, attended overnight polysomnography (PSG) was conducted at an average of 2.1 days post-stroke. Ultimately, 12 LMI patients with significant leisonal symptoms were compared to 7 CSA patients and 36 matched OSA patients (1:3 match for age, gender, BMI, and apnea-hypopnea index [AHI]).

Results: Among 12 LMI patients (11 men, 43.8 ± 8.0 years), mean BMI was 26.4 ± 2.9, and mean AHI was 32.7 ± 18.9. Despite matched AHI severity, LMI patients had significantly higher central AHI (15.2 ± 15.2/hr vs. 1.3 ± 2.5/hr in controls). Lower respiratory arousal index (17.6 ± 13.1 vs. 30.3 ± 16.4 per hour, p < 0.001) and high arousal threshold was more prevalent in LMI patients than OSA group (75.0 vs. 61.1%), while their most respiratory parameters were comparable to CSA patients.

Conclusions: The medullary respiratory center plays a key role in respiratory regulation. In hyperacute LMI, central sleep apnea and impaired respiratory arousal reflex are prominent, even in high-risk OSA patients. Close monitoring and early intervention for CSA in LMI patients are essential, regardless of lesion size, when symptoms are present.

Impaired Recovery Sleep in Aging, Alzheimer's Disease and Lewy Body Disease

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Introduction: Sleep homeostasis is theorized to be governed by the 'Two Process Model' where circadian rhythm (process C) and homeostatic sleep pressure (process S) interact to determine sleep versus wakefulness. Sleep pressure accumulated during prolonged wakefulness increases the duration and intensity of subsequent 'recovery' sleep. Multiple sleep abnormalities are associated with Alzheimer's Disease (AD) dementia and Lewy Body dementia (LBD). This study aimed to determine whether recovery sleep duration and its onset time may also be compromised and explore whether such compromise may arise from abnormalities in process C, S, or their interaction.

Materials and methods: RESTED (Remote Evaluation of Sleep To enhance understanding in Early Dementia) was an observational cohort study with three subgroups: AD Mild Cognitive Impairment (MCI)/dementia, LBD MCI/dementia, and healthy controls (HC). Participants underwent AD/neurodegenerative serum biomarker testing and wrist actigraphy plus daily sleep diaries for 55 nights. Recovery sleep duration was assessed utilising random intercept linear mixed effects models with total sleep time (TST) as the dependent variable. Explanatory variables included preceding night total sleep time as an autoregressive parameter whose estimate (alpha) describes recovery sleep. Negative alpha implies low TST nights are typically followed by higher TST nights, indicating recovery sleep. Interaction terms determined if alpha was affected by participant group or age. Associations between preceding sleep duration and subsequent sleep onset time were assessed in a similarly specified model. Equations reflecting Process C and S were manipulated within a Two Process Model Simulation to determine whether the empirical results could be replicated.

Results: 40 participants (AD=10, LBD=10, HC=20) matched for age and sex completed the study. Alpha was negative in healthy older adults ($\beta=-0.056$, $SE=0.03$, $p=0.083$) indicating an intact compensatory response.

However in AD and LBD cohorts, overall alpha was positive (AD : $\beta=0.263$, $SE=0.05$, $p<0.001$; LBD : $\beta=0.209$, $SE=0.05$, $p<0.001$) indicating a paradoxical response. Phosphorylated-tau₁₈₁/amyloid-beta₄₂ ratio was associated with positive alpha ($\beta=0.063$, $SE=0.022$, $p=0.007$) with other molecular biomarkers of AD pathology demonstrating similar trends. Increasing age was also positively associated with alpha ($\beta=0.011$, $SE=0.004$, $p=0.006$).

Shorter preceding sleep was paradoxically associated with a later sleep onset time in the AD cohort ($\beta=-0.100$, $SE=0.03$, $p=0.006$) with a trend towards a similar relationship in the LBD cohort ($\beta=-0.072$, $SE=0.04$, $p=0.056$). A trend towards the more expected positive association between preceding sleep duration and sleep onset time was found only in the control cohort ($\beta=0.038$, $SE=0.02$, $p=0.104$).

Simulated attenuation of Process C, Process S, or a reduction in sleep threshold within the computational model did not replicate the pattern of these empirical results.

Conclusions: Healthy older adults compensated for shorter sleep with recovery sleep. However, AD, LBD and increasing age impaired recovery sleep in duration and expected time of onset. The strength of the paradoxical relationship in AD / LBD was correlated with markers of AD disease burden.

These results open up new targets to improve sleep in neurodegenerative diseases e.g. targeted behavioral interventions supporting recovery sleep. Finally, our specific disease-related deficits question current conceptual models of homeostatic sleep in these populations.

Induced sleep fragmentation enhances epileptic activity in focal epilepsy: a combined intracranial EEG and polysomnography study

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Introduction: Although complex interactions between sleep and epilepsy have been reported, the directionality of the link between sleep fragmentation and epileptic activity remains poorly understood. To address this critical gap in knowledge, we investigated causality in this relationship by experimentally manipulating sleep stability in individuals with focal epilepsy. Using targeted auditory stimulation to induce sleep arousals, alongside intracranial electroencephalography (EEG) recordings and polysomnography (PSG), we assessed the direct impact of sleep fragmentation on the rates and propagation of interictal epileptiform discharges (IEDs).

Materials and methods: We prospectively recruited 20 adult patients with drug-resistant focal epilepsy undergoing combined stereo-EEG (SEEG) and PSG (scalp EEG, EOG and EMG) as part of their presurgical evaluation. Three patients were excluded from analysis due to technical issues with the auditory stimulation protocol or abnormal sleep patterns that made sleep scoring unreliable, leaving 17 patients for inclusion (8 females, mean age: 37.2 ± 8.1 years). All participants underwent a combined SEEG-PSG night in which the first half entailed sleep fragmentation consisting of induced arousals. Arousals were induced during stable NREM or REM sleep, by delivering auditory stimuli (1 kHz tones, 40-100 dB, 5 s) with reference to real-time PSG-based sleep scoring. We compared the normalised IED counts and number of propagation channels across 3-s periods: the pre-stimulus baseline and either the post-arousal onset time window, or the post-stimulus time window when auditory stimulation did not induce arousals (control). We also examined whether anatomical location (neocortical vs mesiotemporal channels), seizure onset zone (SOZ) involvement (SOZ vs non-SOZ channels) and sleep stage (N2 vs N3 sleep) modulates the relationship between induced arousals and epileptic activity.

Results: Across patients, 25.9 ± 8.9 arousals (median ± interquartile range) were induced by auditory stimulation. Normalised IED counts were significantly increased during the arousal time window compared to the pre-stimulus baseline ($p=0.00059$, Cliff's $d=0.65$), an effect not observed when auditory stimuli failed to evoke arousals ($p=0.070$). We then investigated which factors might modulate the relationship between evoked arousals and interictal discharge activity. Significant effects were observed in neocortical channels ($p=0.00059$, Cliff's $d=0.66$), outside the SOZ ($p=0.00049$, Cliff's $d=0.53$), and in N2 sleep ($p=0.0022$, Cliff's $d=0.61$). In contrast, IED propagation did not show a significant overall change during evoked arousals compared to the pre-stimulus baseline ($p=0.25$).

Conclusions: Our findings demonstrate that experimentally induced sleep fragmentation acutely enhances epileptic spiking, primarily in the neocortex, outside the SOZ and during NREM stage 2 sleep. In contrast, the propagation of epileptic spikes is not influenced by evoked arousals. This suggests that transient sleep arousals selectively enhance local cortical excitability without adequately engaging broader network dynamics required for spike propagation. Taken together, these results highlight that sleep stabilisation is a promising therapeutic avenue for suppressing sleep-related interictal activity in drug-resistant epilepsy by targeting local cortical hyperexcitability.

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International recommendations for sleep and circadian research in aging and Alzheimer's disease: a Delphi consensus study

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Introduction: Sleep and circadian disturbances are highly prevalent among individuals with Alzheimer’s disease (AD) and related dementias, often manifesting years before diagnosis, and could represent a modifiable risk factor for dementia. However, sleep was not formally classified as such in the latest Lancet Commission report of modifiable dementia risk factors. Although there has been a proliferation of research on sleep in the context of aging and dementia over the last decades, consensus guidance is needed to facilitate high-quality research, comparability and consistency. In this context, the *Sleep and Circadian Rhythms Professional Interest Area (PIA)* of the International Society to Advance Alzheimer’s Research and Treatment (ISTAART) conducted an expert consensus study to establish recommendations to harmonize future research efforts in the field.

Materials and methods: A modified Delphi consensus approach was used to establish recommendations. Between December 2022 and September 2023, a steering committee (SC) of 18 experts in the field of sleep, aging and dementia was constituted by invitation of the 2022-2024 chair of the ISTAART Sleep and Circadian Rhythms PIA (Prof. Sharon Naismith). The SC designed the questions and outcomes of an online survey, and the first voting round was open between November 2023 and February 2024 to all PIA members (n~480) and non-member researchers. A second online voting round occurred in May 2024 for questions which did not reach consensus in Round 1 or needed clarity, based on the SC’s recommendations. In July 2024, the results were presented to the SC during a virtual meeting. Final recommendations were discussed during the 2024 Alzheimer’s Association International Conference, and were then approved by all SC members.

Results: Forty complete responses were received during the first round of the Delphi process (12 countries; 60% women; mean years of experience in research: 13). Thirty-eight participants agreed to be contacted again for the second Delphi round, and 32 complete responses were received. After two voting rounds, the group determined by consensus: 1) the most relevant sleep and circadian features to assess in the context of aging and dementia research, 2) recommendations on data acquisition and report in older populations with and without cognitive deficits (including on the use of newly-developed wearable and nearable devices), and 3) high-priority future research directions in the field, including which knowledge gaps should be addressed and which sleep and circadian features, populations and designs should be prioritized.

Conclusions: Final consensus recommendations provide guidance to develop high-quality sleep and circadian research in the context of aging and dementia, and synergize future research to improve comparability and clarity within the field. Similar recommendations will need to be established for clinical practice.

Investigation of Factors that Impact the Accuracy of Auto-detected REM Sleep with Atonia

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Introduction: Accurate, automated detection of rapid-eye-movement (REM) sleep without atonia (RSWA), a prodromal biomarker for alpha-synuclein-related neurodegeneration derived from chin and arm electromyograph (EMG) signal, would enable population-based studies to be conducted inexpensively and conveniently on large samples of REM sleep behavior disorder and Parkinson disease patients compared with healthy controls. This study investigates two factors that could impact the auto-detected RSWA accuracy acquired in the home, i.e., the auto-staging of REM sleep from the frontalis region, and rejection of RSWA during periods with artifact.

Materials and methods: Twenty-three women and 12 men (ages 71.5 ± 8.5 years, 30 diagnosed with mild cognitive impairment and 5 with Alzheimer's dementia) completed two-night in-home Sleep Profiler™ recordings with chin and arm EMG, while 10 participants repeated the procedure one-year later, for a total of 45 "MCI/AD" recordings. A second cohort of 3 women and 11 men with isolated REM sleep behavior disorder (iRBD) were studied for one (n=8) or two-nights (n=6), with chin EMG missing in one case.

Recordings were auto-scored for REM sleep and RSWA using previously described procedures ("auto"), and then visually edited for accuracy ("edited"). The edited studies were processed a third time to reject chin RSWA that overlapped with snoring ≥ 60 dB and/or head movement ("clean").

The total number of 3-second REM mini-epochs (ME) and those with RSWA were tallied across nights when available, and RSWA densities computed by condition. Bland-Altman plots identified biases resulting from edits to the auto-scoring. Abnormal RSWA densities were based on the previously validated thresholds for the chin ($\geq 15\%$), arm (≥ 12.5) and either chin or arm ("any" $\geq 25\%$).

Results: Editing of auto-staged REM reduced total REM Chin-MEs by 90 ± 596 , Arm-MEs by 138 ± 572 , and Any-MEs by 37 ± 149 in MCI/AD cohort, contributing to a Chin-RSWA bias of $0.2 \pm 1.6\%$, Arm-RSWA bias of $0.6 \pm 2.5\%$, and Any-RSWA bias of $0.9 \pm 2.7\%$.

In the iRBD group editing of REM sleep increased total Chin-ME by 170 ± 335 , Arm-ME by 330 ± 633 , and Any-MEs by 117 ± 182 , resulting in a Chin-RSWA bias of $-3.2 \pm 9.4\%$, Arm-RSWA bias of -1.1 ± 5.0 , and Any-RSWA bias of $-1.6 \pm 7.9\%$.

Across three conditions, the proportion of MCI/AD cases with abnormal Chin-RSWA was auto=31%, edited=29% and clean=16%, Arm-RSWA was auto=9% and edited/clean=4%, and Any-RSWA was auto=16% and edited=18% and clean=16%. Only one of the 7 cases with abnormal clean chin-RSWA had concurrent abnormal Arm-RSWA.

In the iRBD group, the proportions with abnormal chin-RSWA were auto=69%, edited=77% and clean=77%, while Arm-RSWA was auto=77% and edited/clean=86%, and Any-RSWA was auto=71%, edited=79% and clean=79%. In one case, a normal Chin-RSWA density classification likely resulted from only 89 total Chin-MEs.

Conclusions: Despite over-reporting auto-staged REM sleep in the MCI/AD group and under-reporting REM in the iRBD group, the distribution of cases with abnormal RSWA densities were similar before and after editing. Rules that rejected Chin-RSWA during periods with snoring or movement had the greatest impact on abnormal RSWA density distributions, reducing the number of presumed false-positive RSWA cases in the MCI/AD group while having no impact on abnormal Chin-RSWA or Amy-RSWA distributions in the iRBD group.

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Locus coeruleus inhibition in tau transgenic mice to treat neuropsychiatric and sleep disturbances in Alzheimer's disease

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Introduction: Alzheimer's disease (AD) is a prominent neurodegenerative disorder affecting more than 55 million people globally, with almost all patients experiencing, alongside cognitive decline, neuropsychiatric symptoms like agitation, apathy or sleep dysfunction. These symptoms are highly challenging to manage. Tauopathy develops in the locus coeruleus (LC) up to decades before AD symptom onset. LC activation mediates the stress response and since LC inactivation is required for induction of REM sleep, we hypothesised inhibiting the LC improves neuropsychiatric symptoms and sleep dysfunction in a mouse model of AD tauopathy. This was tested using pharmacological and chemogenetic inhibition/silencing approaches. For the former, we chronically dosed an orexin 1 receptor (OX1R) antagonist, since OX1Rs are highly expressed on LC neurons and gate excitatory LC input. Then, we used DREADD technology to directly silence LC activity. Olanzapine, a commonly used antipsychotic, was used as a comparator.

Materials and methods: Experiment 1: 64 male and female PS19 mice and wild-type (WT) littermates (8.75-9.5 mo) were dosed daily (p.o.) with the selective, orally available, brain penetrant OX1R antagonist, 1-SORA-51 (60 mg/kg/d) or vehicle (TPGS). Experiment 2: 80 PS19xTH-Cre mice (7-9 mo) underwent bilateral LC injections of hM4Di, an inhibitory DREADD, packaged in an adenovirus vector (AAV-DJ). After 4 weeks, to allow expression of the DREADD construct, mice were dosed daily (i.p.) with either the DREADD agonist J60 (0.01 mg/kg/d), olanzapine (3 mg/kg/d) or vehicle (saline). In both experiments, anxiety- and depressive-like symptoms were assessed using a battery of behavioural tests and polysomnography (PSG) for vigilance states.

Results: 1-SORA-51 reduced hyperlocomotion, as measured by total distance travelled, in male tau transgenic mice (3210.9 mm vs 2072.5 mm) whereas olanzapine did so in both male (7174.0 mm vs 1295.0 mm) and female (3654.6 mm vs 2229.2 mm) PS19 mice. Preliminary analyses suggest J60 administration had weaker effects on depressive- or anxiety-like behaviours than 1-SORA-51 or olanzapine. Both sexes of PS19 mice displayed prominent hyperarousal, as illustrated by a loss, in average percent per hour during the dark/active phase, in total REM (1.3% vs 2.4% in WT) and NREM (25.2% vs 32.3% in WT) and markedly increased wakefulness (73.5% vs 65.2% in WT). Unexpectedly, 1-SORA-51 exacerbated REM sleep deficits (2.2% vs 1.3%) following 2 weeks of treatment in male PS19 mice, however, memory performance was unaffected.

Conclusions: Broad pharmacological inhibition of OX1Rs appeared to be promising in alleviating anxiety-like psychiatric symptoms in PS19 mice, without producing the sedative effects of olanzapine, while the more restricted chemogenetic inhibition of the LC was less effective. Whether this was due to modulation of OX1Rs outside of the LC, or a dominant requirement to modulate LC inputs rather than outputs, is an intriguing question. While OX1R antagonism worsened REM sleep deficits, it did not

negatively affect cognitive performance, suggesting it as a novel and effective daytime treatment option for anxiety-like symptoms in AD.

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Motor Sleep Inertia and Activity-Based Prospective Memory in Early Multiple Sclerosis: An Actigraphic Study

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system, marked by significant clinical heterogeneity. The most common form at onset is relapsing-remitting MS (RRMS). Patients with early-stage RRMS (diagnosed within 24 months) may show increased motor activity around 5:00 a.m., possibly due to hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis. While sleep disturbances have been increasingly studied in MS, transitional sleep–wake dynamics—such as sleep inertia (SI)—remain underexplored. Although actigraphy has been used to study SI in healthy individuals, it has not been widely applied to MS populations. Given MS-related motor and cognitive changes, characterizing SI could offer insight into real-life functioning. Cognitive symptoms are also common in MS. Among these, prospective memory (PM)—the ability to remember to perform intended actions in the future—is particularly relevant, as it plays a key role in daily life, such as remembering to take medications. In this study, PM was assessed through an activity-based task: participants wore an actigraph and were asked to press the event marker upon the last morning awakening. We measured the PM efficiency (in percentage) and the latency between get-up time and button press and its association with motor SI.

Aims:

1. To investigate differences between MS patients and healthy controls (HC) in terms of motor sleep inertia;
2. To assess whether the percentage of accuracy in the PM task differs between HC and individuals with early-stage RRMS;
3. To explore the relationship between motor sleep inertia and performance on the activity-based PM task in both groups.

Materials and methods: We enrolled 35 patients with RRMS (24 females; mean age 31.4 ± 7.74) and 30 HC (21 females; mean age 29 ± 7.07). Participants wore Micro MotionloggerWatch devices on non-dominant wrist for seven consecutive days, pressing the event marker to signal bedtime and wake-up. Data were analyzed using the Action W-2® software, version 2.7.1.

Results: A functional linear model comparing post-wake motor activity in the first 60 minutes (1) revealed a similar pattern across groups, though MS participants showed reduced motor sleep inertia in the first ~10 minutes after morning awakening, suggesting faster motor reactivation. In the PM task (2), both groups showed high compliance, with HC showing slightly higher accuracy (91.4%) than MS (87.7%), though the difference was not statistically significant. FLM analysis showed a broader time window of association between early motor activity and task latency in MS (3), suggesting that reduced inertia correlates with better performance.

Conclusions: Our results indicate (1) reduced motor sleep inertia in individuals with MS, possibly reflecting a heightened adrenal response characteristic of early stages of the disease. This reduced motor inertia appears to (2) be accompanied by a preserved activity-based prospective memory, as MS participants were able to perform the cognitive task at a level comparable to HC. Furthermore, (3) FLM analysis showed that higher early motor activation was associated with faster task initiation in both groups. Notably, the MS group once again exhibited lower sleep inertia compared to HC, and as sleep inertia decreased, task performance improved, resulting in prospective-memory task shorter latency.

Multicenter study on the effect of CPAP on cognitive function in patients with mild cognitive impairment and Alzheimer's disease with OSA (DemCPAP): presentation of the protocol and preliminary data

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Introduction: Obstructive sleep apnea (OSA) is associated with an increased risk of Alzheimer's disease (AD) and its progression. Some studies suggest that continuous positive airway pressure (CPAP) therapy can delay cognitive decline and improve sleep quality in Mild Cognitive Impairment (MCI) and AD. However, large, prospective studies with long-term follow-up are needed to confirm these findings. The DemCPAP study, initiated in April 2024, is enrolling participants to address this gap. The primary objective is to assess, over a 3-year follow-up, the effects of CPAP on cognitive function in patients with amnesic MCI and mild-to-moderate AD who have moderate-to-severe OSA (Group A). These patients will be compared to two control groups: Group B, with the same pathologies where CPAP is not possible or adequate due to patient or caregiver difficulties, and Group C, consisting of patients with MCI or AD without OSA. Secondary objectives include evaluating the impact of CPAP on sleep quality, sleep quantity, and daytime sleepiness. The tertiary objective involves assessing changes in plasma AD biomarkers.

Materials and methods: DemCPAP is a multicenter, prospective study conducted across eight Italian centers specializing in dementia and sleep disorders. The coordinating center is the Sleep Medicine Center, department of neurology at Villa Serena Hospital, Pescara, Italy. The study protocol has been approved by the relevant ethical committees. Patients with amnesic MCI and AD will be enrolled based on specific diagnostic criteria, with the requirement for a valid caregiver. In cases of atypical presentation, biomarker confirmation is required. OSA diagnosis will follow the third edition of the International Classification of Sleep Disorders (ICSD). CPAP titration and treatment will adhere to established guidelines. Baseline assessments include neuropsychological and somnological testing, the Psychomotor Vigilance Task (PVT), polysomnography (PSG), ApoE polymorphism analysis, AD biomarkers (Aβ₄₂, Aβ_{42/40} ratio, TAU), and brain MRI with Scheltens' and Fazekas scales. Participants will be categorized into "cases" (Group A) or "controls" (Groups B and C) based on PSG results and CPAP adherence, assessed three months after titration. A second PSG will evaluate OSA control during CPAP ventilation. At six months, participants will repeat a reduced set of neuropsychological and somnological tests. At 12 and 24 months, extended assessments will be performed, including PVT and reassessment of blood biomarkers at 12 months. At 36 months, extended evaluations and a new brain MRI will be done. In Group A, CPAP adherence will be monitored at each time point.

Results: 28 patients have been enrolled, 27% AD and 73% MCI with OSA present in 54% of MCI and 75% of AD patients. OSA prevalence has been detected in male MCI patients, no sex prevalence in AD. Good CPAP adherence has been observed at three months post-titration in both MCI and AD patients, with no dropouts recorded. Moreover, 18 patients have already been screened for enrollment.

Conclusions: CPAP treatment and good adherence in AD and MCI patients with OSA are expected to improve sleep quality, reduce daytime sleepiness, potentially reduce conversion from MCI to AD, and also improve the clinical course in AD.

Narcolepsy-like symptoms in a 31-year-old male with X-linked adrenoleukodystrophy

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Introduction: X-Linked adrenoleukodystrophy (X-ALD) is a rare inherited neurodegenerative disease, caused by congenital defect in the ATP-binding cassette transporters subfamily D member 1 gene (ABCD1). The mutation is responsible for defective peroxisomal oxidation of very long chain fatty acids, which accumulate in the cells of the central nervous system, testes and adrenal cortex. The typical clinical features of X-ALD include cerebral demyelination, adrenomyeloneuropathy and primary adrenal insufficiency. While the neurological and endocrine features of the disease are well-characterized, data about the impact of the disturbance on sleep and wakefulness among those patients are scarce. We present a case of X-ALD with prominent sleep disturbance, including excessive daytime sleepiness (EDS) and narcolepsy-like symptoms.

Materials and methods: Unattended home-based polysomnography (PSG) was performed using NOX A1 PSG systems, followed by an in-lab multiple sleep-latency test (MSLT). Prior to the PSG a 14-day actigraphy was conducted. The patient was referred to a neurologist and medical geneticist for further evaluation. Genetic testing was carried out through sequence analysis utilizing the Blueprint Genetics (BpG) Leukodystrophy and Leukoencephalopathy Panel.

Results: The patient is a 31-year-old male with primary hypoadosteronism, presenting with chief complaints of EDS, loss of muscle tone upon laughter, and disrupted sleep with enuresis. Objective examination demonstrated spastic gait, lower limb muscle weakness, and persistent ataxia. Wrist-worn actigraphy recording revealed irregular sleep-wake pattern with multiple daytime naps and nocturnal wakefulness episodes. The PSG showed an impaired sleep architecture with decreased REM sleep (13.9%), increased N3 stage (36.3%), increased wake after sleep onset (WASO) of 146.2 min, and periodic limb movements index (PLMI) of 76.2/h. In addition, the arousal index was significantly increased (20.1/h), with arousals being associated with limb movements. The MSLT demonstrated significantly reduced average sleep-onset latency (SOL) of 2 minutes, and one sleep-onset period (SOREMP), indicative of pathological sleepiness. The patient showed difficulty maintaining wakefulness between sessions and had difficulties awakening from sleep, although without signs of sleep inertia. He refused lumbar puncture and cerebrospinal fluid testing for hypocretin levels. The genetic analysis revealed a hemizygous missense variant ABCD1 c.773T>C, p.(Leu258Pro), which is pathogenic for X-ALD.

Conclusions: To the best of our knowledge, this is the first detailed description and analysis of sleep parameters in a patient with X-ALD. It reveals atypical manifestation of X-ALD, presenting with hypersomnolence and altered sleep architecture, including SOREMPs and pathologically reduced SOL. These findings resemble the clinical and electrophysiological characteristics of narcolepsy, highlighting the importance of a broader differential diagnoses in patients with EDS. While narcolepsy remains the primary consideration, the underlying neurologic and endocrine features should be thoroughly investigated and considered as important differential diagnostic markers. This case underscores the importance of evaluating sleep-related symptoms in patients with X-ALD and contributes to the extension of its clinical spectrum.

Neuroimaging findings for poor sleepers after acquired brain injury

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Introduction: Stroke and trauma are the top causes of acquired brain injury (ABI) and more than half of this population suffer from some form of sleep disturbance, which causes caregiver distress and is a treatment challenge. Poor sleep after ABI also hinders participation in rehabilitation activities and therefore, may have an adverse impact on outcomes both directly and indirectly. There is emerging literature on neuroimaging findings of healthy individuals with poor sleep, and studies linking neuroimaging with poor sleep and cognition. However, little is known about neuroimaging findings of poor sleep in people with known structural brain damage after an ABI. The primary aim of the present study is to examine differences in structural and functional Magnetic Resonance Imaging (MRI) findings between ABI patients with poor sleep and those with normal sleep. The secondary aim is to correlate the neuroimaging findings with clinical outcomes of ABI patients.

Materials and methods: 25 patients with ABI were recruited within 3 months of index event concurrently with 49 age and gender-matched healthy controls and underwent baseline assessment involving mood and sleep questionnaires and cognitive tests. 11 ABI patients and 17 controls underwent objective sleep testing because they scored >5 on the Pittsburgh Sleep Quality Index (PSQI). 14 ABI and 40 controls were eligible and completed MRI brain that included structural and resting state functional sequences. Data analysis involved comparing ABI poor sleepers with ABI normal sleepers and comparing ABI poor sleepers with healthy control poor sleepers. Resting state functional MRI data was analyzed using FSL MELODIC to identify important networks common to both ABI poor sleepers and ABI normal sleepers, before being further analyzed with the dual regression to reveal differences in those networks between the two groups.

Results: Preliminary analysis shows differences in the sensorimotor network, default mode network, and cerebellar regions when comparing ABI poor sleepers with ABI normal sleepers. Further analysis ongoing.

Conclusions: Poor sleep after ABI may have a direct impact on brain structure and function, which may correlate with poorer clinical outcomes such as poorer cognitive function. Further work is required to examine if these neuroimaging changes are reversible after successful sleep treatment and whether outcomes can be improved after reversal of these changes.

Non-invasive detection of Hippocampal Interictal Epileptiform Discharges in Epilepsy and Mild Cognitive Impairment Using Zygomatic EEG During Sleep

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Introduction: Interictal epileptiform discharges (IEDs), occurring predominantly during NREM sleep, can disrupt memory consolidation and may contribute to cognitive decline in epilepsy and other neurological disorders. IEDs in the hippocampus and medial temporal lobe (MTL) may also occur in some individuals with amnesic Mild Cognitive Impairment (aMCI), which often represents a prodromal stage of Alzheimer's disease. However, this remains controversial since non-invasive detection of IEDs in deep medial brain regions is extremely challenging via visual annotation. The aim of this study was to develop a quantitative method for non-invasive detection of MTL IEDs to test their occurrence in aMCI during sleep.

Materials and methods: We present an automatic machine learning (ML)-based tool to non-invasively detect and quantify MTL IEDs. We develop and validate the method against ground truth in epilepsy patients, and then apply it in aMCI patients. First, intracranial MTL IEDs from 50 neurosurgical epilepsy patients in three separate medical centers, were detected according to annotations by neurologists. An XGBoost model was trained on simultaneous overnight intracranial EEG and zygomatic EEG ('zEEG', EEG electrodes placed on the upper cheekbone). Second, the model was validated using non-invasive overnight zEEG data in a separate cohort of 44 subjects, including individuals with mesial temporal lobe epilepsy (MTLE) and age-matched healthy controls. Finally, we applied the trained model to overnight zEEG data from 50 elderly participants, including both individuals with aMCI and age-matched healthy controls.

Results: The model successfully detected over 15% of MTL IEDs via zEEG with a precision exceeding 80% in test data, successfully generalizing to new individuals (leave one out approach). We found that MTL IEDs that were successfully detected via zEEG were associated with significantly higher amplitude and spatial spread as recorded intracranially, and that MTL IEDs were associated with pathological burst firing of MTL neurons. Furthermore, the model for detecting MTL IEDs was significantly different than a model trained to detect IEDs in the medial frontal lobe. During validation, IED event rates extracted automatically from zEEG, without any visual inspection, effectively distinguished MTLE patients from healthy controls ($p < 0.0001$). When applied to elderly participants, the model revealed a significantly ($p < 0.018$) higher rate of putative IEDs in individuals with aMCI (age = 71 ± 7 , MoCA = 22 ± 3) compared to healthy controls (age = 70 ± 5 , MoCA = 27 ± 2). Furthermore, there was a significant negative correlation ($r = -0.38, p < 0.01$) between the rate of putative IEDs identified by the model and MoCA scores in both healthy participants and individuals with aMCI.

Conclusions: Our work advances early diagnostics by enabling non-invasive detection of deep brain epileptiform activity during sleep, offering new biomarkers for intervention and disease monitoring.

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Optimising Positive Airway Pressure (PAP) Therapy in a Patient with Cervical Spinal Cord Injury and Untreated Severe Obstructive Sleep Apnoea (OSA): A Case Report

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Introduction: Sleep disordered breathing is common in individuals with spinal cord injuries (SCI). This often contributing to impaired rehabilitation outcomes. We present a case of a patient with previously diagnosed but untreated severe OSA, who sustained a cervical SCI. He subsequently underwent intensive rehabilitation in the Ventilatory Rehabilitation Unit, was successfully initiated on PAP therapy and had with improvement in functional outcomes.

Materials and methods: A case report of a patient with untreated severe OSA managed in a ventilatory rehabilitation unit following cervical spinal injury.

Results: A 52-year-old male with known severe OSA which was confirmed by polysomnography: Apnoea-Hypopnoea Index [AHI] 91.8, Oxygen Desaturation Index [ODI] 87.9, nadir SpO₂ 58%. He had had previously declined Positive Airway Pressure (PAP) therapy due to the great discomfort he experienced with PAP therapy.

He presented to the hospital after sustaining from a fall from a chair, with resultant tetraparesis. Magnetic Resonance Imaging of the cervical spine showed cervical spondylosis and degenerative disc

disease, worse at C3-4 to C5-C6 with moderate spinal canal and moderate to severe bilateral foraminal stenosis. He then underwent surgical decompression and instrumentation of his cervical spine before he was transferred to a rehabilitation centre for intensive tertiary rehabilitation.

On admission to the rehabilitation centre, his demonstrated improvement in his strength and had residual mild weakness in his limbs.

During his stay in the rehabilitation centre, he was noted to have daytime somnolence which significantly impaired his engagement in therapy. History revealed that he fell from the chair as he dozed off while sitting on the chair. Examination revealed a body mass index (BMI) of 40 kg/m², neck circumference of 38.5 cm, Epworth sleepiness scale (ESS) of 19 and STOP-BANG Score 7.

He was re-counselled and agreed for initiation of PAP therapy. Initial autoCPAP (10–12 cmH₂O) was poorly tolerated due to discomfort. He could only tolerate PAP therapy for up to 2 hours a night. This prompted reduction to CPAP 5 cmH₂O. Concurrent troubling symptoms of allergic rhinitis were managed with intranasal corticosteroids and oral antihistamines. As nasal symptoms improved, a structured PAP acclimatisation protocol was implemented. This included adjustment of ramp settings, progressive increase in pressure settings and duration of PAP therapy.

Gradually, the patient achieved improved tolerance, with nightly use extending to 8 hours. Compliance data showed that AHI had reduced to 21. ESS had also improved to 10. He reported marked reduction in daytime somnolence, enabling full participation in physiotherapy. On discharge, he achieved significant improvement in his functional status and required only minimal assistance for ambulation and activities of daily living.

Conclusions: Effective initiation and acclimatisation to PAP therapy in the inpatient setting in this patient not only led to significant improvement in sleep-related symptoms and functional rehabilitation outcomes. This could also reduce his risk of falls which could prevent further injuries.

Structured, individualised PAP therapy acclimatisation with close multidisciplinary support facilitated better adherence, especially in this patient who was previously non-compliant.

Acknowledgments: We would like to thank the multidisciplinary team in the Ventilatory Rehabilitation Unit

Outcomes of poor sleep quality after acquired brain injury in the subacute phase - preliminary data from a longitudinal study

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Introduction: Trauma and stroke are the 2 commonest causes of acquired brain injuries (ABI). Studies show more than 50% of ABI patients experience sleep disturbances. Clinical experience shows that sleep-wake disturbance is one of the most challenging problems to manage as it causes high levels of caregiver distress in both the hospital and the community and does not seem to respond well to available pharmacological treatments even at high doses. In the hospital setting, sleep-wake disturbance is a reason for the use of physical restraints and in the community setting, sleep-wake disturbance is an important reason for institutionalization. Moreover, it is also a major hindrance to participation and progress in rehabilitation efforts. Effective management of these sleep disturbances is therefore a critical need for clinical practice. There are very few studies in current literature that have specifically examined the association between abnormal sleep after ABI and neuropsychiatric outcomes such as mood, behaviour, cognition and overall function. The primary aim of this study was to measure and characterize sleep abnormalities at 3, 6 and 12 months after ABI using both subjective and objective measures, and their impact on neuropsychiatric outcomes.

Materials and methods: 25 adult ABI subjects and 49 healthy controls were recruited and underwent assessment with sleep and mood questionnaires and cognitive tests. Study subjects with a score of 5 or more on Pittsburgh Sleep Quality Index (13 ABI and 22 controls) underwent objective sleep testing

with overnight ambulatory polysomnography, actigraphy monitoring and sleep diary charting for 1 week. Data from subjects with both objective and subjective measures were analyzed and compared.

Results: 1. Frequency of poor sleep quality in ABI patients high (72%), not significantly different from gender-matched control group (67.35%)

2. No difference in objective sleep measures on overnight polysomnography & wrist actigraphy likely due to small sample size & sample heterogeneity

3. ABI patients with poor sleep had poorer performance on sustained attention tests than healthy controls with poor sleep.

Conclusions: Poor sleep in ABI patients may affect cognitive performance in sustained attention.

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Post-stroke sleep disordered breathing and the effect of positive airway pressure treatment. A systematic review and meta-analysis of randomized control trials

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Introduction: Sleep-disordered breathing (SDB), primarily Obstructive Sleep Apnea (OSA) is both a known risk factor of cerebrovascular events and a consequence of them.

OSA negatively impacts cerebrovascular health through blood pressure and heart rate fluctuations. This increases stroke recurrence risk and hinders neuroplasticity. It also impairs cognitive function and mood, often leading to depression and excessive daytime sleepiness.

Positive airway pressure (PAP) therapy is the gold-standard of OSA treatment and existing research shows that PAP therapy benefits stroke survivors with OSA, but findings across studies vary.

The aim of this meta-analysis of Randomized Control Trials was to investigate the favorable outcome of PAP therapy in patients with OSA after a stroke.

Materials and methods: Records were identified from Embase Elsevier Database (Embase, Medline/PubMed, Preprints, PubMed-not-Medline).

The study aimed to investigate the effect of PAP on vascular events, neurological deficit, functional independence, depression, sleepiness and cognitive function.

After screening 72387 records, 21 RCTs were included in the systematic review with 1457 patients with stroke (753 patients in the PAP group and 704 in the standard of care (SOC) or sham-CPAP group)

Results: Recurrent vascular events were evaluated in 7 studies (364 patients under PAP and 274 controls). The recurrent vascular events in the PAP group were significantly lower compared to the control group: OR 0.45 (95% CI 0.28 to 0.78; $p < 0.01$).

Neurological deficit was evaluated in 7 randomized clinical trials (332 patients received PAP and 306 in the control group). A significant improvement was achieved with the application of PAP treatment: OR -0.30 (95% CI -0.47 to -0.14; $p < 0.01$).

Ten studies evaluated functional independence (410 patients in the PAP group and 390 controls). It was shown that PAP treatment did not significantly improve functional independence: OR 0.25 (95% CI -0.11 to 0.60; $p = 0.17$).

Five studies evaluated sleepiness after the application of PAP treatment (106 patients in the PAP group and 107 controls). The application of PAP treatment improved daytime sleepiness OR: -0.96 (95% CI -1.47 to -0.45; $p < 0.01$).

Five studies evaluated improvement of depression (136 patients in the intervention arm and 172 in the control group). Analysis showed that the application of PAP treatment reduced depression levels: OR -0.58, (95% CI -1.05 to -0.11; $p = 0.02$)

Cognitive function was evaluated in 6 studies (166 patients receiving PAP group and 216 controls).

Statistical analysis showed that PAP treatment improved cognitive function: OR1.10 (95% CI 0.35 to 1.86; $p=0.02$).

Conclusions: Positive airway pressure treatment is effective and feasible in patients with stroke.

PAP treatment can reduce recurrent vascular events and improve recovery and rehabilitation of these patients.

Screening of sleep disordered breathing in these patients should not be delayed even in the acute post-stroke phase.

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Prevalence of obstructive sleep apnea and screening questionnaire performance in highly drug-resistant epilepsy

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Introduction: Obstructive sleep apnea (OSA) is common among patients with drug-resistant epilepsy (DRE); however, data are limited for those with highly drug-resistant epilepsy (HDRE), defined as requiring three or more antiepileptic drugs. This study aimed to determine the prevalence of OSA in patients with HDRE and to evaluate the performance of existing screening questionnaires to identify the most suitable tool for assessing OSA risk.

Materials and methods: We conducted a cross-sectional study in 41 adults with HDRE. All participants underwent overnight polysomnography (PSG) and completed five screening questionnaires: STOP-BANG, SA-SDQ, Berlin Questionnaire, NoSAS, and NH-OSA. The discriminatory performance of each tool was assessed using receiver operating characteristic (ROC) curve analysis. A novel scoring model BANGS was developed using logistic regression.

Results: The prevalence of OSA was 75.6%, with severity classified as mild (26.8%), moderate (29.3%), and severe (19.5%). For an apnea-hypopnea index (AHI) ≥ 5 , the STOP-BANG questionnaire demonstrated the highest area under the curve (AUC) at 0.771 (95% CI: 0.62–0.92), with 74.2% sensitivity and 80% specificity. The newly developed BANGS score, based on BMI ≥ 23 , age ≥ 40 , neck circumference ≥ 40 cm, male gender, and snoring, achieved 71.4% sensitivity and 100% specificity for predicting moderate-to-severe OSA.

Conclusions: This is the first study to report OSA prevalence in patients with HDRE, revealing a notably high rate. Nearly half of the patients had moderate-to-severe OSA. STOP-BANG demonstrated acceptable diagnostic performance, while the BANGS score showed strong specificity and may serve as a useful screening tool. Routine OSA screening should be considered in patients with HDRE.

Rare Pediatric Genes: A Case of Obstructive Sleep Apnea in a Patient with Cornelia de Lange

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Introduction: Cornelia de Lange syndrome (CdLS) is a rare genetic disorder affecting 1 in 10,000 newborns. It is characterized by growth restriction, developmental delays, and high rates of various comorbid conditions. Approximately 25% of individuals with CdLS experience epilepsy, for which vagal nerve stimulators (VNS) can be used as a treatment. However, VNS has been associated with obstructive sleep apnea (OSA) through various mechanisms including decreased airflow and change in respiratory effort. This report highlights a CdLS patient with OSA initially attributed to VNS implantation.

Materials and methods: A 13-year-old male with a history of CdLS, chronic epilepsy managed with VNS, and a history of adenotonsillectomy at a young age presented to the sleep clinic for OSA management. Two years post-VNS implantation, his epilepsy remained poorly controlled on EEG. Restless sleep and excessive daytime sleepiness (EDS) were quite debilitating and thought to be worsening his seizure burden.

Results: A sleep study was ordered which revealed severe pediatric OSA (apnea-hypopnea index (AHI) of 14.8/h, central apnea index (CAI) of 0.4/h, and oxygen nadir of 81%). Initially, VNS-induced worsening of OSA was suspected, and nighttime VNS settings were adjusted accordingly. His mother reported continued restlessness during sleep, but no witnessed apnea and ongoing sleepiness. Patient underwent repeat adenoidectomy with ENT. Post-operative sleep study confirmed persistent, residual severe OSA (AHI 18.1, RDI 46, oxygen nadir 74%). Post-operative sleep study confirmed persistent severe OSA (AHI 18.1, RDI 46, oxygen nadir 74%). The patient began therapy with APAP 5–15 cm H₂O. Adherence was poor prior to desensitization/education and improved notably thereafter. On APAP, his residual AHI improved to 1.3. Symptoms of hypersomnolence improved drastically with a decrease in seizure burden and resolution of restless sleep. Eventually, a very low dose of modafinil was also trialed with complete resolution of EDS issues, to avoid interaction with metabolism of antiepileptic medications.

Conclusions: This case underscores the complexity of managing OSA in patients with rare syndromes and various comorbidities. While VNS was initially suspected to exacerbate OSA, settings adjustment proved ineffective, highlighting the need for comprehensive evaluation. Despite repeat surgical interventions, PAP therapy ultimately proved to be the most efficacious treatment, demonstrating that even patients with syndromic conditions can achieve effective treatment & adherence with appropriate interventions. Seizure burden and hypersomnolence should be treated aggressively and concurrently to improve quality of life. Adjunct medications for EDS can be utilized as well, with collaboration amongst specialists proving quite useful. Providers must remain informed about the unique needs of the complex pediatric population to deliver optimal care, including those with vagal nerve stimulators.

Rationale and Study Design of Phase-3 Clinical Development Program for Samelisant (SUVN-G3031) in the Treatment of Excessive Daytime Sleepiness in Patients with Narcolepsy

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Introduction: Samelisant (SUVN-G3031) is a potent and selective inverse agonist of the histamine H₃ receptor. It acts by modulating the histaminergic system, which plays a critical role in the regulation of the sleep–wake cycle. Samelisant demonstrated both wake-promoting and anticataplectic effects in animal models of narcolepsy. The objective of the Phase-3 study is to assess the efficacy and safety of Samelisant for the treatment of excessive daytime sleepiness (EDS) in narcolepsy patients.

Materials and methods: Samelisant was evaluated in orexin knockout mice and orexin-B saporin (SAP)-lesioned rats to assess its effects on sleep–wake patterns and cataplexy using electroencephalography (EEG). Samelisant was evaluated as a monotherapy in a Phase-2 proof-of-concept, double-blind, randomized controlled trial (NCT04072380) for the treatment of EDS in patients with narcolepsy, with or without cataplexy. Building on the robust preclinical evidence and positive outcomes from the Phase-2 clinical study, a Phase-3 clinical trial for Samelisant is planned. The design of this proposed study will be outlined in the results section.

Results: In orexin knockout mice, Samelisant significantly increased the time spent in wake period and reduced cataplexy-like episodes. Similarly, in orexin-B SAP-lesioned rats, it demonstrated wake-promoting effects and led to a significant decrease in direct transitions from wakefulness to rapid eye movement sleep (DREM episodes), a hallmark of narcolepsy. In the Phase-2 study, on day 14, Samelisant demonstrated a statistically significant and clinically meaningful reduction of 2.1 points in the Epworth Sleepiness Scale (ESS) total score compared to placebo ($p < 0.024$). The improvement in the primary endpoint was further supported by statistically significant benefits on key secondary endpoints, including the Clinical Global Impression–Severity (CGI-S), Patient Global Impression of Change (PGI-C), and Clinical Global Impression of Change (CGI-C). Samelisant was found to be safe and well tolerated in the study population.

The proposed global Phase-3 study will be a placebo-controlled, double blind randomized, parallel-group study. The study will recruit about 216 narcolepsy patients with an established diagnosis of

narcolepsy according to the ICSD-3-TR or DSM-5-TR. After a screening period of 4-weeks, eligible patients will follow a titration schedule to gradually increase their dose of the investigational product for initial four weeks followed by stable dose treatment for additional eight weeks.

The primary endpoint of the study will be change from Baseline in total ESS score at Week 12.

Secondary endpoints will include change from Baseline in Maintenance of Wakefulness Test (MWT) score, CGI-S score and Narcolepsy Severity Scale (NSS) at Week 12.

Other exploratory endpoints will be change from Baseline in weekly rate of cataplexy (WRC), CGI-C, PGI-C, sustained attention to response task (SART) score and Functional Outcomes of Sleep Questionnaire (FOSQ-10) scores at Week 12.

Conclusions: The Phase-3 study is expected to begin in the second half of 2025. Study results from this Phase-3 study will provide further insight into the therapeutic potential of Samelisant for the treatment of narcolepsy.

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Relationship between polysomnography findings and sleep bruxism in patients with multiple system atrophy

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Introduction: The objective of this study is to analyze the relationship between findings in polysomnography (PSG) and the frequency of sleep bruxism (SB) in patients with multiple system atrophy (MSA).

Materials and methods: We recruited 15 patients with neurological diseases who simultaneously underwent PSG and electromyography (EMG) of the masseter using a wearable device in Fukuoka University Hospital from August 2020 to December 2024. The breakdown of the 15 patients was as follows: 7 with MSA (5 males and 2 females; mean age, 70.3±12.1 years) and 8 with Parkinson's and related disorders (PRD; 6 males and 2 females; mean age, 70.0±13.1 years). The association between findings in PSG and the frequency of SB was analyzed. SB episodes were classified as phasic, tonic, or mixed based on the American Academy of Sleep Medicine criteria.

Results: The mean apnea-hypopnea index (AHI), sleep efficiency (SE, %), and periodic leg movement index (PLMI, /h) were 27.0±21.5, 68.4±11.7, and 52.6±48.5 in the MSA group, and 20.2±5.0, 77.7±11.1, and 4.4±3.1 in the PRD group, respectively. SB (/h), phasic (/night), and tonic (/night) episodes were 27.2±21.4, 73.2±100.7, and 33.7±11.1 in the MSA group, and 33.9±32.8, 110.9±167.3, and 15.0±13.1 in the PRD group, respectively. The frequencies of PLM and tonic episodes in the MSA group were significantly higher than those in the PRD group (p=0.02, p=0.01, respectively). The MSA group showed a significant negative correlation between SE and SB episodes (r = -0.893, p<0.01). The proportion of tonic episodes in SB was 17.6% in the MSA group, which was significantly higher than 7.4% in the PRD group (p < 0.001). There was no significant correlation between tonic episodes and PLMI.

Conclusions: These results suggest the possibility of increasing frequencies of PLM and tonic episodes, and of reducing the quality of sleep with the occurrence of SB in patients with MSA.

Rest-activity rhythm and risk of cognitive impairment: A systematic review and meta-analysis

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Introduction: Although rest-activity rhythm (RAR) disruption is widely recognized as a risk factor for cognition, its influence on cognitive impairment remains unclear. The study is to evaluate the

association of RAR with cognitive impairment, including cognitive decline, mild cognitive impairment (MCI) and dementia.

Materials and methods: Two reviewers systematically searched PubMed, Embase, and PsycInfo for studies published from inception to February 2025, which were observational studies published as full-length articles in peer-reviewed journals related to the association of RAR and cognitive decline, MCI and dementia, and this review followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.

Results: A total of 11 longitudinal studies comprising 97,963 participants were included, with an average follow-up time of 4.95 years. It showed that individuals with lower amplitude (effect size, -0.062; 95% CI, -0.119 to -0.006), higher least active 5-hour period (effect size, 0.060; 95% CI, 0.014 to 0.105), higher intradaily variability (effect size, 0.015; 95% CI, 0.003 to 0.027), and phase-advanced (effect size, 0.114; 95% CI, 0.037 to 0.190) exhibited a higher risk of cognitive impairment. Lower amplitude (effect size, -0.092; 95% CI, -0.155 to -0.029), lower relative amplitude (effect size, -0.078; 95% CI, -0.116 to -0.039), and higher least active 5-hour period (effect size, 0.059; 95% CI, 0.025 to 0.093) were associated with mild cognitive impairment (MCI) and dementia. Lower amplitude (effect size, -0.006; 95% CI, -0.010 to -0.002) was associated with cognitive decline. But no association was found between either the most active 10-hour period or the midline estimating statistic of rhythm and cognitive impairment.

Conclusions: This meta-analysis found that RAR was associated with cognitive impairment. Higher amplitude and regular acrophase were protective factors for cognitive impairment, but higher least active 5-hour period increased the risk of cognitive impairment. The results suggested that a regular circadian rhythm pattern such as high-intensity exercise during daytime and a deep resting state during night could be useful in early-stage cognitive impairment management.

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Sativex (Nabiximols) on the sleep symptoms of agitated late-stage dementia patients - A study comparing questionnaire-based and wearable-based results

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Introduction: Sleep disturbances are common in late-stage dementia patients, especially in those co-morbid with behavioural symptoms such as agitation, causing considerable burden to their caregivers and increasing their own risk of fall. Despite non-pharmacotherapies have been suggested as the first line treatment, these symptoms are by far managed by hypnotics, sedentary antidepressants, or even antipsychotics, which at times cause more harm than benefit to these vulnerable patients. Cannabis and cannabinoids may be a feasible and safer option for sleep problems in this vulnerable population but has not been previously examined in randomised controlled trials.

Materials and methods: This study uses the data from the STAND (Sativex (nabiximols) for the treatment of Agitation & Aggression in Alzheimer's Dementia) trial, which is an 8-week (4 weeks of intervention followed by 4 weeks of observation) randomised, double-blind, placebo-controlled trial conducted in the UK. Nabiximols is a 1:1 mixture oral spray of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), and the trial's protocol, the feasibility study confirming the digital inclusivity of applying wearable device as an auxiliary assessment in this cohort, and the primary outcomes on agitation have been recently published. This study further evaluates nabiximols' effect on the participants' sleep.

Out of the 29 participants living with late-stage dementia, 28 (14 female) who accepted wearing the device with sufficient wearing rate (>80%) were included. The participants' sleep symptoms were assessed with the caregiver-rated sleep item score of the Neuropsychiatry Inventory-Nursing Home version (NPI-NH) at baseline, week 2 and week 4. Device-measured sleep variables, including sleep duration, onset and offset time, efficiency, Wake-After-Sleep-Onset duration and the Sleep Regularity Index (SRI), were calculated using unadjusted GGIR R package. The mean between-arms differences

were estimated using mixed linear models, adjusting for relevant covariates such as age, sex, and severity of dementia.

Results: The prevalence of sleep problem was high at baseline, regardless of the measuring tool (62.1% NPI-sleep item ≥ 4 , and 51.9% actigraphy-measured sleep efficiency $< 85\%$) and the trial group assigned; and the participants in both arms had a very low SRI throughout the trial period (Placebo: 22.3 ± 3.9 during week 1-2, and 24.2 ± 4.3 during week 3-4; nabiximols: 31.2 ± 4.2 during week 1-2, and 28.8 ± 4.7 during week 3-4). Sleep as measured by the NPI-NH sleep item was significantly improved in the nabiximols group compared to the control group from baseline to week 4 ($F_{2,24} = 5.176$, $p=0.009$). However, none of the actigraphy-measured sleep outcomes attained statistical significance between the two arms.

Conclusions: Care home-dwelling late-stage agitated dementia patients appeared to sleep poorly with very low sleep regularity, compared with people with similar dementia severity or of similar age. Despite not sufficiently powered, preliminary NPI-NH-based results of this study suggest sleep symptoms might be ameliorated following 4 weeks of nabiximol treatment. Although the improvements were not corroborated in device-based outcomes, the longitudinal and objective device-based variables provide holistic information regarding the overall circadian rhythmicity change, which might facilitate the development of novel therapeutic targets for late-stage dementia patients.

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Sleep AD: exploring the feasibility of a new approach to sleep research using at-home EEG remotely with people with prodromal and mild Alzheimer's

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Introduction: Modifying sleep quality is an untapped opportunity with potential to delay progression of Alzheimer's disease (AD). Whilst in-laboratory polysomnography remains the gold-standard, the approach is expensive, burdensome and fails to capture a typical night's sleep. The future of sleep trials is home-monitoring with commercially-available electroencephalography (EEG) devices. We aim to identify the optimal approach balancing reliability, comfort, efficiency and accuracy, for AD sleep intervention trials. We previously demonstrated that EEG headbands can be utilised remotely with this cohort, and now seek greater spatial resolution. Sleep AD assessed the feasibility, acceptability and sensitivity of using 32-channel EEG sleep caps remotely. We hypothesised that this would yield behaviourally-relevant sleep neurophysiology sufficient for clinical trials.

Materials and methods: We used a single-centre prospective observational feasibility study design. Participants with Mild Cognitive Impairment or mild AD completed baseline sleep and mood questionnaires, and provided a blood sample for AD biomarker analysis. Recordings were conducted over 3 consecutive nights; researchers attended evenings and mornings to set-up and test/reset equipment. Participants completed a Sleep Consensus Diary and feedback questionnaire. We used Brain Products actiCAP slim sleep caps with 32 active electrodes, and a matching wireless EEG LiveAmp amplifier and battery pack, worn in harness. Participants completed an overnight memory task on the final evening, and had the option to wear a wrist pulse oximeter for nights 2-3.

Results: Of 62 screened, 31 were invited, and 11 recruited. Recruitment stopped early (our original target was $n=50$) when interim analysis proved conclusive. Participants had a mean (SD) age of 71.3 (9.1), 4/11 were female, mean (SD) Montreal Cognitive Assessment score was 18.9 (6.0). One participant withdrew after completing baseline measures. Two completed <3 nights due to kit discomfort. Sleep data was recorded from 10 participants over a total of 28 nights. We achieved optimal recordings on 11/28 (39%) nights; sub-optimal full recordings on 5/28 (17.9%) nights; and partial/no data on 12/28 (42.9%) nights. 91% of optimal recordings were achieved on nights 2-3. On night 1, 90% of participants reported disrupted sleep, primarily due to discomfort. On nights 2-3, sleep ratings improved but mild discomfort/sleep disruption were frequently reported. Overnight memory testing appeared feasible and well-tolerated. Experiences of wearing a pulse oximeter were mixed. Participants reported satisfaction with taking part and liked the home-monitoring approach.

Conclusions: Our approach to use 32-channel sleep caps remotely yielded just 39% of recordings with data sufficiently sensitive for micro-architectural analysis. Data completeness was below expectations and insufficient for intervention trials. Despite iterative set-up improvements, ground/reference signals

were frequently lost due to cap movement or adherence loss; real-time adjustments were not possible remotely. The 3 consecutive night design aimed to provide an adjustment night prior to more typical sleep on subsequent nights. Whilst partially successful, the scheduling was onerous for researchers. Despite withdrawals, feedback was unanimous that the concept of home-monitoring was appealing. We consider the approach of EEG home-monitoring with this cohort worth repeating, if we can develop a reliable and comfortable set-up with an alternative device.

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SLEEP CHANGES AFTER ACQUIRED BRAIN INJURY AND ITS IMPACT ON RECOVERY OUTCOMES - A SCOPING REVIEW OF THE LITERATURE

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Introduction: Background

While sleep and Acquired Brain Injuries (ABI) have an intimate relationship, there are limitations to elucidating the underlying aetiology of sleep disturbances and the effects of sleep on ABI outcomes. Differing disease trajectory, iatrogenic influences and the numerous challenges in sleep research further confound the relationship between sleep and ABI.

Objective

To summarize the research findings of the relationship between acquired brain injury (ABI) and sleep, and the relationship between post-ABI sleep disturbances and ABI outcomes as well as the methodological limitations that would affect the applicability of the results.

Materials and methods: Design

A scoping review was conducted from research published within 5 years from 2019-2023.

Methods

Sources of evidence were PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Cochrane and Embase. MeSH terms used were “**sleep [title] AND stroke [keywords] OR brain injury [keywords]**” in PubMed and adapted accordingly to other search engines. Studies were included if they met the criteria: Adult sample >21 years old; Papers with objective or subjective measures of sleep; Papers published within 5 years from 2019-2023; Papers that measured sleep **after** stroke or brain injury; Unpublished papers (conference abstracts); Translated papers (official translations from other languages); Observational or epidemiological quantitative studies.

Results: Results

The search yielded 4336 articles. After 1472 duplicates were removed, 2864 abstracts were screened. 93 articles were found to meet the inclusion criteria. There were ample descriptions of sleep disturbances measured both subjectively and objectively occurring after stroke, but no convincing elucidation of the extent of causality and causal mechanisms of stroke and disturbed sleep.

There are also convincing correlations between sleep disturbance and poorer stroke outcomes, however the findings suffer from a lack of clarity of which type of sleep disturbance causes which specific outcome and the lack of a plausible causal mechanism.

There is a clear relationship between TBIs and sleep related disorders and symptoms. The wide variety of sleep measures and their combinations allowed for a greater breadth of evidence but the heterogeneity in measures used, and methodologies poses a challenge for direct comparison between studies.

There is also a general direction towards sleep disturbances having significant effects on patient outcomes, of particular interest would be the time taken to recover post-TBI. Patients were also more likely to experience psychological issues like depression and anxiety with poor sleep.

Conclusions: Conclusion

Future research and interventional trials can only proceed after the dilemma between small low-powered studies using precise but resource-heavy measurements and large high-powered studies using imprecise measurements can be satisfactorily resolved, and there is more detailed understanding of post-ABI sleep pathophysiology in humans.

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Sleep Disturbances and Cognitive Functions in Dementia with Lewy Bodies and Alzheimer's Disease

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Introduction: Sleep impairment is prevalent in individuals with Dementia. Dementia with Lewy Bodies (DLB) and Alzheimer's Disease (AD), two most common subtypes of dementia, have different pathogenesis and course. Cognitive decline in DLB is characterized by early visual-spatial and executive dysfunction, with memory being relatively preserved initially, alongside symptoms like fluctuating attention and visual hallucinations. AD presents with early memory loss due to hippocampal involvement, with visual-spatial and executive impairments emerging in later stages. Here, we hypothesize that sleep disturbances and cognitive functions manifest distinctly in these two neurodegenerative conditions due to their unique pathological mechanisms.

Materials and methods: Participants diagnosed with DLB (n=8) and AD (n=10) underwent assessments using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and wore Sleep Profiler™ EEG Sleep Monitors for two consecutive nights at baseline, 6-month follow-up, and/or 12-month follow-up. All paired data were aggregated across subjects for analysis. Sleep metrics such as sleep efficiency, REM sleep percentage, and non-REM hypertonias (NRH) were evaluated. Linear mixed models with a random intercept were applied to assess the relationship between three sleep metrics RBANS subdomain scores. Four models were used to examine the association between 1) sleep efficiency and immediate memory, 2) REM sleep and delayed memory, 3) NRH and attention, and 4) NRH and visuospatial scores, adjusting for age, dementia subtype, and interactions between dementia subtype and sleep metrics.

Results: In the DLB group, higher sleep efficiency was associated with lower immediate memory scores (beta = -0.7, 95% CI -1.2, -0.1, p=0.02), while higher NRH was linked to better attention (beta = 0.9, 95% CI 0.1, 1.7, p=0.03). No significant associations were found between the sleep metrics and RBANS subdomains for the AD group. However, the difference in the association between sleep efficiency and immediate memory between the two dementia groups was statistically significant (p = 0.04), suggesting different sleep-cognitive interactions across dementia types.

Conclusions: The direction of the associations in DLB were opposite of what we predicted. Future studies with larger samples and information about the relationship between longitudinal changes in sleep metrics and cognitive function are necessary to determine whether repeated objective sleep metrics would provide clinically relevant digital sleep biomarker for dementia.

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Sleep EEG Characteristics in People with Parkinson's Disease Dementia: A Retrospective Polysomnographic Analysis

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Introduction:

Dementia prevalence is rising worldwide, with one new case every three seconds and projected global costs of USD 2 trillion by 2030. In Taiwan, 7.54% of adults ≥65 years (about 319,000 cases) are

affected. About 26% of community-dwelling patients experience sleep disturbances, which increase agitation, caregiver burden, and cognitive decline. Insomnia and sleep apnea elevate Alzheimer's and vascular dementia risk (RR 1.49 and 1.47), likely through neuroinflammation, impaired glymphatic clearance, and disrupted sleep–wake cycles. EEG studies show accelerated background slowing in dementia, with increased 8 Hz power and reduced entropy in Alzheimer's disease. Sleep EEG features—architecture, spindles, slow oscillations, coherence—differentiate dementia or MCI from controls, though subtyping remains limited.

This retrospective study (2020–2023) analyzed polysomnographic data from dementia patients at our Sleep Medicine Center to (1) characterize demographics and sleep physiology, (2) strengthen clinical practice, (3) identify research opportunities, and (4) promote cross-disciplinary collaboration.

Materials and methods: This exploratory study included patients with dementia or cognitive impairment confirmed by neurologists/psychiatrists at our hospital. Diagnoses were cross-referenced with ICD-10 codes, and all cases verified in electronic records. Two subprojects were undertaken:

1. Basic Sleep Physiology: Extracted demographics (sex, age, education, dementia type) and polysomnographic measures—total sleep time, latency, stage distribution (N1–REM), sleep events, oxygen saturation, mean heart rate, and periodic limb movement index. Data were de-identified and analyzed descriptively and by ANOVA across subgroups.

2. Sleep EEG Analysis: EEG signals from frontal, central, and occipital regions were processed with computer science support, involving pre-processing, feature extraction, classification, and post-processing. Patterns were compared across dementia subtypes.

Results: Of 46 identified cases, 33 unique remained after excluding duplicates. Records showed 24 cognitively normal individuals, 4 with subjective cognitive decline, 3 with Parkinson's disease (PD), and 2 with epilepsy. The three PD cases were included for further analysis. Preliminary spectral mapping revealed EEG differences across groups, suggesting sleep EEG may serve as a biomarker of dementia-related changes.

Conclusions: Spectral EEG analysis showed group-level differences between PD and controls. PD patients demonstrated altered delta activity and more pronounced theta power changes. Within-group analysis revealed that controls had no significant alpha–beta differences, whereas PD patients showed marked beta reduction relative to alpha. This alpha–beta imbalance may reflect impaired transitions between wakefulness and light sleep, linked to basal ganglia and cortical degeneration. Elevated Theta abnormalities are consistent with prior studies connecting Theta oscillations to cognition and memory, possibly underlying decline and disease progression in PD. These findings reinforce the value of sleep EEG for distinguishing PD dementia from normal aging and for monitoring progression.

This exploratory study highlights spectral EEG features as potential biomarkers for PD dementia. Future directions include predictive modeling of dementia progression, integrating subjective sleep measures with physiological data for risk scores, and applying machine learning to automate dementia subtyping. Despite limitations, the study demonstrates the value of institutional datasets in advancing early diagnostic tools and stratification strategies for dementia care.

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Sleep Efficiency and Short-Term Topographic Memory in Stroke Survivors: Preliminary Results

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Introduction: Sleep plays a critical role in memory and learning tasks. About 90% of stroke patients have sleep disturbances. We have previously demonstrated differential effects of sleep efficiency based on the territory of stroke. This study aimed to assess short term topographical memory consolidation using the Four Mountain Task (4MT) in stroke patients compared to age-matched controls, pre- and post-sleep.

Materials and methods: Ischemic stroke patients (3 months old, chronic phase) and healthy volunteers, underwent the 4MT before and after an overnight polysomnography. The 4MT evaluates short term topographic memory by asking participants to recognize previously seen landscapes with four mountains. Reaction times and accuracy were recorded. Correlation between sleep efficiency and post-sleep task performance was analyzed.

Results: A total of 14 stroke patients and 14 controls were included in the study. The mean age of stroke patients was 47.3 years (SD: 8.4), while controls had a mean age of 44 years (SD: 9.39). Males comprised 50% of the stroke group and 57.1% of the controls. Reaction times improved after sleep in both groups (Patients: 4305 ms to 3920 ms; Controls: 3720 ms to 3345 ms), suggesting sleep-dependent memory improvement. Accuracy remained stable in patients and improved slightly in controls. No significant group differences were noted in overnight change scores. A significant negative correlation ($p = -0.48$, $p = 0.01$) was observed between sleep efficiency and post-sleep reaction time across all participants, suggesting that sleep dependent memory improvement.

Conclusions: Short term topographical memory benefit from sleep in stroke survivors, with reaction time improvements linked to better sleep efficiency. These findings suggest that preserving sleep quality may support cognitive recovery post-stroke.

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Sleep Microarchitecture Disruptions in Ischemic Stroke: Insights from Polysomnography

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Introduction: Sleep microarchitecture, including spindles, K-complexes, and slow waves, plays a critical role in neuroplasticity and recovery. However, alterations in these features following stroke remain underexplored. This study aimed to compare sleep microarchitecture features in ischemic stroke patients versus healthy controls and to identify lesion locations associated with disrupted sleep parameter using voxel-based lesion-symptom mapping (VLSM).

Materials and methods: Ischemic stroke patients (within one month of onset) and healthy controls underwent overnight polysomnography (PSG). Sleep EEG was manually scored using AASM manual 2023 and microarchitecture was analyzed using the YASA toolbox. Spindle features (count, density, amplitude, duration, frequency) and K-complexes were extracted during Stage N2. Slow-wave features (amplitude, slope, duration) were analyzed during Stage N3. REM parameters were also assessed. VLSM analysis was performed in 25 stroke patients using manually segmented lesion masks co-registered to MNI space. Non-parametric mapping with FDR correction ($p < 0.05$) was applied.

Results: Thirty ischemic stroke patients (mean age: 51.4 ± 10.2 years; 20 males, 10 females) within one month of onset and thirty age- and gender-matched healthy controls (mean age: 50.8 ± 9.6 years; 20 males, 10 females) underwent overnight polysomnography (PSG). Stroke patients had significantly lower spindle density (mean: 0.49/min vs. 0.83/min, $p < 0.01$) and amplitude (mean: 11.2 μV vs. 15.4 μV , $p = 0.02$) compared to controls, particularly over fronto-central channels. Spindle count was also reduced (mean: 147.3 vs. 235.7, $p = 0.01$), with decreased average duration (mean: 0.75 s vs. 0.89 s, $p = 0.03$). During N3 sleep, stroke patients exhibited lower slow wave amplitude (mean: 59.2 μV vs. 78.5 μV , $p = 0.01$) and slope (mean: -1.47 $\mu V/ms$ vs. -2.18 $\mu V/ms$, $p = 0.01$). REM density showed a trend toward reduction (mean: 1.9/min vs. 2.6/min, $p = 0.07$). VLSM analysis revealed that reduced sleep efficiency correlated with lesions in the right dorsolateral prefrontal cortex ($Z = 4.85$, 672 voxels), right superior frontal gyrus ($Z = 4.32$), right anterior cingulate cortex ($Z = 4.10$), left inferior parietal lobule ($Z = 3.95$), and right insular cortex ($Z = 3.82$).

Conclusions: Stroke survivors demonstrate disruptions in sleep microarchitecture, particularly in spindles and slow waves. Alterations in sleep efficiency are linked to lesions in frontal and parietal regions regulating attention and arousal. Disruptions of microarchitecture could be a potential biomarker for sleep alterations post stroke.

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Sleep Misperception in Epilepsy Patients with Nocturnal Spiking

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Introduction: Patients with epilepsy frequently experience comorbid insomnia, complicating both conditions. Accurate sleep assessment in this population is crucial for treatment but potentially confounded by spike rate provoking awakenings leading to increased sleep fragmentation. This study enlists three sleep assessment methods (electronic self-report sleep diary, actigraphy, and high-density (hd)EEG-PSG) in patients with epilepsy and insomnia to evaluate the effect of spikes on subjective sleep perception and objective actigraphy measurements compared to the gold standard hdEEG-PSG.

Materials and methods: Participants with focal epilepsy and insomnia underwent hdEEG-PSG “adaptation” and “baseline” sleep recordings 1 week apart. Epileptic spike rate was manually annotated by an epileptologist (MCN). Patients also completed insomnia severity index (ISI) questionnaires, electronic sleep diaries, and actigraphy (Actigraph-wGT3X-BT). hdEEG-PSG was recorded using the 10-10 system and scored using modified AASM criteria in 10-second epochs within SleepWorks (Natus). The parameters of ‘wake after sleep onset’ (WASO), ‘awakenings’, ‘time in bed’ (TIB), ‘total sleep time’ (TST), ‘sleep latency’ (SL), and ‘sleep efficiency’ (SE) were provided by Actilife (Actigraph) software and SleepWorks post-scoring. Sleep diary parameters were based on answering the question of “In total, how long were you awake during the night?” for WASO, duration between participants’ recollection of lights out to last awakening for TIB, TIB minus SL minus WASO for TST, $TST/TIB \times 100$ for SE, and awakenings were taken directly from diary response. Misperception was calculated as $(|X - hdEEG-PSG| / 0.5(X + hdEEG-PSG)) \times 100$ where X is the diary or actigraphy value.

Results: Ongoing recruitment has yielded 5 participants to date – 2 of whom have been fully analyzed (50% female). Patient 1 (P1) had 383 spikes (49.3/hour). P2 had 648 spikes (108.7/hour). P1 had severe insomnia (ISI=22.9). P2 had moderate insomnia (ISI=17.7). Excluding the first night effect (i.e. “adaptation”) and compared to hdEEG-PSG (100%), respective diary and actigraphy responses were severely misperceived for both WASO (P1 136.4%, 35.4%; P2 142.9%, 79.1%) and awakenings (P1 189.4%, 160.7%; P2 182.7%, 174.5%). In contrast, P1 had only below 10% misperception on sleep diary vs. hdEEG-PSG for TST (5.8%) and SE (6.8%); and actigraphy vs. hdEEG-PSG for SE (6%). Similarly, P2 diary vs. hdEEG-PSG for TIB was 5.3%, TST 8.6%, and SE 3.3%; and actigraphy vs. hdEEG-PSG for TIB was 3.9%, TST 9.1%, and SE 5.2%.

Conclusions: Our ongoing research demonstrates that misperception of WASO and awakenings is exacerbated in people with insomnia and epilepsy compared to other sleep parameters when recorded via electronic diaries and actigraphy vs. gold standard hdEEG-PSG. While P2 with moderate insomnia was able to perceive more parameters concordant with hdEEG-PSG than P1 with severe insomnia, P2 was still unable to perceive WASO and number of awakenings precisely. Of note, both subjective diaries and objective actigraphy were unable to correctly identify the number and total duration of awakenings during sleep. Given that epileptic spikes may disrupt sleep quality and continuity, this begs the questions of whether (1) the high nocturnal spike rates in our epilepsy patients preferentially and covertly increase WASO and awakenings, and (2) actigraphy is properly attuned to measuring sleep in those living with epilepsy.

Sleep Research in Children with Autism Spectrum Disorder

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Introduction: Sleep problems are a common comorbidity for children with autism spectrum disorder (ASD) and research in this area has a relatively long history. Within this review, we first outline historic patterns in the field of sleep and ASD. Second, we conducted a systematic update and coded these studies based on their alignment with historic patterns.

Materials and methods: To identify articles for this study, we built and executed comprehensive searches in the bibliographic databases PubMed, PsycINFO (EBSCOhost platform), and Web of Science Core Collection. The search strategy combined terms related to autism and sleep. The “autism” keywords searched included *autism*, *autistic*, *Asperger’s*, and *pervasive developmental disorder not otherwise specified (PDD-NOS)*. The “sleep” keywords included *sleep*, *sleeping*, *circadian*, *waking*, *night*, *melatonin*, *clock gene*, and *rest*. Controlled vocabulary terms for these keywords were included for each database, as appropriate.

Results: Research on ASD and sleep over the past two decades has primarily focused on four principal areas: (1) documenting the prevalence and types of sleep problems, (2) sleep problem treatment options and efficacy, (3) how sleep problems are associated with other behavioral, contextual, or biological elements, and (4) the impact of child sleep problems on families and care providers. The systematic update in this paper includes empirical studies published with terms for sleep and ASD within the title, keywords, or abstract. In sum, 60 studies fit the inclusion/exclusion criteria and most fit within the historic patterns noted above. Notable differences included more global representation in study samples, studies on the impacts of COVID-19, and a growing body of work on sleep problems as an early marker of ASD. The majority of studies focus on correlates of sleep problems noting less optimal behavioral, contextual, and biological elements are associated with sleep problems across development for children with ASD.

Conclusions: Recommendations for future directions include continued expansion of global and age representation across samples, a shift toward more treatment and implementation science, and studies that inform our mechanistic understanding of how sleep and ASD are connected.

Sleep spindles and slow oscillations predict amyloid beta, tau pathology, and cognition in persons with mild to moderate Alzheimer’s Disease

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Introduction: Sleep plays vital roles in brain-health and cognition, including regulating clearance of β -amyloid (A β) and tau proteins that hallmark Alzheimer’s disease (AD). There is a bidirectional relationship between sleep and AD. Changes in sleep physiology can predate cognitive symptoms by decades in AD. Sleep assessments including features of NREM sleep correlated with AD pathology or cognitive decline offer the potential for early, non-invasive screening for AD risk before the onset of clinical symptoms and provide novel therapeutic targets to slow AD progression. However, the majority of available research has investigated associations between NREM sleep physiology and AD pathology or cognition in healthy older adults, but far less is known about *these in persons who already have AD*. It remains unclear which sleep characteristics predict cognitive and neurodegenerative changes after AD onset. Our research addresses these important knowledge gaps for the role of sleep physiology in AD and AD progression.

Materials and methods: Using data from a prospective cohort study of mild-to-moderate AD (n=60, 30 female, mean age 74.7) in Lleida, Spain, we analysed non-rapid eye-movement sleep spindles and slow oscillations (SO) at baseline and their associations with baseline amyloid-beta and tau, and with cognition from baseline to three-years follow-up.

Participants underwent overnight polysomnography (PSG), blood and cerebrospinal fluid draws for amyloid-beta 42, phosphorylated (pTau-181) and total-tau at baseline, and neuropsychological assessment at baseline, 12, 24 and 36 months with the Mini-Mental Status Examination (MMSE), California verbal learning test (CVLT), Rey-Osterrieth Complex Figure Test (ROCF), Alzheimer’s Disease Assessment Scale–Cognitive Subscale (ADAS-Cog).

PSG was scored along American Academy of Sleep Medicine guidelines. Spindle and SO detection were performed using in-house, open-source software packages developed at Concordia University, following Moelle (2011) recommendations for spindles and Staerens's (2015) recommendations for SO. Associations between SO and spindle and SO duration, density, power, amplitude, AD biomarkers, and cognition from baseline to 36 months were investigated with false discovery rate-adjusted generalised linear models, controlling for age, sex, apnoea-hypopnea index.

Results: We found previously unreported associations between spindle characteristics, biomarkers, and cognition in persons with AD. Higher spindle and SO density, duration, amplitude and power predicted significant changes in amyloid-beta 42 ($\beta = 69.3$, $p = 0.001$), phosphorylated (pTau-181) ($\beta = 7.92$, $p = 0.001$) and total-tau, and tau/A β 42 ($\beta = -0.52$, $p = 0.001$), clinically and statistically significantly lower Alzheimer's Disease Assessment Scale Cognitive Subscale (better cognitive performance) ($\beta = -9.0$, $p = 0.001$) and higher Mini-Mental State Examination scores (better cognitive performance) ($\beta = 15.2$, $p = 0.01$) from baseline to 36-months, and significant changes in verbal and visual memory on the ROCF and CVLT. Spindles and SO activity also mediated the effect of pTau181/a β 42 on cognition (41-81%), while pTau181/a β 42 moderated the effect of spindles and SO on cognition.

Conclusions: Our findings demonstrate that spindle and SO activity during sleep constitute predictive and non-invasive biomarkers of neurodegeneration and cognition in AD patients and novel treatment targets for delaying cognitive decline and AD progression. Sleep microarchitecture can, therefore, also provide novel therapeutic targets for preserving brain-health in older adults at risk of AD or in the early stages of AD.

Slow-wave-heart rhythm coupling during sleep in older adults with and without mild cognitive impairment: effects of phase-locked acoustic stimulation

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Introduction: Cognitive dysfunction is a hallmark of neurodegeneration, which is often associated with both cardiac autonomic dysfunction and reduced slow-wave (SW) activity (Chen et al., 2023). Therefore, slow-wave-heart rhythm (SW-HR) coupling, although largely underexplored, may be a promising biomarker for cognitive decline and a therapeutic target. Phase-locked acoustic stimulation (PLAS) of SW activity improves cognition in older adults (Wunderlin et al., 2023). However, little is known about the effects of PLAS on SW-HR coupling. We investigated SW-HR coupling in older adults with mild cognitive impairment (MCI) and without MCI. We further described how PLAS, compared to a sham intervention, affects SW-HR coupling in older adults with mild cognitive impairment (MCI) and without MCI.

Materials and methods: This is a secondary analysis of a partially randomized controlled trial (Wunderlin et al., 2023) including 57 older adults (age: 70.2 ± 4.5 years, 64% women) with MCI (16 participants, 28%) and without MCI (41 participants, 72%), who underwent a baseline nocturnal sleep assessment using high-density EEG (128 electrodes) and full polysomnography. No-MCI group was randomized to three-night PLAS (27 participants, 47%) or sham stimulation (14 participants, 25%), whereas the MCI-group received only three-night PLAS. Three groups were matched by demographics and apnea-hypopnea index. SW-HR coupling was quantified using previously described (Fabus et al., 2024; Naji et al., 2018) and newly conceptualized metrics. We compared SW-HR coupling between the groups and over time within groups on the level of individual electrodes, if applicable. The significance level was set at $\alpha = 0.05$.

Results: This is the first study to comprehensively characterize the cortical topography of brain-heart interactions. Temporal SW-HR coupling was bidirectional and predominantly involved latero-posterior regions. HR was moderately associated with SW amplitude in occipital and right insular regions and weakly with SW globality. At baseline, compared to no-MCI, the MCI group had significantly lower temporal coherence across all cortical areas and weaker coupling of HR with SW amplitude in central regions not reaching statistical significance. In both MCI- and no-MCI group, PLAS significantly decreased temporal SW-HR coherence in fronto-central and posterior regions. In MCI group, PLAS significantly decreased SW-amplitude-HR coupling in posterior and right insular regions. HR coupling with SW-globality followed the overall directional trends without reaching statistical significance.

Conclusions: Our findings extend previous observations implicating posterior and insular brain regions in cardiac autonomic functioning during sleep. The MCI group showed a reduced SW-HR coupling at baseline, suggesting early dysregulation of neurocardiac integration in central frontal networks. PLAS, while reported to enhance the coupling between SW and sleep spindles (Wunderlin et al., 2023), seemed to reduce SW-HR coupling in our analysis, particularly in MCI, which may be related to the limited physiological reserve in response to external modulation. PLAS-induced shifts in autonomic dynamics warrant further investigation of long-term physiological outcomes.

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Subjective-objective sleep discrepancy in older adults with Alzheimer's disease and Lewy body disease

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Introduction: Sleep fragmentation and reduced total sleep time have been reported in aging and neurodegenerative conditions such as Alzheimer's disease (AD) and Lewy body disease (LBD). Such relationships are reliably demonstrated in polysomnography studies, but less consistent patterns are found in studies utilising self-report measures, particularly in cognitively impaired populations potentially subject to recall bias. Here, we aimed to examine the presence and utility of sleep discrepancy (the discordance between subjective and objective measures of sleep) in AD and LBD compared to healthy older adults.

Materials and methods: Adults aged 50 or older with mild cognitive impairment or dementia due to probable AD or LBD and age-matched cognitively unimpaired older adults were enrolled in a prospective cohort study measuring sleep across eight weeks. Subjective sleep quality and subjective estimates of core sleep parameters (total sleep time, sleep efficiency, and sleep latency) were derived from a baseline Pittsburgh Sleep Quality Inventory (PSQI) and compared to mean values of objective parameters derived from 8 weeks of wrist actigraphy complemented by daily digital sleep diaries. The resulting discrepancies were compared across cohorts before being used to predict cohort membership (AD, LBD, or control).

Results: 40 participants (mean age 71 years; probable AD = 10, probable LBD = 10, controls = 20) completed the study, providing a mean of 53 nights of actigraphy per participant. Mean PSQI subjective sleep quality ranked from best to worst in the AD, control and then LBD cohorts, with mean LBD sleep quality significantly worse than AD. However, participants with both AD and LBD generally overestimated their total sleep time and greater sleep efficiency subjectively compared to actigraphy (i.e., underestimated their sleep disturbance). Participants with AD also underestimated their sleep latency. Higher objective sleep efficiency was associated with better subjective sleep quality in the controls, but not in individuals with AD or LBD. Sleep discrepancy for total sleep duration, sleep efficiency, and sleep latency, combined with self-reported subjective sleep quality, discriminated between participant groups with 80% accuracy and was more accurate than subjective or objective measures alone.

Conclusions: Caution is warranted when relying on subjective measures in patients with mild cognitive impairment or dementia due to underestimation of sleep disturbance compared to objective parameters. However, subjective measures combined with wrist actigraphy and digital sleep diaries may have diagnostic utility and provide a more comprehensive profile of sleep than either subjective or objective measures alone. Wrist actigraphy and digital sleep diaries offer a low-cost and convenient pragmatic way to measure naturalistic sleep in older adults with and without cognitive impairment and could be useful in clinically as well as in research settings.

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The interplay between orexin, neurodegeneration, cognition and sleep microarchitecture in mild to moderate Alzheimer's Disease

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Introduction: Cerebrospinal fluid (CSF) orexin levels are higher in MCI and AD and associated with sleep deterioration, increasing risk of cognitive decline and Alzheimer's disease (AD) progression. Orexin-A is a key sleep-wake cycle regulator. Dual orexin receptor antagonists improve sleep in AD and insomnia and may reduce tau and A β deposition in older adults. However, little research has investigated associations between sleep microarchitecture, orexin, neurodegeneration biomarkers, cognitive decline, or mental health in AD. Using data from a prospective cohort study of mild-to-moderate AD (n=60, 30-female, mean age=74.7), we analysed non-REM sleep spindles, slow oscillations (SO), and their associations with CSF orexin, AD biomarkers, cognition, and mental health over three years. Participants underwent polysomnography (PSG) and CSF draws for β -amyloid (A β), ptau181, total tau, orexin, and other biomarkers and at baseline, neuropsychological assessment with the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) and Neuropsychiatric Inventory (NPI) at baseline and 12 months, and Mini-Mental Status Examination (MMSE) at baseline, 12, 24, and 36 months. PSG was scored along American Academy of Sleep Medicine guidelines. Spindle and SO detection were performed using in-house, open-source software packages developed at Concordia University, following Moelle (2011) recommendations for spindles and Staresina's (2015) recommendations for SO. Associations between SO and spindle characteristics (duration, density, power, amplitude) and orexin, A β 42 and tau at baseline, and baseline orexin and cognition from baseline to 36 months were investigated with false discovery rate-adjusted generalised linear models, controlling for age, sex, apnea-hypopnea index.

Materials and methods: Using data from a prospective cohort study of mild-to-moderate AD (n=60, 30-female, mean age=74.7), we analysed non-REM sleep spindles, slow oscillations (SO), and their associations with CSF orexin, AD biomarkers, cognition, and mental health over three years.

Results: We found previously unreported, predictive associations between SO, duration, density, amplitude, and CSF orexin. Orexin also predicted increased ptau181, total-tau, ptau/A β 42, total-tau/A β 42. Increased orexin predicted worse cognitive performance (higher ADAS-cog, lower MMSE) from baseline to 36-months and increased neuropsychiatric symptom severity (NPI) from baseline to 12 months. Orexin also moderates relationships between spindles, SO, cognition, and mental health.

Conclusions: Orexin levels are associated with neurodegeneration biomarkers and cognitive deterioration in AD and moderate relationships between sleep microarchitecture and cognitive changes over time. Orexin may thus constitute a potential target for sleep-related interventions for cognition in neurodegenerative disorders. Sleep microarchitecture, through its associations with orexin and other important biomarkers of brain health, can also provide novel therapeutic targets for preserving brain-health in older adults at risk of AD or in the early stages of AD.

Other

Acoustic Properties of Healthy Vs. OSA Patients

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Introduction: OSA and snoring are prevalent conditions affected by the vocal tract anatomy and physiology. These changes may provide non-invasive markers for diagnosing and differentiating

between OSA and healthy individuals. Comprehensive evaluation of acoustic variations across postures and their clinical implications remains elusive.

Materials and methods: We analyzed audio recordings from 59 patients stratified into three groups: OSA (n=20, 288 recordings), Snoring (n=20, 150 recordings), and Healthy (n=19, 150 recordings). Each patient provided five phonemes (/a/, /i/, /u/, /m/, /n/) in sitting and supine postures, totaling 588 recordings. Acoustic parameters, including fundamental frequencies (FFT and pYIN), vocal stability (jitter, shimmer), spectral characteristics (spectral centroid, flatness), and formant frequencies (F1, F2, F3), were analyzed. Positional effects and group-level differences were evaluated using statistical methods. Machine learning models, including k-Nearest Neighbors (KNN), were applied to assess the diagnostic accuracy of acoustic markers.

Results: The mean fundamental frequency (FFT) across all recordings was 111.29 Hz (± 43.67 Hz), ranging from 8.36 Hz to 194.52 Hz. The mean fundamental frequency (pYIN) was 131.67 Hz (± 22.04 Hz), with a range of 86.32 Hz to 350.25 Hz. Measures of vocal stability indicated a mean jitter of 0.24% ($\pm 0.10\%$) and a shimmer of 3.51% ($\pm 1.81\%$). Spectral features revealed a mean spectral centroid of 1056.14 Hz (± 349.20 Hz), while the mean spectral flatness was 0.0002 (± 0.00036), indicative of tonal characteristics. Formant frequencies averaged F1 = 500.12 Hz (± 120.45 Hz), F2 = 1500.32 Hz (± 220.87 Hz), and F3 = 2500.45 Hz (± 300.14 Hz). Supine recordings exhibited a slightly higher mean spectral centroid compared to sitting, suggesting subtle positional effects. MFCCs, capturing detailed frequency characteristics, exhibited variability, with MFCC1 ranging from -20.45 to 30.15 and MFCC12 from -47.09 to 39.05.

Significant group-level differences were observed in spectral flatness ($F=37.95$, $p<0.001$) and MFCC1 ($F=104.25$, $p<0.001$), with OSA showing distinct patterns compared to Snoring and Healthy groups. Positional effects, particularly MFCC1 mean delta ($F=4.22$, $p=0.020$), further distinguished OSA from others. Among nasal sounds, /m/ demonstrated greater discriminatory power (F_2 , $F=4.84$, $p=0.0096$). The KNN model exhibited superior classification performance (test accuracy: 94%), highlighting the potential of these features for OSA diagnosis.

Conclusions: Acoustic features, particularly MFCC1 and spectral flatness, provide promising markers for distinguishing OSA. Positional changes amplify these distinctions, underscoring the relevance of dynamic assessments. Future research should refine feature extraction and explore larger datasets to enhance diagnostic precision.

A Cross-Sectional Pilot Study on the Craniofacial Markers of Obstructive Sleep Apnea in a South Indian Population

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Introduction:

Obstructive Sleep Apnea (OSA) is a prevalent disorder that results in intermittent upper airway obstruction during sleep, leading to fragmented sleep and systemic effects. Specific anatomical features can predispose individuals to this condition by affecting the patency and stability of the upper airway. Variations in cranial base and maxillary length can influence upper airway morphology and contribute to OSA. Most studies on craniofacial anatomy and OSA have been conducted in Western or East Asian populations. There is a need for research focused on the Indian population to account for ethnic and genetic variations in craniofacial morphology, which can help identify specific risks for obstructive sleep apnea.

Materials and methods:

Study design: Cross-sectional descriptive study

Primary Objective:

To identify craniofacial markers associated with symptomatic obstructive sleep apnea (OSA) in a South Indian population.

Secondary Objective:

To assess the relationship between anthropometric measurements (BMI, waist-hip ratio, neck circumference) and craniofacial markers in patients with symptomatic OSA.

Sample size estimation: Pilot study with thirty patients.

Sampling strategy: Consecutive sampling

d. Inclusion criteria:

- Adults > 18-years of age
- Symptomatic and asymptomatic newly diagnosed OSA individuals were determined by ESS and STOP-BANG scores.
 1. Symptomatic OSA Group: Participants with ESS >7, and diagnosed with OSA confirmed by Level 3 PSG.
 2. Asymptomatic OSA Group: Participants with ESS <7 and no symptoms, though mild OSA may be detected via PSG.

e. Exclusion criteria:

1. Prior treatment for OSA(surgical/PAP therapy)
2. History of craniofacial surgery or trauma
3. Pregnancy

Craniofacial imaging : MRI scan, where in single sequence of T1 SPACE 3D imaging / T1 MPRAGE with a single CT screening image was done.

- Soft palate length (mm)
- Tongue length (mm)
- Retropalatal Distance (Anteroposterior and transverse in mm)
- Retroglossal Distance (Anteroposterior and transverse in mm)
- Submental fat (mm)
- Hyoid – Sella Distance
- Hyoid – Nasion Distance
- Hyoid – Supramental distance.

These measurements were analyzed by the radiologist and correlated with indices of OSA severity.

Results: In the 26 patients included in this analysis, 18 had ESS>7 and 8 had ESS <7.

Continuous variables were described as median and IQR, while the Categorical variables were expressed as proportions.

Mann U test was used to compare the groups. Correlations were assessed using the Kendall Taus test. Majority of the patients were male. There was no statistically significant difference between the baseline characteristics of the two groups.

There was a positive correlation between tongue length, submental fat and the neck circumference.

There was a significant correlation between the hyoid to sella distance and neck circumference.

However this is a pilot study. The present study will be used to power further work exploring the various craniofacial measurements and its impact on the evaluation and management of OSA

Conclusions: There are previous studies performed in caucasian, asian and specifically north indian populations with OSA. However, there are racial and regional differences in craniofacial features. These are likely to have a differential impact on the presentation and course of illness in patients with OSA. Further studies are aimed at developing scientific knowledge in this area of sleep medicine research in India.

Acknowledgments: My Students

An Estimate of Waste Produced by CPAP Treatment in the United States

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Introduction: Obstructive sleep apnea (OSA) is a global public health concern, affecting up to 1 billion people worldwide. While continuous positive airway pressure (CPAP) remains the primary treatment for moderate to severe OSA, it is resource-intensive and generates considerable material waste. In the United States, where an estimated 4.8 million patients are treated with CPAP, the broader healthcare system produces 5.9 million tons of solid waste and 665 million metric tons of CO₂-equivalents annually. The environmental footprint of sleep medicine—particularly CPAP therapy—has not been quantified. The purpose of this study was to inform this discussion by estimating the total solid waste produced by the treatment of moderate-severe OSA with CPAP in the US over a 10 year period.

Materials and methods: We modeled waste generation under a steady-state CPAP-treated population (4.8 million or 24 million patients), assuming an annual 15% exit and entry rate to maintain population stability. Each new patient was assigned a CPAP machine at initiation; existing users contributed waste from ongoing consumable use. Waste calculations included machine and accessory weight (masks, tubing, filters) based on typical published product specifications. We evaluated scenarios by varying mask type distributions (even split of full face, nasal and nasal pillow masks; representative split based on CMS data), tubing type (heated tubing; simple tubing), and machine replacement schedule (every 5 years; every 7 years) to create total waste estimates.

Results: The solid waste associated with the treatment of the 4.8 million patients currently diagnosed with moderate-severe OSA in the US over a 10 year period ranged from 88.718 kilotons to 104.453 kilotons depending on model parameters. The highest amount of waste was produced when patients used climate line tubing and replaced their machine every 5 years, regardless of mask mix (104.408-104.453 kilotons); waste was reduced by 15% when patients used simple tubing and replaced their machines every 7 years (88.718-88.763 kilotons). 64.6% of all waste produced during the 10 year treatment period was due to supply refills (masks, tubing, water reservoirs).

Conclusions: The treatment of OSA with CPAP is a resource-intensive therapy that produces significant plastic and electronic waste, contributing to environmental degradation. Over 10 years, U.S. CPAP use generates ~100 kt of solid waste—less than insulin therapy (~1,019 kt) or hemodialysis (~10,452 kt), but far more than laparoscopic surgery (~25.9 kt). These estimates reflect only the mass of discarded materials and do not capture the full carbon footprint, which would also include upstream emissions from manufacturing, energy use, and transportation. Nevertheless, equipment choices can meaningfully reduce waste. Extending the usable lifespan of CPAP machines and selecting lighter components—such as simple tubing—could reduce total waste by up to 16 kt, or approximately 16% over a decade. These findings highlight the importance of improving medical device durability and advancing circular economy strategies to mitigate the environmental impact of long-term therapies in sleep medicine and beyond.

A Pilot Study of Sleep Measurements in Japanese Infants

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Introduction:

Sleep in early life is crucial for healthy brain development. Nevertheless, the majority of existing studies have focused on adults and school-aged children, and surprisingly little is known about the role of sleep in infants' perceptual, social, and cognitive development. The current study was conducted to serve as a pilot to validate measures of sleep for infants as a foundation for future investigations of the associations between infant sleep and social-cognitive development.

Materials and methods: Twelve infants aged between 2-12 months ($M = 7.82$, $SD = 3.9$; 5 female and 7 male) from Sendai city, Japan, participated in the study. Their sleep was continuously monitored for at

least over a week (min. 7 nights, 8 days) using an actigraphy (Micro Motionlogger®, Ambulatory Monitoring Inc.) with their sleep data analysed by the Sadeh algorithm, with metrics such as total sleep time (TST), sleep efficiency (SE) and wakefulness after sleep onset (WASO) derived. All parents completed the Brief Infant Sleep Questionnaire-Revised (BISQ-R) online and those who habitually tracked infant sleep with a diary were invited to share the records.

Results:

83.33% of the participants reported having a regular habit of tracking their infant's sleep. According to actigraphy measurements, on average, infants spent 52.78% ($SD = 4.38$) of their time asleep. The sample's mean nighttime sleep duration per night was 10 hours 30.76 minutes ($SD = 61.83$) and napping duration per nap was 1 hour 20.39 minutes ($SD = 34.47$). Average nighttime SE was at 92.54% ($SD = 4.10$), and WASO was 50.16 minutes ($SD = 35.74$). 75% of parents underestimated durations of nighttime sleep, at around 3.90% (i.e. 24.60 minutes, $SD = 5.17\%$). However, parents were equally as likely to overestimate and underestimate durations of naps - where on average, parents overestimated the durations of naps by 2.16% (i.e. 1.74 minutes, $SD = 10.96\%$). With nighttime and daytime sleep combined, 75% of parents underestimated their infant's sleep duration, at around 4.36% (i.e. 236.94 minutes, $SD = 6.06\%$). Correlational analysis revealed that better actigraphic sleep efficiency (SE) was positively correlated with healthier parent-reported sleep patterns (BISQ-R infant subscale), $r = .746$, $p = .013$. Parents' sleep monitoring confidence positively correlated with average napping durations per nap, both measured by the actigraphy, $r = .756$, $p = .030$, and reported by the parent, $r = .688$, $p = .028$, suggesting that parents' higher sleep monitoring confidence was associated with longer naps of their infants.

Conclusions: We showed that parental reports relative to actigraphy underestimates nighttime sleep frequency and duration and overestimates daytime sleep duration. A key component of the BISQ-R was found to significantly correlate with objective measures of infant sleep. This pilot work is promising and lays a foundation for future work in the relationship between infant sleep and social-cognitive development, reinforcing the value and potential of parent-reported infant sleep data.

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A Quest for a Histaminergic or Orexinergic Biomarker for Sudden Infant Death Syndrome

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Introduction: Sudden infant death syndrome (SIDS) is defined as the death of an infant under one year of age which occurs during the sleep and remains unexplained after a complete evaluation of death scene, infant history and postmortem investigation. In industrialized countries, SIDS is still the leading cause of post-neonatal death (between one month and one year). The occurrence of SIDS during sleep at a specific developmental period, especially between 2 and 6 months of age, suggests an association with a dysfunction in the maturation of sleep-wake regulation particularly the brain arousal systems. Indeed, polysomnographic recordings have shown that SIDS victims exhibit altered arousability, characterized by fewer arousals at the end of the night and an increased prevalence of incomplete arousals compared to age matched healthy infants. SIDS risk factors, for example, ventral sleep position, bed-sharing, overheating, infections, ante or postnatal cigarette exposure, prematurity have shown to decrease the arousability from sleep. Therefore, the present study investigates whether the

Orexin (Ox) and Histaminergic (HA) systems, two major wake-promoting systems, are altered in SIDS victims.

Materials and methods: In the first part of this study, we evaluated Ox and HA levels in CSF between infants died of SIDS, infants died of known causes (ED) and healthy control infants (C) still alive. CSF samples for Ox measures were collected from 61 controls, 38 SIDS cases and 32 infants died of ED. In the second part, we attempted to assess whether Ox and HA cell numbers are altered in SIDS. 11 SIDS and 8 ED were cell counted in the postmortem posterior hypothalamus following immunocytochemistry of Orexin -A (Ox-A) and histidine-decarboxylase (HDC, the HA synthesizing enzyme). We subdivided the HDC- and Ox-ir neuronal populations into rostral, central and caudal parts in order to quantify their respective cell number and then compare them between SIDS patients and ED control subjects.

Results: Ox levels were not statistically different in dead infants compared to controls infants, and in SIDS compared to ED. However, the decrease in Ox values in controls was not observed between the age of 0-2 months to 2-6 months in died infants ($p=0.02$), explaining higher Ox values between 2-6 months in deceased infants compared to controls ($p=0.04$). The CSF samples for HA measurement were collected from 42 other controls and 52 other SIDS cases. Compared to healthy controls, the HA and its direct metabolite *trans*-methylhistamine (*t*-MeHA) levels were extremely high in SIDS victims likely due to a postmortem cell release. More Ox-ir neurons were found in rostral ($p=0.04$) and caudal ($p=0.03$) subdivisions in SIDS compared ED controls but not in central subdivision ($p=0.60$). However, no difference was observed in terms of their morphology or in the number of HDC-positive neurons in SIDS patients compared to controls in either rostral, medial and caudal parts of the posterior hypothalamus.

Conclusions: Although no dysfunction of these systems was directly demonstrated, the elevated orexin cell counts and CSF levels in SIDS infants suggest an increased orexin release prior to death, potentially due to prolonged or repeated stressors such as hypoxia.

Are occupational therapists' sleep education and professional development needs being met in Aotearoa New Zealand?: Preliminary survey findings

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Introduction: Healthy sleep plays an important role in recovery from illness and injury and in positive rehabilitation outcomes. Good sleep health is also vital for mental and physical health, waking functioning and engagement in purposeful activities, all of which are encompassed in occupational therapy's scope of practice. However, recent US research suggests that most occupational therapists receive little, if any, in the way of undergraduate education on sleep and have limited access to sleep-focused continuing professional development to support their practice. The aim of our study was to investigate how much sleep-focused education and professional development occupational therapists in Aotearoa New Zealand (NZ) currently receive, to help identify unmet needs and inform future sleep education and resource development.

Materials and methods: We developed an online survey in Qualtrics (with a paper-based option) informed by previous international research and adapted for the NZ context. The survey was disseminated via formal and informal occupational therapy networks. Inclusion criteria was being a registered occupational therapist currently practising in NZ. Questions included whether participants received education about sleep in their entry-level occupational therapy programme (yes/no) and, if so, how many hours, plus whether sleep was incorporated in postgraduate occupational therapy studies they had engaged in. Therapists were also asked to report the number of sleep related continuing professional development/education hours they received in the past 2 years and whether occupational therapists in NZ should be better prepared to evaluate and treat sleep after graduation from entry-level occupational therapy programmes (yes/no).

Results: The sample ($n = 116$) comprised 7% Māori (Indigenous) and 93% non-Māori participants with a mean (SD) age of 43.3 (14.1) years. Most (92%) respondents identified as female (8% male), and one fifth had been practising for either 5 years or less (23%) or for more than 30 years (21%). Less than one fifth (18%) of participants reported receiving sleep education in their entry-level occupational therapy

training and, of those who did, 26% estimated this to have been a total of 1 hour, 21% estimated this to have been for 2 to 3 hours and 53% could not remember how much time was dedicated to sleep. Of the 37% of participants who had undertaken postgraduate occupational therapy studies, 13% reported this including a sleep component. Over half (56%) of respondents reported receiving no sleep-related continuing professional development in the last 2 years, 29% received 1 to 2 hours, 9% received 3 to 4 hours, and 7% received 5 or more hours. All participants (100%) who answered the question on whether occupational therapists should be better prepared to evaluate and treat sleep after graduating (n = 101) responded 'yes'.

Conclusions: Preliminary survey findings indicate a need to support occupational therapists via enhanced sleep education and resources spanning the course of therapists' careers. Future research to understand facilitators and barriers to implementing undergraduate and postgraduate sleep education and continuing professional development initiatives is warranted.

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Association between sleep disturbances and cryptogenic ischemic stroke in young adults

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Introduction: Incidence of cryptogenic ischemic stroke (CIS) in young adult is increasing, as are sleep problems including insomnia, poor sleep quality and sleep apnea. We analyzed the association of sleep disturbances, perceived stress and CIS in a large multicenter study.

Materials and methods: Altogether 337 patients (median age 40.6 years, 45.1% women) with a recent CIS and 337 sex- and age-matched stroke-free controls were included. Responses to the Basic Nordic Sleep Questionnaire (BNSQ), Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS)—assessing condition prior stroke—were analyzed. A conditional logistic regression model adjusting for depression, obesity, smoking, physical inactivity, snoring, and stress at work or home was used to assess associations between sleep problems and CIS.

Results: Compared to controls, patients reported more frequent difficulties falling asleep on ≥ 3 days/week (72.7% vs. 47.8%, $p=0.002$), awaking too early in the morning (76.3% vs. 47.8%, $p<0.001$), and poor subjective sleep quality (68.5% vs. 46.8%, $p<0.001$). In conditional logistic regression analysis, poor subjective sleep quality (BNSQ item 6) was independently associated with CIS (OR 2.62, 95% CI 1.03–6.65, $p=0.042$). A combination of stress and total sleep time of 5-6 hours or less showed a strong but statistically trend-level association with CIS (OR 8.05, 95% CI 0.95–68.37, $p=0.056$). Stress alone (OR 1.93, 95% CI 1.10–3.38, $p=0.022$) and current smoking (OR 2.03, 95% CI 1.01–4.06, $p=0.046$) were also significantly associated with stroke. No significant differences were observed in global PSQI or ESS scores between the patients and controls.

Conclusions: Poor subjective sleep quality, stress, and smoking were independently associated with cryptogenic ischemic stroke in young adults. Short sleep together with stress showed a very strong but statistically borderline significant association with CIS. These findings highlight the relevance of modifiable sleep and psychosocial factors in the risk profile of young stroke patients. Association with sleep, stress and stroke risk warrant further investigation.

Association Between Sodium Intake and Risk of Hypertension, Heart Failure, Stroke, and Myocardial Infarction: A Systematic Literature Review and Meta-analysis

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Introduction: Substantial evidence supports a strong relationship between excess sodium consumption and increased cardiovascular morbidity and mortality risk. Accordingly, US and international health and nutritional guidelines recommend limiting dietary sodium intake to reduce the risk of cardiovascular disease. Certain medications can contribute to sodium consumption in excess of recommended limits (<2300mg/day for most adults); for example, some narcolepsy medications contain up to 1640mg of sodium per nightly dosage. This up-to-date systematic literature review (SLR) and meta-analysis qualitatively and quantitatively evaluated the relationship between sodium intake and the risk of hypertension (HTN), stroke, heart failure (HF), and myocardial infarction (MI).

Materials and methods: A comprehensive SLR was conducted using Embase®, MEDLINE®, CENTRAL®, conference proceedings, and clinical trial registries to identify evidence published up to 7 December 2023. Study selection, data extraction, and risk of bias assessments (Cochrane RoB2.0 and Newcastle-Ottawa Scale) were conducted manually by two independent human reviewers. For title and abstract screening, one human reviewer was replaced with an artificial intelligence-based tool (GPT-4). Discrepancies were resolved by a third human reviewer. Studies meeting prespecified PICOS criteria, including observational or interventional designs assessing associations between higher vs lower sodium levels (variably defined across studies) and the incidence of HTN, stroke, HF, or MI in adults (≥18 years) were eligible for meta-analysis. Pooled effect estimates were derived using STATA v18.5 SE. Both fixed-effects and random-effects models were applied to eligible studies in base-case and subgroup (sodium levels assessed via 24-hour urine excretion) analyses. Statistical heterogeneity and publication bias were assessed using the I-square statistic and funnel plots, respectively.

Results: The SLR included 145 studies reporting HTN, stroke, HF, and MI; low risk of bias was observed in most studies. Higher sodium/salt intake was significantly associated with increased risk of HTN (83/102 studies), stroke (15/30), HF (6/7), and MI (3/13). The 74 studies (HTN=59; stroke=9; HF=5; MI=4) eligible for meta-analysis demonstrated that higher sodium intake was significantly associated with increased odds/risk of HTN (odds ratio [OR]: 1.56, 95% confidence interval [CI]: 1.44–1.68), stroke (hazard ratio [HR]: 1.63, 95% CI: 1.28–2.09), HF (HR: 1.48, 95% CI: 1.14–1.94), and MI (OR: 2.97, 95% CI: 1.81–4.86). Subgroup analyses of studies using 24-hour urine excretion to measure sodium were comparable to those observed in the base case for HTN (OR: 2.48, 95% CI: 1.66–3.71) and HF (HR: 1.41, 95% CI: 1.15–1.73). A directionally similar trend to the base case was observed for stroke (HR: 1.39, 95% CI: 0.85–2.30) and MI (OR: 2.62, 95% CI: 0.92–7.46). Statistical heterogeneity was low in MI, moderate in stroke and HF, and high in HTN studies. Funnel plots showed no asymmetry in MI, possible asymmetry in stroke and HF, and substantial asymmetry in HTN studies.

Conclusions: This current SLR and meta-analysis are consistent with and expand the robust evidence base that higher sodium intake is significantly associated with increased risk of HTN, stroke, HF, and MI. Findings support clinical and health authority recommendations to limit sodium intake to mitigate cardiovascular risk.

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Association Between Sodium Intake and Systolic and Diastolic Blood Pressure: A Systematic Literature Review and Meta-analysis

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Introduction: US and international health organisations, including the USDA, AHA, ACC, and WHO, recommend limiting dietary intake of sodium (<2300 mg/day for most adults) to protect cardiovascular health. Chronic use of certain medications can lead to substantially higher sodium consumption, with some narcolepsy treatments containing up to 1640 mg of sodium per 9 g nightly dosage. Despite the well-established evidence that excess sodium intake is directly linked to increased blood pressure, the majority (89%) of US adults consume more sodium than the recommended 2300 mg/day limit. This systematic literature review (SLR) adds to previous SLRs by using more expansive criteria and provides an up-to-date meta-analysis to qualitatively and quantitatively evaluate the relationship between sodium intake and systolic and diastolic blood pressure (SBP; DBP).

Materials and methods: A comprehensive SLR was conducted using Embase®, MEDLINE®, CENTRAL®, conference proceedings, and clinical trial registries to identify evidence published up to 7 December 2023. Study selection, data extraction, and risk of bias assessments (Cochrane RoB 2.0, Newcastle Ottawa Scale) were conducted by two independent reviewers. For the title and abstract screening, one human reviewer was replaced with an artificial intelligence-based tool (GPT-4). Any discrepancies were resolved by a third human reviewer. Studies meeting prespecified PICOS criteria, including observational or interventional designs with ≥ 2 years of follow-up assessing the association between higher vs lower sodium levels (variably defined across studies) and SBP/DBP in adults (≥ 18 years), were eligible for meta-analysis. Pooled effect estimates were derived using STATA v18.5-SE. Both fixed-effects and random-effects models were applied to eligible studies in base-case and subgroup (sodium levels assessed via 24-hour urine excretion) analyses. Statistical heterogeneity and publication bias were assessed using the I-square statistic and funnel plots, respectively.

Results: Fifty-seven studies were included in the SLR irrespective of duration of follow-up; low risk of bias was observed in most studies. Higher sodium/salt intake was significantly associated with an increase in SBP (39/57 studies) and DBP (37/55). Across studies with ≥ 2 years of follow-up eligible for meta-analysis ($n=27$), higher sodium intake was significantly associated with increases in SBP (weighted mean difference [WMD], change from baseline [CFB]: 3.39, 95% confidence interval [CI]: 1.73–5.05 [$n=15$]; WMD, absolute mean difference [AMD]: 4.21, 95% CI: 2.52–5.90 [$n=23$]) and DBP (WMD, CFB: 1.61, 95% CI: 0.61–2.61 [$n=13$]; WMD, AMD: 1.81, 95% CI: 1.30–2.32 [$n=20$]). Subgroup analyses of studies measuring sodium levels with 24-hour urine excretion were similar for AMD in SBP (WMD, AMD: 2.69, 95% CI: 0.43–4.96 [$n=10$]) and DBP (WMD, AMD: 1.33, 95% CI: 0.40–2.26 [$n=10$]), confirming the robustness of the findings. Statistical heterogeneity was high for SBP and DBP; the funnel plot showed moderate asymmetry, suggesting potential publication bias.

Conclusions: This current SLR and meta-analysis confirm and further strengthen the evidence base for the relationship between higher sodium intake and increased blood pressure. Findings underscore the importance of reducing sodium consumption, as recommended by clinical and health authority guidelines, to manage blood pressure and protect cardiovascular health.

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Associations between napping habits with mood and insomnia symptoms in young adult nappers of Hong Kong

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Introduction: While the links between nighttime sleep and mental health are increasingly recognised with converging evidence, the effects of daytime naps remain unclear, with mixed conclusions on whether they are beneficial or detrimental to our mood. This study aims to establish how common napping is among young adults in Hong Kong and to examine whether differences in their napping habits are associated with mood and insomnia symptoms.

Materials and methods: As a part of the Formation and Transformation of Beliefs in Chinese online panel survey study, 1374 young adults (79% female, 82.39% students) aged 18–35 years ($M=22.83$) completed a self-reported questionnaire of their napping patterns across three dimensions (duration, timing, and frequency; as a multiple choice question), negative mood states (Depression Anxiety Stress Scale-21), and insomnia symptoms (Insomnia Severity Index).

Results:

More than half (61.21%) of the participants were considered nappers, who took at least one nap per week. This prevalence was similar between students (61.22%) and workers (61.16%). Paired t-tests revealed significantly higher stress levels, $t(1222.8)=2.788$, $p=.005$, and insomnia symptoms, $t(1191.3)=2.789$, $p=.005$, in non-nappers than nappers, while depression and anxiety levels showed no significant differences between the two groups. ANOVA tests examined the differences in sleep and mood symptoms among nappers with varying napping duration, frequency, and timing. There was a significant effect of napping duration on depression, $F(3,837)=5.989$, $p<.001$, anxiety, $F(3,836)=4.448$,

$p=.004$, stress, $F(3,836)=7.294$, $p<.001$, and insomnia, $F(3,837)=5.329$, $p=.001$. Post hoc Tukey analysis showed that individuals who napped for > 2 hours had higher levels of depression ($p<.001$), anxiety ($p=.003$), stress ($p<.001$), and insomnia ($p=.008$) compared to those who napped for 30-60 minutes. They also had higher anxiety ($p=.012$) and stress ($p<.001$) levels compared to those who napped for < 30 minutes, and higher stress ($p=.027$) compared to those who napped for 1-2 hours. Napping frequency was associated with insomnia symptoms, $F(3,837)=3.395$, $p=.018$, with those napping > 6 times a week reporting more insomnia symptoms than those napping once ($p=.049$) or 4-5 times a week ($p=.015$) - but no significant mood symptom associations. Nap timing showed no significant relationship with depression or anxiety levels, but was significantly associated with insomnia, $F(6,833)=4.818$, $p<.001$, and stress levels, $F(6,833)=2.554$, $p=.019$. Those who napped between 12:00-12:59 reported higher insomnia symptoms than those who napped before 12:00 ($p=.026$) and after 13:00 ($p<.001$). Higher stress levels were reported for those who take naps at 15:00-15:59 compared to 13:00-13:59 ($p=.028$).

Conclusions: Napping was found to be common among young adults in Hong Kong. Non-nappers had significantly more insomnia and mood symptoms than nappers. Sleep and mood symptoms among nappers varied with nap duration, frequency, and timing, with habits such as napping for over 2 hours, more than 6 times per week, or around midday each being linked to negative effects on mood and insomnia.

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Auditory sleep modulation to treat depression

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Introduction: Major depressive disorder (MDD) is a leading cause of reduced quality of life due to illness worldwide. Recent studies suggest that selectively suppressing slow wave sleep (SWS) may induce rapid antidepressant effects. This project examines the impact of SWS suppression (without sleep deprivation) on depressive symptoms, sleep patterns, and brain activity, using auditory stimulation and high-density EEG during sleep. It also tests a synaptic plasticity model of therapeutic sleep deprivation in MDD, assessed via tDCS and TMS protocols.

Materials and methods: The study is a single-centre, doubled-blinded, randomized, sham controlled, repeated measures within-subject (stimulation and sham) clinical trial including 30 patients with MDD and 30 healthy controls (project-ID 2023-01804). Participants take part in four sleep laboratory nights (adaptation, baseline, stimulation and sham in counterbalanced order) and a daytime follow-up assessment. We test the hypothesis that auditory-closed loop suppression of slow wave sleep improves depressive clinical symptomatology (Montgomery-Åsberg Depression Rating Scale, MADRS) compared to sham stimulation and explore indices of brain plasticity.

Results:  A total of 16 participants (14 healthy controls (age = 37.8 ± 5.8 , $f = 8$) and 2 subjects with MDD (age = 41.5 ± 2.5 , $f = 2$) have been included so far in the study and analysis. Results show effect on the healthy controls. Stimulation led to a significant reduction of SWS by about 50%, with an associated increase in sleep stage N1, without significant changes in neither wake duration nor in arousal indices across vigilance states, other changes in architecture across the night. The continuity of SWS as well as wake was reduced. SWA as well as the number of SWs were reduced during SWS, without changes in any other frequency band nor changes in any vigilant state apart from N3. While SWA propensity dissipates across undisturbed sleep, it stayed constant across the night during stimulation, as reflected by a higher accumulation rate of SWE in the second half of the night as compared to sham.

Additionally, TMS and tDCS protocols revealed reduced long-term potentiation (LTP-like) inducibility and increased synaptic strength following a night of SWS suppression compared to an undisturbed night.

Conclusions: Preliminary results of the study demonstrate feasibility and potential efficacy of the protocol. The ongoing study aims to inform future treatment developments.

A Workforce Planning Model for Sleep Medicine Specialist Training Using Mathematical Optimization

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Introduction: Obstructive sleep apnea (OSA) affects about 30% of Singapore's adult population, yet it remains largely underdiagnosed. With anticipated increases in diagnosis and treatment rates, proactive workforce planning for sleep medicine specialists is essential. This study develops a mathematical model assessing the training requirements for sleep physicians to meet the projected demand for OSA treatment.

Materials and methods: Training as a sleep medicine specialist takes 13 years: 6 years of medical school, 3 years of junior residency, 3 years of senior residency, and 1 year of a sleep fellowship. We estimated the demand for sleep physician full-time equivalents (FTEs) using two approaches considering Singapore's projected population: (1) a patient-to-physician ratio based on a South Korean study, OSA prevalence and diagnosis rates in Singapore, and (2) population-to-physician ratios from the US, Australia, and South Korea. A mathematical model was created to estimate required training numbers of sleep physicians, factoring in current sleep physician data and the national retirement age.

Results: Currently, 42 sleep physicians (aged 39-62, mean age 49.6) operate at 0.2 FTE across various departments in Singapore. To meet projected demands for 2043-2062, we assessed training needs from 2025 to 2034. Using a patient-to-physician ratio with a 30% diagnosis rate and 0.5 FTE for new physicians, projected training requirements are 11 (2025-2028), 7 (2029-2031), and 8,12,14 for 2032-2034. If FTEs increase to 0.7, the needs decrease to 8 (2025-2028), 6 (2029-2030), and 5, 4, 11, 10 for 2031-2034.

Conclusions: These findings can aid policymakers in planning sleep medicine specialist capacity to address Singapore's future OSA demand.

Costs and benefits of a Meta and tiktok public campaign to promote the usage of a sleep hygiene phone app

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Introduction:

Social media platforms are a great source of medical information for a general audience. Unfortunately the quality of information is poorly controlled and many instagram or tiktok accounts do not provide reliable links to validated apps or scientific content. Moreover, while social media campaigns are often evaluated for visibility and engagement, their actual cost-effectiveness and impact on health-related behaviors remain underexplored. Leveraging their reach and engagement potential, we developed a targeted social media campaign to promote the use of a mobile application designed to support sleep hygiene. This study examines both the costs and benefits of such a campaign, assessing its ability to drive adoption and sustained use of a sleep hygiene app in a real-world context.

Materials and methods: KANOPEE, a free sleep hygiene app, was made available on the Google Play Store and Apple App Store. A grant from the French Regional Health Agency funded a social media campaign, which ran from January 11, 2023, to May 30, 2025. The campaign consisted of paid ads on META platforms (Facebook, Instagram, Messenger) and TikTok, with short video content explaining the consequences of poor sleep hygiene and the benefits of using KANOPEE. Ads targeted adults aged 18 and older, regardless of gender. Due to GDPR restrictions, these campaigns were traffic-oriented, meaning they were optimized to maximize redirection to the app's download pages without being able to link it to an actual download.

Results:

The total cost of the campaign was €30,000. It reached 14,414,918 people and generated 139,937 redirections to the app download pages, at an average cost-per-click of €0.21. Notably, the cost per redirection varied by platform and operating system: Android users were reached at a lower cost (€0.17) compared to iOS users (€0.60). All age groups were exposed to the campaign, but engagement was highest among individuals aged 55 and older. META platforms primarily reached this senior audience, while TikTok proved more effective in engaging younger demographics.

Conclusions: This study demonstrates that targeted social media campaigns can serve as a cost-effective strategy to promote evidence-based mobile health tools such as KANOPEE. With more than 14 million individuals reached and nearly 140,000 redirections to app download pages, the campaign highlights both the scalability and demographic specificity of digital outreach. Importantly, platform/device-related differences in cost-efficiency underscore the need for tailored strategies when allocating resources. While GDPR-related constraints limited direct measurement of downloads and app use, these findings suggest that social media constitutes a promising avenue to increase awareness and potential adoption of sleep hygiene interventions at the population level.

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Cross-cultural comparison of the association between childcare arrangements and nap duration at age 3.5 in the Quebec (ELDEQ) and French (ELFE) birth cohorts

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Introduction: Nap duration varies across preschool years. No study has investigated associations between childcare arrangements and nap duration between cohorts from different cultural background. Our objective was to examine whether childcare arrangements (1-unstructured with family members, 2-semi-structured in family daycares, 3-structured in a center-based childcares or schools) are associated with nap duration at 3.5 years old.

Materials and methods: Data are based on maternal reports from ELDEQ (n=1950) and ELFE (n=12236). Multinomial logistic regression models were adjusted for child (sex, age, breastfed, nighttime duration, bedtime), maternal (immigrant status, age, education) and family characteristics (siblings, income).

Results: In Quebec, 30% of children attended a structured childcare arrangement compared to 73% of children in France. At 3.5 years old, 37% in Quebec Vs 8% in France took no nap or <1h, 52% in Quebec Vs 58% in France napped from 1h to 2h, and 11% in Quebec Vs 34% in France napped ≥2h. Compared to children in a structured childcare arrangement, children in an unstructured arrangement had 3.26 (Quebec, 95%CI=2.25-4.71) or 5.03 (France, 95%CI=4.26-5.93) times the odds of taking no nap or a short one and children in a semi-structured arrangement had 1.83 (Quebec, 95%CI=1.32-2.53) or 2.16 (France, 95%CI=1.60-2.93) times the odds of taking no nap or a short one compared to children who napped from 1h to 2h. In France, children in an unstructured arrangement had 2.95 (95%CI= 2.65-3.29) times the odds of taking a long nap and children in a semi-structured arrangement had 3.41 (95%CI=2.93-3.97) times the odds of taking a long nap compared to children who napped from 1h to 2h.

Conclusions: Attending a childcare arrangement other than a structured one is associated with short nap duration (Quebec and France) or long nap duration (France) at 3.5 years old compared to children who napped from 1h to 2h.

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Development of search strategies for meta-research related to sleep

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Introduction: Although the number of systematic reviews and meta-analysis published in sleep medicine has been increasing, there is a growing concern regarding their overall reliability and external validity. Recent meta-epidemiological studies demonstrate that the average methodological quality of sleep-related systematic reviews is often poor, therefore impairing the process of evidence synthesis. Developing reliable search strategies is a challenging aspect of systematic reviews, often resulting in methodological biases and impacting their overall quality. Using standardized search strategies is an alternative to prevent methodological biases and increase the quality and reproducibility of systematic reviews. The current study aimed at developing a series of search filters for meta-research in sleep medicine.

Materials and methods: First, a comprehensive list of sleep disorders, conditions, and related topics for which search filters was created. The list included all disorders, isolated symptoms and normal variants disclosed on the International Classification of Sleep Disorders (3rd edition, text revision – ICSD-3-TR), as well as emergent or proposed disorders, and sleep-related conditions not primarily related to a disorder. In some cases, more than one search filter was developed for a single sleep disorder, in order to provide different levels of sensitivity and specificity. All search strategies were design specifically for a PubMed search, by combining controlled vocabulary (Medical Subject Headings terms – MeSH) and free terms, encompassing the disorder name, alternative nomenclature (as disclosed by the ICSD-3-TR), entry terms listed on MeSH, and clinical experience. Each search filter was developed based on an iterative process, being tested, modified and retested until a reasonable sensitivity and specificity is achieved.

Results: In total, 71 sleep-related conditions were listed for the development of search filters. This includes 40 sleep disorders listed in ICSD-3-TR (16.9%), 3 proposed sleep disorders (sexsomnia, upper airway resistance syndrome, and restless sleep disorder – 4.2%), 7 isolated symptoms (9.9%), 6 sleep-related medical or neurological disorders (listed in ICSD-3-TR appendix A – 8.5%), 3 additional conditions (sleep deprivation, chronotype and dreaming – 4.2%), and 12 supracategories, composed by the combination of two or more filters into a conceptual topic (16.9%). In total, 91 search filters were created, as some sleep disorders resulted in more than one search filter. Due to the number and length of the search filters, they cannot be disclosed in the current abstract (for instance, most have more than 100 words and the longest one has 311 words). However, all these search filters are already publicly available at Open Science Framework (<https://osf.io/tdqyp/>).

Conclusions: Efforts towards methodological standardization in sleep-related systematic reviews are needed to ensure the quality and reliability of these studies. Utilizing standardized search filters is an effective way to enhance their accuracy, transparency, and reproducibility. These search filters are valuable supporting tools for researchers aiming at developing their own systematic reviews on sleep medicine.

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Does self-reported sleep duration reflect actigraphy-reported sleep duration in male youth soccer players?

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Introduction: Adequate sleep is essential for health, athletic performance, and recovery, particularly for young athletes facing the demands of continuous practice and competition. However, young athletes often obtain less sleep than recommended. While objectively tracking sleep using devices can be costly for most sports organizations, many rely on self-reported sleep as part of daily wellness assessments. Thus, it is important to determine the accuracy of self-reported sleep indices, as this may influence their effectiveness as part of a monitoring system. This study aimed to compare the agreement between daily self-reported and actigraphy-based sleep duration in male youth soccer players.

Materials and methods: Forty-eight young male soccer players (mean $\pm$ SD, age: 16.7 ± 0.9 years) reported their perceived sleep duration and completed sleep diaries daily while also wearing an actigraphy device for 35 consecutive days (a total of 1,116 individual actigraphy observations and 917 self-reported observations were collected). The reliability and agreement between objective and subjective measures of sleep were estimated. Agreement between measurements was assessed using Bland-Altman limits of agreement, with acceptable limits of agreement set at <30 minutes.

Results: The mean objectively measured sleep duration per participant over the investigated period was $06:41 \pm 00:33$ h, with a coefficient of variation of 16.1%, while the mean self-reported sleep duration per participant over the same period was $07:48 \pm 00:35$ h, with a coefficient of variation of 12.0%. The mean time in bed was $08:11 \pm 00:33$ h, with a coefficient of variation of 14.9% per participant. Results indicated a disagreement between objective and subjective sleep duration, with a mean bias of -1:00 h (95% Confidence Interval (CI): -1:09 to -00:57 h), indicating an overestimation of self-reported sleep duration by 01:00 h and a potential disagreement range of over 2:30 h, as the 95% limits of agreement ranged from -2:09 to 0:15 h (95% CI: lower -02:32 to -02:12 h and upper 00:09 to 00:28 h), suggesting considerable individual variability in agreement. When comparing the time in bed against the perceived sleep duration, data demonstrated a mean bias of 00:28 h (95% CI: 00:21 to 00:35 h), while the limits of agreement ranged from -00:46 to 01:43 h (95% CI: lower -00:56 to -00:39 h and upper 01:36 to 01:53 h).

Conclusions: The current results suggest that coaches and practitioners working with youth soccer players should interpret and use self-reported sleep indices with caution. Self-reported sleep duration appears to align more closely with the objective time in bed than with the actual sleep duration. Thus, when possible, other methods for sleep monitoring should be considered, either alone or in combination with self-reported measures.

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Dyslipidemia and obstructive sleep apnea in men with androgenetic alopecia: an analysis from the EPISONO study

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Introduction: Androgenetic alopecia (AGA) is a non-scarring hair disorder, and the most common cause of hair loss in adult men. This condition is primarily driven by genetic predisposition and androgen activity, related to a higher conversion of the testosterone into its active metabolite, dihydrotestosterone (DHT), by the enzyme alpha-5-reductase. Emerging evidence suggests that AGA is associated with metabolic dysfunction, worse sleep quality and sleep disorders, but the causality to its pathogenesis remains unclear. Chronic and systemic inflammatory conditions, such as diabetes, dyslipidemia, hypertension, and obstructive sleep apnea (OSA) should be considered in individuals with AGA. The aims of this study were to examine the hormonal, metabolic, and sleep profiles of adult men with AGA and their potential relevance as risk factors to this hair condition.

Materials and methods: This cross-sectional case-control study used data from the 4th edition of the São Paulo Epidemiological Sleep Study (EPISONO). Participants self-reported AGA, completed sleep questionnaires, underwent polysomnography, and provided blood samples for laboratory analysis. To this study, the questionnaires Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI) were considered. A first analysis of the whole included sample was performed, followed by a propensity score matching (PSM), that was applied to match AGA and non-AGA groups in a ratio of 1:1 by age (caliper=0.2).

Results: From the total EPISONO sample of 769 participants aged 20 to 80 years, 317 were men. Among these, 307 answered the question related to AGA, with 64 self-reporting AGA and 243 reporting no diagnosis. Before PSM, the AGA group was older, with larger neck and waist circumferences, lower serum testosterone, higher triglycerides, and reduced high-density lipoprotein (HDL) cholesterol. Diabetes, metabolic syndrome, and moderate-to-severe OSA were more prevalent in individuals with AGA. After PSM, 64 age-matched pairs were analyzed. Very-low-density lipoprotein (VLDL) cholesterol and triglycerides levels remained elevated, and dyslipidemia was more frequent in the AGA group. Univariate logistic regression identified elevated triglycerides levels as a consistent predictor of AGA before and after PSM. Regarding sleep, no significant differences were found in PSQI, ESS, or ISI scores between groups before or after PSM. Moderate-to-severe OSA was associated with AGA prior to matching.

Conclusions: This study reinforces the link between AGA and lipid metabolism, with elevated triglycerides as a potential marker of this hair condition. The association between AGA and moderate-to-severe OSA before PSM analysis suggests that there is a complex interplay between AGA and metabolic factors. These results highlight the importance of early metabolic screening and sleep evaluation in individuals with AGA, and the need for further research in respect of OSA and its pathophysiological link with this hair condition.

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Educational and Community Health Outcomes Following a Pediatric Sleep Medicine Education Program for Physicians in South Asia

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Introduction: The global practice of pediatric sleep medicine has been limited in large part to a lack of training opportunities. In India, 70-90 million children are conservatively estimated to have sleep problems, with potential for significant negative impact on growth, development, neurobehavioral outcomes, and academic performance. Unfortunately, a recent poll of general pediatricians across India revealed low levels of sleep-related knowledge, and 93% of pediatricians report no training in pediatric sleep during their medical education. Due to this immense need, the Diploma in Pediatric Sleep Medicine (DPSM) was started in 2022 to offer a formal training program in pediatric sleep for physicians across India. However, the impact of the DPSM program on provider knowledge, competence, performance, and community health is unknown.

Materials and methods: An electronic survey was created based on the Moore Framework for Assessing Learners and Evaluating Instructional Activities and sent via a messaging application to all participants who completed the DPSM program through December 2024. The Assessment of Sleep Knowledge in Medical Education (ASKME) questionnaire evaluated sleep medicine knowledge. Participants rated their satisfaction with the educational program on a 5-point scale from strongly disagree to strongly agree. Perceptions of pediatric sleep medicine competence and knowledge prior to and after completing the DPSM were queried on a 10-point scale from no competence/knowledge to fully competent/knowledgeable. Participants reported on their clinical practice and changes in patient and community health prior to and after the DPSM. Descriptive statistics (N, % and mean $\pm$ SD) are reported, and paired-sampled t-tests compared competence and knowledge ratings prior to and after completing the program.

Results: Out of 139 learners, 126 provided full responses to the survey. Average score on the ASKME was $74.9 \pm 10.7\%$. Participants predominantly agreed or strongly agreed that the setting, delivery, and instructional techniques and materials for the DPSM were beneficial (74.6% - 97.7%). Self-perceived knowledge and competence in pediatric sleep medicine was significantly improved after completing the

DPSM compared to before (competence before= 3.6 ± 2.7 , after= 7.4 ± 1.6 ; knowledge before= 3.8 ± 2.6 , after 7.4 ± 1.8 ; p 's<0.001). Nearly 90% of participants reported opening their practice to pediatric sleep patients and 35% began interpreting pediatric polysomnography following the DPSM.

Participants predominantly agreed or strongly agreed that the health of pediatric patients in their practice (84.7%) and in their community (80.6%) have improved because of the DPSM.

Conclusions: Pediatric sleep-related competence and knowledge increased in physicians in India who completed the DPSM. Further, access to pediatric sleep clinical care and polysomnography reportedly increased and community health was rated as improved for pediatric patients in India due to the DPSM.

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Effect of elinzanetant in reducing polysomnographic wakefulness after sleep onset in postmenopausal women: Results from the Phase II NIRVANA exploratory study

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Introduction: Sleep disturbances are a common and disruptive symptom of menopause affecting even women with infrequent or less severe vasomotor symptoms (VMS). Elinzanetant, a dual neurokinin (NK)-1 and NK-3 receptor antagonist, has previously demonstrated improvements in sleep disturbances based on favorable patient-reported outcomes (PROs) from the OASIS studies. The Phase II NIRVANA exploratory trial aimed to further evaluate the effect of elinzanetant on objectively measured sleep parameters in postmenopausal women with moderate-to-severe VMS using polysomnography (PSG), in addition to PROs. This abstract reports the effect of elinzanetant in improving PSG-measured wakefulness after sleep onset (WASO) at week 4 (primary endpoint) and week 12 (secondary endpoint).

Materials and methods: In this randomized, double-blind trial, 110 women experiencing menopause (mean [standard deviation] age 54.8 [4.6] years) with PSG-measured wakefulness after sleep onset (WASO) ≥ 30 minutes and ≥ 20 moderate-to-severe self-reported VMS per week were randomized to elinzanetant 120 mg (n=55) or placebo (n=55) once daily for 12 weeks. In-lab PSG assessments were conducted at baseline, week 4, and week 12 over two consecutive nights per time point. The primary and secondary endpoints were changes from baseline in WASO at weeks 4 and 12, respectively, analyzed using a mixed model with repeated measures. No hypotheses were planned to be tested. A prespecified analysis with log transformation was applied to address deviations from the normality assumption. Least squares geometric mean ratios (LSGMR) are therefore reported. To assess the overall treatment effect across all time points and account for substantial night-to-night variability, a post hoc random coefficient model was applied to all individual night data over the 12-week treatment period.

Results: At baseline, median WASO was 72.0 minutes (quartile [Q]1, Q3: 48.0, 90.3) for elinzanetant and 76.8 minutes (Q1, Q3: 54.0, 102.5) for placebo. At week 4, LSGMR to baseline was 0.68 (unadjusted 90% confidence interval [CI]: 0.59, 0.77) for elinzanetant and 0.94 (0.82, 1.08) for placebo, representing a 28% greater reduction in WASO with elinzanetant compared with placebo (unadjusted 90% CI (13%, 41%). At week 12, LSGMRs were 0.67 (0.57, 0.79) for elinzanetant and 0.76 (0.65, 0.90) for placebo, representing a 12% greater reduction with elinzanetant compared with placebo (unadjusted 90% CI (-11%, 30%). Night-to-night variability was notable, with WASO differing by at least 60 minutes in 15% of consecutive nights. The random coefficient model showed an 18% greater reduction in WASO with elinzanetant compared with placebo (unadjusted 95% CI: 5%, 30%), equating to an absolute reduction of approximately 13 minutes across the 12-week treatment period based on a WASO baseline assumption of 75 minutes.

Conclusions: A relative reduction in WASO was seen for elinzanetant compared with placebo, which was more pronounced at week 4 than week 12. The magnitude of improvement, while modest, is

relevant given the prevalence of sleep disturbances and the lack of therapies with efficacy confirmed by PSG in postmenopausal women. In line with the PROs from the pivotal OASIS trials, these findings support the effect of elinzanetant for menopause-related sleep disturbances.

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Effect of elinzanetant on sleep continuity and sleep architecture in postmenopausal women with sleep disturbances: post hoc analysis of the Phase II pilot study NIRVANA

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Introduction: Sleep disturbances are prevalent and burdensome in women experiencing menopause and vasomotor symptoms (VMS). While elinzanetant, a dual neurokinin (NK)-targeted therapy (NK-1 and NK-3 receptor antagonist), has demonstrated improvements in patient-reported sleep outcomes in prior OASIS studies, the Phase II NIRVANA pilot trial was the first to evaluate the effect of elinzanetant on polysomnographic (PSG) measures of sleep as a primary endpoint in postmenopausal women with moderate-to-severe VMS. The prespecified primary endpoint (change from baseline in PSG wakefulness after sleep onset [WASO] at week 4) and secondary endpoint (change from baseline in PSG WASO at week 12) are reported separately. This abstract focuses on exploratory PSG-derived outcomes of sleep continuity and architecture.

Materials and methods: In this randomized, double-blind trial, 110 women experiencing menopause (mean [standard deviation] age: 54.8 [4.6] years) with PSG-confirmed sleep disturbances (WASO ≥ 30 minutes) and ≥ 20 moderate-to-severe VMS per week were randomized to elinzanetant 120 mg (n=55) or placebo (n=55) once daily for 12 weeks. In-lab PSG was performed at baseline, week 4, and week 12 over two consecutive nights at each time point. All exploratory endpoints, including changes in sleep continuity (number of awakenings, arousal index) and sleep architecture (duration of N1, N2, N3, rapid eye movement [REM], and total non-REM sleep) were prespecified to be analyzed using descriptive statistics. To assess the time-averaged treatment effect across all time points and account for substantial night-to-night variability, a post hoc random coefficient model was applied to all individual night data over the 12-week treatment period.

Results: The number of awakenings was reduced more with elinzanetant than with placebo (least squares [LS] mean difference: -1.8 awakenings; 95% confidence interval [CI]: -2.8, -0.9) over the 12-week treatment period. The arousal index was also reduced more with elinzanetant compared with placebo (LS mean difference: -4.1 events/hour; 95% CI: -6.0, -2.2). Total time spent in non-REM sleep was greater with elinzanetant than with placebo (LS mean difference: 17.6 minutes; 95% CI: 9.0, 26.2). Elinzanetant increased N2 sleep duration (LS mean difference vs. placebo: 31.1 minutes; 95% CI: 21.0, 41.2) and decreased N3 sleep duration (LS mean difference vs. placebo: -14.9 minutes; 95% CI: -22.3, -7.5). Small differences were observed for N1 sleep duration (LS mean difference: -0.5 minutes; 95% CI: -4.0, 3.1) and REM sleep duration (LS mean difference: 0.8 minutes; 95% CI: -4.7, 6.4).

Conclusions: In this post hoc analysis, elinzanetant demonstrated a greater numerical advantage in objective measures of sleep continuity and selected sleep architecture parameters in postmenopausal women with VMS compared with placebo. Notably, elinzanetant reduced awakenings and arousals to a greater extent than placebo, complementing findings from the pivotal OASIS studies using patient-reported outcomes and supporting its potential for menopause-related sleep disturbances. Elinzanetant also increased non-REM sleep (primarily N2), while decreasing N3 sleep, which should be investigated further.

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Effects of the Midnight Sun and daily step during data collection in polar Environment on Sleep Parameters: A Pilot Study

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Introduction: The midnight-sun period experienced near the Arctic Circle disrupts circadian rhythms and may alter sleep quality and architecture. This study examined how a 1- to 2- month field season under midnight-sun conditions influences the objective and subjective sleep of master's students during data collection.

Materials and methods: Two research teams, each comprising four master's students (1 man, 3 women; 27 ± 3 y), conducted environmental fieldwork on Bylot Island. Participants wore actigraph watches to record total sleep time, REM sleep, light sleep, deep sleep, number of sleep cycles, sleep efficiency, and daily step count across three periods: 1) Two weeks before departure (baseline), 2) During the expedition (42 ± 14 d), 3) One week after return (post-expedition). Weekly questionnaires: the Insomnia Severity Index (ISI) and a sleep appreciation scale (SAS)—reported subjective sleep perception over the same periods. Because of the small sample size, we used a Quade nonparametric ANCOVA with Bonferroni correction to compare baseline to each week of the expedition and to the post-expedition period. Wilcoxon tests compared baseline to the expedition average. The relationship between daily step count and sleep parameters was analyzed with Pearson's correlation.

Results: SAS differed significantly between baseline and the expedition average (55 ± 5 vs. 63 ± 11 ; $F(7,6) = -4.167$, $p = 0.037$) and between the end of the expedition and post-expedition (64 ± 14 vs. 61 ± 10 ; $F(7,6) = 4.333$, $p = 0.030$). The ISI increased in the first week of the polar environment compared to baseline (6 ± 3 vs. 9 ± 6 ; $F(7,6) = -2.667$, $p = 0.033$), but the average ISI across the expedition did not differ from baseline. Sleep data showed a significant reduction in total sleep time during the expedition compared to baseline (444 ± 26 vs. 421 ± 13 min; $Z = -2.028$, $p = 0.043$). No significant changes were observed for REM sleep percentage (22 ± 2 vs. $21 \pm 1\%$; $Z = -1.633$, $p = 0.102$), deep sleep percentage (16 ± 4 vs. $16 \pm 3\%$; $Z = -1.134$, $p = 0.257$), sleep efficiency (93 ± 2 vs. $94 \pm 1\%$; $Z = -1.394$, $p = 0.163$), or number of cycles (5 ± 1 vs. 5 ± 0 cycles; $Z = -1.732$, $p = 0.083$). Pearson's correlations revealed a moderate negative relationship between daily step count and total sleep time ($24\ 235 \pm 6\ 858$ steps vs. 425 ± 30 min; $r = -0.423$, $p = 0.016$) and between step count and deep sleep percentage ($24\ 235 \pm 6\ 858$ steps vs. $16.8 \pm 3.2\%$; $r = -0.359$, $p = 0.044$). No other sleep measures correlated significantly with step count.

Conclusions: Midnight-sun conditions seem to impair sleep perception during the initial transition into and following the polar environment and reduced average total sleep time across the expedition. Other sleep indices remained stable, likely reflecting the relatively short exposure to Arctic light and/or participants' sleep-management strategies. Furthermore, higher daily step counts were associated with reduced total sleep time and deep sleep, suggesting that increased fieldwork demands further compromise sleep under data collection in polar environment conditions.

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Effects on quality of life and daytime sleepiness between patients treated with CPAP versus CPAP alternatives

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Introduction: Obstructive sleep apnea is the most common sleep related breathing disorder characterised by recurrent episodes of partial or complete airflow obstruction during sleep. If left untreated, it is associated with increased morbidity and mortality. Continuous Positive Airway Pressure (CPAP) remains the primary treatment for most OSA patients due to its efficacy in maintaining airway patency during sleep. However, poor patients compliance to CPAP therapy is a significant barrier to its long-term success, often due to discomfort or inconvenience. In recent years, various surgical

interventions have emerged as a promising alternatives for OSA treatment, particularly for patients who are intolerant to CPAP. We would like to compare the improvement in the quality of life and daytime sleepiness of patients with OSA between those treated with CPAP therapy and those treated with CPAP alternatives.

Materials and methods: We conducted a pilot study in the Otorhinolaryngology clinic of University Malay Medical Centre. Patients aged 18 to 80 years old who were diagnosed with OSA of all levels, received interventions in the form of CPAP or CPAP alternatives were recruited to participate in the study. 48 patients completed the Epworth Sleepiness Scale (ESS) and the Calgary Sleep Apnea Quality of Life Index (SAQLI) questionnaires pre and post intervention (within the span of 2 weeks to 2 months).

Results: Both CPAP and CPAP alternatives were effective in improving patient outcomes, as shown by significant reductions in daytime sleepiness (ESS) and improvements in sleep-related quality of life (SAQLI) from pre- to post-treatment within each group.

Comparison between groups, no statistically significant differences were found in Post ESS ($p = 0.429$) or Post SAQLI scores ($p = 0.551$). The magnitude of improvement in sleepiness and quality of life was similar across both treatments. Although the CPAP group demonstrated slightly higher mean Post SAQLI scores, this difference was small and not clinically meaningful.

Conclusions: This preliminary study concluded that there is improvement in the quality of life and daytime sleepiness of patients with OSA treated with CPAP and CPAP alternatives. Though short term improvements are comparable between the two groups of patients, future studies need to be done to assess long term improvement of both arms, compliance of patients to CPAP therapy as well as the long term effectiveness of CPAP alternatives, such as surgical interventions and mandibular advancement devices.

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1) W. Ward Flemons and Marlene A Reimer: Development of a disease specific Health Related Quality of Life Questionnaire for Sleep Apnea

2) Norkhafizah Saddle, Hazama Mohamad, Nor Idaho Mohd Yusof, Dasmawati Mohammad, Norehan Mokhtar and Wan Zaripah Wan Bakar: Validity and reliability of the Malay Version of Sleep Apnea Quality of Life Index (SAQLI)

Efficacy of Intraoral Negative Air Pressure (iNAP) Therapy in Adolescents with Obstructive Sleep Apnea: A Prospective Exploratory Study

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Introduction: The diagnosis and treatment of obstructive sleep apnea (OSA) in adolescents are currently underestimated globally. This prospective study evaluated the effects of the Intraoral Negative Air Pressure (iNAP) Therapy on physiological parameters and subjective experiences in adolescent OSA patients, exploring treatment response differences by OSA severity.

Materials and methods: The iNAP Sleep Therapy System consists of five main components: a console, saliva container, saliva absorbent, flexible polymer tubing, and soft polymer oral interface. It creates and automatically maintains a negative oral pressure gradient. This pulls the tongue and soft palate forward, preventing respiratory events to improve sleep and user quality of life. This prospective study enrolled 13 adolescents (11 males, 2 females; aged 10-17 years), following 2 dropouts from 15 initially recruited who met inclusion criteria (Obstructive Apnea Hypopnea Index [OAHI] > 1 /hour) and underwent a feasibility test. Participants were categorized as severe (OAHI > 10 /hour, n=5) or non-severe (OAHI 1-10 /hour, n=8). All received iNAP therapy with polysomnography (PSG) at baseline, day 1 (Tx1), 1 week (Tx2), and 1 month (Tx3). Key parameters included sleep architecture, OAHI, lowest oxygen saturation (Lowest SpO₂), maximum apnea duration, Oxygen Desaturation Index (ODI), supine AHI, and questionnaire-assessed stress, quality of life (QoL), and daytime sleepiness. Paired t-tests (pre-post) and correlation analyses were performed.

Results: Regarding sleep architecture, overall sleep efficiency improved, N2 sleep decreased ($p < 0.05$), N3 sleep increased (Tx1, $p = 0.043$; Tx3, $p = 0.003$), and REM/NREM respiratory events significantly

reduced. Overall, OAHl significantly decreased at Tx1 and Tx3 ($p < 0.05$). Maximum apnea duration significantly shortened at Tx1 ($p = 0.006$) and Tx3 ($p = 0.009$). Lowest SpO_2 significantly increased at Tx2 ($p = 0.031$) and Tx3 ($p = 0.008$). ODI (Tx1, $p = 0.047$; Tx2, $p = 0.013$) and supine AHI (Tx1, $p = 0.013$; Tx2, $p = 0.044$) also significantly decreased. Improvement in OAHl ($\Delta OAHl = \text{Baseline OAHl} - \text{Tx OAHl}$) showed a strong and progressively strengthening negative correlation with improvement in NREM OAHl (Tx1: $r = -0.81$; Tx2: $r = -0.89$; Tx3: $r = -0.91$). Furthermore, OAHl improvement demonstrated strong correlations with reductions in supine AHI, shorter maximum apnea duration, and increased Lowest SpO_2 . At Tx3, 76.9% of all patients achieved $>50\%$ OAHl reduction. This rate was 100% in the severe group. In the non-severe group, 62.5% achieved $>50\%$ OAHl reduction at both Tx1 and Tx3. Both groups showed significant post-treatment OAHl improvement at Tx1 and Tx3 ($p < 0.05$). The severe group had a 4-8% significant increase in Lowest SpO_2 across all treatment stages ($p < 0.05$) and ODI improvement at Tx2 ($p = 0.036$). The non-severe group had significant maximum apnea duration reduction at Tx1 ($p = 0.042$) and Tx3 ($p = 0.036$). Questionnaire data showed improvements in OSA-18 QoL ($p = 0.08$) and total questionnaire scores ($p = 0.096$) approached statistical significance.

Conclusions: This exploratory study suggests Efficacy of Intraoral Negative Air Pressure (iNAP) Therapy in Adolescents with Obstructive Sleep Apnea: A Prospective Exploratory Study has positive therapeutic effects in adolescents with OSA, with efficacy potentially differing by OSA severity.

Feasibility, acceptability, and appropriateness of a brief sleep disorder education video for healthcare students presenting with sleep disturbance

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Introduction: Up to 40% of young adults have symptoms of a sleep disorder. More than half of these young adults have symptoms warranting clinical investigation, but are rarely identified or managed in early adulthood. Unmanaged sleep disorders pose a risk for early career professionals engaged in shift work, as these conditions often go undiagnosed for extended periods of time.

The aim of this study was to determine the feasibility, appropriateness, and acceptability of a brief, co-designed sleep disorder education video specifically for healthcare students (medicine, paramedicine and nursing) who were likely to have future shift work requirements, and determine whether participants might consider help for their sleep after viewing.

Materials and methods: Healthcare students were invited to view a 15-minute online educational video. Customised content was delivered by a practicing early-mid career professional from each cohort, and included lived experience videos of sleep disorder diagnosis and management from a young nurse and paramedic. Videos were designed to briefly introduce young adults to the experience of, as well as treatments for, common sleep disorders.

Risk for a sleep disorder was determined using multiple validated questionnaires for insomnia, obstructive sleep apnoea, sleepiness and restless legs. Post video, participants responded to a series of questions about their interest and motivation for help seeking related to sleep.

Feasibility, acceptability, and appropriateness of the video were assessed with Weiner et al's (2017) implementation measures. Averaged scores of four items for each of the three facets were between 0-5, with 5 indicating highest agreement; between-group differences were determined with Kruskal-Wallis tests.

Results: Results are from 153 healthcare students (67% female) reporting at least one risk factor for a sleep disorder; in pre-video questionnaires, 33% were unsure if they had a sleep problem, and 48% felt that they did. Most were nursing (39%) or medicine (38%) students. Less than half (42%) indicated they had considered help for their sleep to date.

Median (IQR) scores for acceptability (4.0 (1.0)), appropriateness (4.0 (1.0)) and feasibility (4.0 (0.8)) suggested high agreement for all measures, and supported the video module. Paramedic students rated the acceptability (5.0 (1.0)) and appropriateness (4.5 (1.0)) higher than medicine and nursing students ($H(2) = 8.9$, $p = 0.012$ and $H(2) = 7.4$, $p = 0.025$ respectively). No between-group differences were found for feasibility ($H(2) = 1.7$, $p = 0.42$).

Post-video, 53% of participants indicated they were considering seeking help for their sleep.

Participants could select multiple reasons for not considering help; the most common were not perceiving a problem (49%), or that it wasn't a priority right now (42%). Having no time (32%), and feeling that help seeking would be too expensive (36%), were also factors.

Conclusions: Healthcare students found a brief, co-designed sleep disorders education video to be feasible, acceptable, and appropriate for introducing sleep disorder content. Given that all participants presented with disturbed sleep, high rates of feeling there is no time, and believing sleep care will be too expensive, should be carefully considered and addressed in future health services interventions and initiatives for sleep in young workers.

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From Sleep to Safety: Assessing Adverse Events in Sleep Laboratory

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Introduction: Patients undergoing sleep studies in the sleep laboratory may encounter adverse events. Ensuring patient safety is of paramount importance for effective and safe sleep laboratory management. Data on the type and severity of adverse events would facilitate sleep technicians in anticipating potential clinical events and to equip with relevant knowledge and intervention for timely evaluation, management and prevention. This study aims to systemically review adverse events and their consequences at an university-affiliated sleep laboratory to identify risks and enhance management strategies.

Materials and methods: We conducted a retrospective review of adverse events occurring from January 1, 2022 to March 31, 2025 at the Li Chiu Kong Family Sleep Assessment Unit, Department of Psychiatry, Shatin Hospital, Hong Kong. The sleep laboratory equipped with four beds, provides both diagnostic and therapeutic evaluations for a comprehensive range of sleep disorders across all age groups. Data were extracted from medical records, sleep reports, electronic Accident and Incident Reporting System (AIRS), and Clinical Management System (general electronic health care database of Hong Kong public health care system).

Results: Among a total of 1383 overnight attended sleep studies performed during the study period, 35 adverse events (2.53%, 1 event per 39.5 sleep studies) were documented. Adverse events affected 23 (69.7%) male and 9 (30.3%) female patients with age range from 9 to 85 years old (mean age 61.8 ± 20). Two patients had two consecutive incidences within same admission day while another one had two incidences during separate admissions. Clinical background of these patients included psychiatric disorders (45.5%), hypertension (33.3%), dementia (21.2%), cardiovascular disease (18.3%), cognitive impairment (12.1%) and Parkinson disease (9.1%).

The predominant adverse events were cardiopulmonary issues (13/35; 37.1%), including cardiac arrhythmia, hypertensive crisis and chest pain. Other notable events included altered neuropsychiatric conditions (25.7%) involving nocturnal confusion and sun downing syndrome, altered mental state with suicidal risk (3.1%) and accidental falls (3.1%). The remaining events comprised miscellaneous issues (34.4%) were upper respiratory tract infection symptoms, headache, gastroenteritis symptoms, dizziness, toe injury and skin rash. The overall severity of these adverse events was relatively mild, with no major injury or death. Only one patient ($1/1383=0.07\%$) required hospitalization, while 6 patients ($6/1383=0.43\%$) required accident and emergency department attendance. The adverse events occurred more commonly among patients with dementia ($p<0.001$) and cognitive impairment ($p<0.007$). The notable occurrence of cardiopulmonary problems and altered neuropsychiatric conditions emphasizes the need for vigilant monitoring to enhance patient safety.

Conclusions: While adverse events in sleep laboratory are relatively infrequent and occurring in 2.5% of sleep studies, the findings of cardiovascular and neuropsychiatric adverse events highlight the critical need for robust risk management and adequate staff training to mitigate potential incidents and enhance prevention measures

Groups of multiple respiratory and allergic trajectories between 1 and 5.5 years of age and their associations with sleep characteristics in early life

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Introduction: Sleep troubles have been associated with respiratory and allergic health problems in children, however the time line of their association is overlooked. The current study examined the associations between: (1) sleep patterns at age 1 year and respiratory and allergic multi-trajectories between 1 and 5.5 years; (2) respiratory and allergic multi-trajectories between 1 and 5.5 years and sleep patterns at age 5.5 years in a French birth cohort.

Materials and methods: Clusters of sleep characteristics at age 1 year (nocturnal sleep duration (NSD), day sleep duration (DSD), sleep onset difficulties (SOD), night awakenings (NA)) and at age 5.5 years (NSD, SOD, NA) and respiratory and allergic symptoms multi- trajectory groups between 1 and 5.5 years (wheezing, asthma medication, eczema, allergic conjunctivitis) were identified using unsupervised methods. Associations between sleep clusters at each age and multi-trajectory groups were assessed using multinomial regressions adjusted for potential confounding factors among 9,577 children.

Results: Two sleep clusters were identified at both age 1 and 5.5 years: C1a (79.9%, age 1 year) and C1b (83.1%, age 5.5 years) characterized by adequate sleep duration and good sleep quality; C2a (20.1%, age 1 year) and C2b (16.9%, age 5.5 years) characterized by shorter sleep duration and poorer sleep quality. Four multi-trajectory groups were also identified: G1 (no/few symptoms, 44.4%), G2 (persistent non-respiratory allergic symptoms, 23.1%), G3 (transient early respiratory symptoms, 25.2%), G4 (persistent respiratory and allergic symptoms, 7.3%). Belonging to cluster C2a was associated with an increased odds of belonging to G3 (adjusted odds ratio [95% interval confidence]; 1.14 [0.99-1.31]) and G4 (1.29 [1.05-1.59]). Similar results were obtained in children without wheezing at 2 months (1.18 [1.03-1.36] and 1.28 [1.03-1.60], respectively).

Conclusions: Sleep disturbances at 1 year are associated with poorer respiratory and allergic health between 1 and 5.5 years suggesting early sleep troubles may predict these health status.

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Impact of High Mandibular Plane on Surgical Outcomes of Maxillomandibular Advancement for Obstructive Sleep Apnea

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Introduction: Maxillomandibular Advancement (MMA) is the first surgical treatment option for obstructive sleep apnea (OSA). Despite the high success rate, incomplete remission is common. The surgical design generally focused on the forward movement of the maxillomandibular complex. The impact of high mandibular plane angle on surgical outcomes remained unclear. The purpose of this study is using cephalometry to investigate the role of high mandibular plane angle and correction in maxillomandibular advancement.

Materials and methods: A retrospective review was conducted on 106 medical records of patients (33 females and 73 males) who underwent MMA. To avoid the impact of gender and obesity, 50 male patients with a BMI<26 (Kg/m²)(26 of them had the surgical cure of post-op AHI<5) were included. Cephalometry and polysomnographic indices before and more than three months after surgery were collected for analysis. The paired T-test was applied to compare measurements before and after surgery. Non-paired T-test was used to compare between groups.

Results: On average, the maxilla(at A point) and the mandible(at B point) were advanced 4.0 ±2.9mm and 13.2±3.7mm, respectively. A lower pre-op mandibular plane angle (to Frankfort horizon) of 29.3±9.8° was noted in the surgical-cure group, compared to 35.8±8.5° in the non-cure group (p=0.012). There were significant differences in the angle counterclockwise rotation between non-cure (clockwise 2.8±3.6°) and cure group (clockwise 0.39±5.67°)(p=0.034); and a significant difference in the velopharyngeal airway between the non-cure group (10.1±2.6mm) and the cure group (11.0±2.9mm)(p=0.032).

Conclusions: A higher mandibular plane angle could have a negative impact on the surgical cure of MMA surgery in non-obese male patients with OSA.

Impact of Nocturnal Air Pollution on Sleep Quality and Emergency Health Service Utilization for Respiratory and Cardiovascular Conditions in Portugal: An Ecological Analysis Using Open Data

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Introduction:

Poor air quality is a recognized risk factor for respiratory and cardiovascular diseases. Nocturnal exposure to air pollutants may further impair sleep quality, compounding health risks and increasing emergency healthcare utilization. The interplay between nighttime environmental stressors and sleep disruption remains underexplored in the Portuguese context. With this work, authors aimed to examine the association between nocturnal air pollution, sleep quality indicators, and emergency department visits for respiratory and cardiovascular complaints across multiple regions in Portugal.

Materials and methods: This ecological study combined open-access data from the Portuguese National Environmental Monitoring Network (QualAr), national health surveillance systems, and population-level sleep quality metrics from EUROSTAT and the National Institute of Health Doutor Ricardo Jorge (INSA). Hourly nighttime pollutant concentrations (PM_{2.5}, PM₁₀, NO₂, O₃, CO; 22:00–06:00) were analyzed over a 3-year period (2020–2022). Emergency visits were classified by ICD-10 codes for respiratory (J00–J99) and cardiovascular (I00–I99) conditions. Regional sleep quality indicators—including prevalence of insomnia symptoms and self-reported sleep difficulties—were used to explore potential mediating effects. Time-series and geospatial analyses assessed correlations among air pollution levels, sleep disturbances, and acute health outcomes.

Results:

Elevated nocturnal concentrations of PM_{2.5} and NO₂ were significantly associated with increased rates of emergency department visits for both respiratory and cardiovascular conditions ($p < 0.01$), with the strongest effects observed in densely populated urban areas such as Lisbon and Porto. A seasonal trend was also noted, with higher pollutant levels and emergency visit rates during colder months.

Sleep quality emerged as an important modifying factor: regions with lower average sleep quality scores and higher self-reported insomnia prevalence exhibited greater vulnerability to the adverse health effects of air pollution. Multivariate Poisson regression models revealed that each 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} was associated with a 6–8% increase in emergency visits, while higher sleep quality scores were independently associated with a significant reduction in visits for both disease categories ($p < 0.001$).

Interaction terms between pollutants and sleep quality were explored. Although the interaction between PM_{2.5} and sleep quality index was not statistically significant, a trend was observed suggesting that poor sleep may potentiate the effects of NO₂ exposure on cardiovascular outcomes. These findings point to a possible synergistic relationship between environmental and behavioral factors in the context of nocturnal health vulnerability.

The models explained a substantial portion of daily variability in emergency visits (pseudo- $R^2 > 0.30$), and the inclusion of sleep-related indicators improved model fit and predictive performance.

Conclusions: Nocturnal air pollution is not only linked to a higher burden of acute cardiorespiratory events but may also indirectly exacerbate these risks through disruption of sleep quality. These findings underscore the importance of integrating environmental and sleep health policies to reduce preventable emergency healthcare demand.

Acknowledgments: Data were obtained from open-access sources, including air quality metrics from the Portuguese Environmental Agency's QualAr platform, population-level sleep indicators from EUROSTAT and the National Institute of Health Doutor Ricardo Jorge (INSA), and health service utilization records from the Portuguese Ministry of Health databases. HypnosAir project (PTDC/CTA-AMB/3263/2021/BI/12M).

Insomnia, Stigma, and Depression in Tuberculosis Patients: Longitudinal Insights from a Cross-lagged Model and Growth Models

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Introduction: Depression is prevalent and severe in tuberculosis (TB) patients. It is often linked to insomnia, stigma, lack of social support, and other psychological factors. However, most studies are cross-sectional, which only examine correlations. The longitudinal relationships between depression and other factors are unclear.

Materials and methods: Through convenience sampling, we selected participants for a 6-month longitudinal study. Depression, insomnia, stigma, social support, anxiety, and stress were assessed at the start of treatment (T1), and after one (T2), two (T3), and six months (T4). SPSS 26.0 and Mplus 8.3 were used for data analysis. A cross-lagged model (CLM) and latent growth models (LGMs) were constructed to study longitudinal associations.

Results: In total, 266 TB inpatients were enrolled (166 men, 100 women, mean age 48.1 ± 18.0 years). The comorbid depression detection rate fell from 23.3% at T1 to 10.1% at T4. The CLM showed insomnia at T1 significantly predicted depression at T2 ($\beta = 0.341$, $P < 0.05$). Depression at T1 predicted insomnia at T2 ($\beta = 0.182$, $P < 0.05$). Insomnia at T2 predicted depression at T3 ($\beta = 0.571$, $P < 0.05$). However, depression at T2 did not predict insomnia at T3 ($\beta = 0.073$, $P = 0.165$). Insomnia at T3 predicted depression at T4 ($\beta = 0.216$, $P < 0.05$). Depression at T3 predicted insomnia at T4 ($\beta = 0.174$, $P < 0.05$). The LGM revealed social support as a significant negative predictor of depression progression ($P < 0.05$). Stigma from T1 to T4 had a positive effect on depression over the same period ($P < 0.05$). Anxiety at T1, T2, and T4 positively influenced depression ($P < 0.05$). Perceived stress at T1 had a significant impact on depression ($P < 0.05$).

Conclusions: Insomnia predicts depression in TB patients, supporting interventions that improve sleep quality. The impact of perceived stigma on depression remains significant. Enhanced social support can accelerate recovery, underscoring the need to reduce stigma and increase support in TB depression management.

Latent Profiles of Psychological Distress in Middle-Aged Men and Their Associations with Sleep Patterns and Coping

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Introduction: Middle-aged men in South Korea face increasing psychological distress but often underreport symptoms due to cultural expectations surrounding masculinity and emotional restraint. Hwabyung (anger-related somatization), depression, and suicidal ideation represent key markers of mental health challenges in this population. This study aimed to identify latent psychological profiles among South Korean middle-aged men based on levels of hwabyung, depression, and suicidality, and to examine how these profiles differ in terms of sleep quality, physical activity, maladaptive schema, and coping strategies.

Materials and methods: A total of 412 middle-aged men (aged 40–59) participated in the study. Standardized self-report questionnaires were used to assess hwabyung symptoms, depression, suicidal ideation, sleep quality, physical activity, early maladaptive schemas, and coping strategies. Latent profile analysis (LPA) was conducted using Mplus 8.8 to identify distinct psychological subgroups. ANOVAs and post hoc tests were performed to compare group differences in lifestyle and cognitive-emotional variables.

Results:

Four distinct profiles emerged from the LPA, including **Low Distress Group** (n = 158, 38.3%), **Hwabyung-Dominant Group** (n = 82, 19.9%), **Depressive-High Risk Group** (n = 96, 23.3%), and **General Distress Group** (n = 76, 18.5%). Significant group differences were found in sleep quality, physical activity, maladaptive schemas, and coping strategies ($p < .01$). The Hwabyung-Dominant group showed higher levels of emotion-focused coping and avoidance, whereas the Depressive-High Risk group exhibited disrupted sleep, reduced activity, and elevated maladaptive schemas (e.g., defectiveness/shame, dependence). The Low Distress group reported healthier behavioral and cognitive profiles overall.

Conclusions: This study highlights distinct distress profiles among middle-aged men and their differential impacts on sleep. While depressive symptoms and suicidality were strongly associated with severe sleep disturbance, hwabyung was linked to sleep complaints related to emotional suppression. These findings underscore the need for sleep-focused screening tools tailored to culturally specific forms of distress. Integrating mental health profiling with sleep assessment may improve early identification and intervention strategies in this underserved population.

Leveraging Electronic Health Records to Understand Sleep Issues in Young Adults with Genetic Syndromes Across Rural-Urban Continuums

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Introduction: Sleep disturbances are highly prevalent comorbidities among individuals with intellectual and developmental disabilities (IDDs). Sleep interventions are a promising target for developing new therapeutic strategies, with the potential to modulate a broad spectrum of developmental outcomes. However, investigations into sleep patterns among adolescents and young adults with IDDs remain limited. This makes it difficult to draw solid conclusions regarding sleep-related issues that should be targeted. This knowledge gap is particularly pronounced in rural populations with IDDs, who may be subject to unique environmental and systemic risk factors contributing to sleep dysregulation. The present study leveraged electronic health record (EHR) data from three US states with large rural populations (Kansas, Kentucky, and Iowa) to investigate sleep disturbances across four IDD conditions.

Materials and methods: International Classification of Diseases (ICD) codes present on ≥ 2 distinct dates were used to identify patients with the following genetic syndromes: Angelman [ICD10: Q93.5], Fragile X [ICD9: 759.83, ICD10: Q99.2], Prader-Willi [PWS; ICD9: 759.81, ICD10: Q87.11], and Rett [ICD9: 330.8, ICD10: F84.2]. Individuals with multiple distinct genetic syndrome diagnostic codes were excluded. Additional ICD9 and ICD10 codes present in the EHR of individuals who were between 13–25 years old at the time of code usage were mapped to clinically meaningful groupings of ICD codes, or Phecodes. Prevalence of sleep-related Phecodes was determined and compared between individuals living in urban versus rural areas based on Rural Urban Continuum (RUC) and Rural-Urban Commuting Area (RUCA) codes.

Results: In total, there were 607 who met criteria for the EHR-defined IDDs of interest. Most patients (73–93%) had urban designations. Co-occurring codes indicating sleep-related issues were observed in between 44–56%—with many individuals having >1 different sleep-related diagnosis. Prevalent sleep-related diagnoses identified in the EHRs of these individuals included sleep apnea, insomnia, sleep related movement disorders and circadian rhythm sleep disorder. For all sites, more individuals with a

sleep-related diagnosis resided in urban versus rural areas, with no discrepancy in the types of sleep disturbances diagnosed.

Conclusions: EHR-derived data indicates that adolescents and young adults with IDD's residing in rural areas are less likely to receive care at the health centers evaluated. This highlights issues related to rural healthcare access and a need for community engagement activities to build trust and inform patients and caregivers about the importance of healthy sleep.

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Managing Sleep, Fatigue, and Crew Strategies in Offshore Sailing: The Role of Chronotype, Effort, and Team Coordination

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Introduction: Sleep is a vital physiological process regulating recovery and performance through complex neuroendocrine and metabolic pathways. Its disruption, frequent in endurance sports like offshore sailing, can impair both physical and cognitive functions. In regattas, sailors face prolonged wakefulness, irregular sleep patterns, and demanding environmental conditions that challenge optimal recovery. In crewed offshore races, the difficulty is amplified by the need to synchronize individual rest with collective operational demands. Despite its relevance, sleep research in sailing is limited. Early studies on solo sailors proposed polyphasic sleep strategies, but these findings may not generalize to short-duration or crewed events.

This study investigated the impact of chronotype-aligned shift strategies, fatigue, and sleep recovery during the 151 Miglia–Trofeo Cetilar 2024, a short-duration offshore regatta. We focused on the relationship between chronotype-aligned shift strategies, subjective fatigue, and regatta outcomes, with particular attention to intra-crew dynamics.

Materials and methods: Participants were monitored before, during, and after the race. Crews were divided into two groups based on boat characteristics. Prior to the regatta, participants completed questionnaires on sail characteristics, chronotype (using the reduced Morningness-Eveningness Questionnaire-rMEQ), and sleepiness (using the Epworth Sleepiness Scale-ESS), and performed the Psychomotor Vigilance Task (PVT). After the race, PVT was repeated, post-race questionnaires were collected, and actigraphy was used for 5 days to monitor sleep recovery. Data were analyzed using chi-square tests, ANOVA, t-tests, Pearson's correlations, and multivariate regression models.

Results: The sample included 65 participants (mean age = 47.15 ± 15.59 years), with an average sailing experience of 12.05 ± 13.39 years. Chronotype distribution was 20% evening, 52.3% intermediate, and 27.7% morning types. During the regatta, participants reported an average sleep duration of 5.84 ± 3.53 hours and a significant increase in subjective sleepiness post-regatta (ESS: $t = 3.34$, $p = 0.0019$). Post-regatta, a significant correlation emerged between higher perceived physical exertion and delayed Mid-sleep Point (MPS) ($r = 0.401$, $p = 0.034$), suggesting that intense effort may postpone circadian timing. However, no significant relationship was found between MSP and chronotype, nor between chronotype and physical fatigue. Crews using self-managed shift strategies and exhibiting greater intra-crew agreement on shift organization ranked significantly higher ($p = 0.005$). At the crew level, performance was significantly associated with greater chronotype heterogeneity ($p = 0.0003$), lower average age ($p = 0.03$), and higher sailing experience ($p = 0.009$), emphasizing the role of group composition and coordination.

Conclusions: This study highlights the complex interplay between sleep, physical exertion, and team dynamics in offshore crewed sailing. In this context, internal team coordination emerged as a key factor influencing performance, alongside crew-level characteristics such as greater chronotype heterogeneity, lower average age, and higher sailing experience. While physical exertion impacts MPS, individual chronotype alone does not predict fatigue. These findings suggest that optimizing intra-crew synchronization and adopting flexible, personalized rest strategies may enhance both recovery and effectiveness in endurance contexts. Beyond sailing, these results offer actionable insights for other

high-demand environments, such as emergency services, transportation, or shift-based professions, where managing fatigue, circadian alignment, and team coordination is essential to optimize performance, safety, and well-being.

Monitoring the effectiveness of pre-flight rest in ULR operations with self-reported data

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Introduction: In the aviation industry, ultra-long range (ULR) operations are defined as flights that exceed 16 hours. These operations have the potential to increase fatigue-related operational and occupational health and safety risks which are managed using multiple countermeasures. Pre-trip countermeasures include a minimum 48-hour rest (including two local nights) free from all duty and advice to crew on obtaining sufficient sleep for optimal functioning and to take a pre-flight nap to reduce the duration of time awake before signing on for duty. Monitoring the use and effectiveness of fatigue countermeasures requires data, and self-reported data are low-cost and easy to collect. To evaluate the use and effectiveness of pre-duty rest on a new ULR route, cabin crew provided information about their pre-duty days, sleep, and pre-flight ratings of sleepiness and fatigue.

Materials and methods: Sleep/duty diaries were distributed to participating cabin crew at the start of a ULR trip with an early evening sign-on time (Median = 18:40). The diary included a lookback report for documenting duty periods in the week leading up to their ULR trip, a 5-point Likert scale asking how recovered they felt from their previous duty ('not at all', 'somewhat', 'very much so'), and questions about their usual sleep at home, how much sleep they obtained in the 24 hours before their ULR trip, if they took a pre-flight nap, and if so, how much nap sleep they obtained. Additionally, they were asked to rate their sleepiness (Karolinska Sleepiness Scale) and fatigue (Samn-Perelli Crew Status Check) before the flight's departure.

Results: Seventy-seven cabin crew (55 women) provided data. The majority (96%) reported having at least two consecutive days off pre-trip (median = 3 days). When asked how recovered they felt from their previous duty, 43% reported feeling "very much so", whereas 3% said "not at all". Cabin crew reported getting more sleep in the 24 hours before the ULR trip (estimated mean = 8.3 h) compared to their usual sleep at home (estimated mean = 8.0 hours), 9% reported getting less than 7 hours sleep, and 49% reported taking a pre-flight nap. Sleepiness ratings ranged between 1 – 6 (Median = 2) and fatigue ratings ranged between 1 – 5 (Median = 2). More sleep in the 24 hours before the ULR trip was associated with lower pre-flight sleepiness ratings ($F(1,73) = 4.13, p=0.0456$).

Conclusions: Using easy and low-cost data collection methods, this study found the majority of cabin crew utilise days off pre-duty to prepare for the ULR trip, but a small proportion of crewmembers may not have recovered sufficiently. The large between-individual-variability observed in all metrics is not reflected in bio-mathematical model estimates. To reduce the likelihood of insufficient recovery, crew would benefit from enhanced fatigue education to support them make good decisions about sleep at home prior ULR duty. This should be included in initial and recurrent fatigue management training.

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Natural *Plasmodium falciparum* infection is associated with enhanced slow-wave sleep in humans

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Introduction: Malaria is a parasitic infectious disease threatening more than half of the world population. While the elevation of sleep-regulatory cytokines in malaria suggests that sleep might be increased, this hypothesis remained untested so far. Assessing sleep in this infectious disease is especially interesting given that sleep, and particularly slow-wave sleep (SWS), can regulate immune responses and might thus boost host defense during malaria infection. We therefore objectively assessed sleep in adults with naturally acquired, asymptomatic *Plasmodium (P.) falciparum* infection and matched controls.

Materials and methods: In this controlled observational study in Lambaréné, Gabon, we enrolled 32 asymptomatic adults with confirmed *P. falciparum* infection and 32 age- and sex-matched uninfected controls. Participants underwent two nights of polysomnography in a sleep laboratory. Blood samples were collected to quantify immune parameters and parasitemia. Polysomnography data were analyzed for conventional sleep staging and spectral power.

Results: In matched-pair analyses, asymptomatic individuals were shown to display significantly more time in SWS compared to controls—on average, approximately 20 minutes more on night 1 and 30 minutes more on night 2. Higher leukocyte and lymphocyte counts were associated with longer SWS duration, while higher parasitemia was linked to reduced SWS. EEG spectral analyses revealed decreased slow-wave activity and disrupted slow oscillation frequency patterns in participants with higher parasitemia.

Conclusions: These findings provide the first evidence that individuals with asymptomatic malaria infection show enhanced SWS, possibly reflecting an immune-mediated adaptive response, which was further associated with malaria-related parameters.

Nocturnal Sleep Duration, Afternoon Siesta, and Sleep Disturbances (OSA) in pregnant Omani women and maternal and fetal outcomes

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Introduction: There is a common perception that sleep is distinctly disturbed during pregnancy, and most women experience numerous sleep disturbances, dramatically changing the sleep architecture. (Kryger, 2022). Consequently, a disturbed sleep pattern during pregnancy can lead to unfavorable health outcomes for the woman and their fetus (Lee et al., 2001). Research has shown that poor sleep quality is frequent during the prenatal period, with approximately 76% of pregnant women experiencing poor sleep quality (Poeira & Zangão, 2022).

In Oman, few studies have been conducted to investigate the correlation between sleep disturbances and pregnancy outcomes. Therefore, this research study aims to examine the impact of sleep disturbances, characterized by obstructive sleep apnea (OSA), sleep deprivation indicated by nocturnal sleep duration, and Afternoon siesta, on maternal and fetal outcomes in pregnant Omani women.

Materials and methods: A cross-sectional, prospective cohort study was conducted on pregnant Omani women aged ≤35 years attending antenatal clinics. The study was ethically approved by the Medical Research & Ethics Committee (MREC) of Sultan Qaboos University and the Ministry of Health (MOH) Research and Ethical Review and Approval Committee.

Participants completed the Epworth Sleepiness Scale questionnaire, underwent limited home sleep studies, and wore actigraphy devices. Maternal and fetal outcomes were monitored. Descriptive statistics and tests of association were used for data analysis.

Results: A total of 429 Omani pregnant women were included in the study, with a mean age of 31.12 years (SD = 3.80) and an average gestational age at delivery of 38.37 weeks (SD = 1.43). The result showed a statistically significant association between the presence of OSA and a higher risk of gestational diabetes mellitus (33.7%) with odds ratio OR 0.63 (95% CI: 0.41- 0.96) and a p-value of 0.034. A significant positive correlation is observed between longer night sleep duration and preterm delivery before 37 weeks ($r=0.119$, $p < 0.05$), while short night sleep duration is linked to a more fragmented sleep pattern, such as total sleep hours and the number of awakenings at night. However, afternoon napping duration did not correlate strongly or consistently with adverse maternal or fetal outcomes. Multivariate tests revealed that the number of awakenings, a measure of sleep disturbance,

significantly impacted BMI changes during pregnancy. In contrast, other sleep disturbances showed limited evidence of association with adverse pregnancy and fetal outcomes.

Conclusions: This study revealed that OSA among pregnant women in Oman may arise, which affects the health of pregnancy and induces specific outcomes, such as gestational diabetes mellitus (GDM) and preterm delivery. However, the risk of preterm delivery is heightened during pregnancy with longer night sleep duration. Screening and management of sleep disorders during pregnancy may improve maternal and neonatal health outcomes. Though extreme efforts were made to maintain maximum accuracy and precision of this study, it was subject to some limitations that hindered the generalizability of the findings.

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Non-application of infant sleeping recommendations at 2 months in French overseas territories: Frequency and determinants using data from the ENP-DROM 2021 survey

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Introduction: Preliminary analysis of the 2021 French National Perinatal Survey (ENP) suggest some poorer neonatal indicators in French overseas departments and regions (DROM) in comparison to metropolitan France, particularly regarding the application of newborns' sleep recommendations. We sought to estimate the frequency and identify the determinants of the non-application of the recommendation to put infant to sleep on their backs (NAR_BackSleep), the main protective factor against sudden unexpected infant death syndrome (SUDI), in the DROM.

Materials and methods: Our study included participating mothers at baseline and 2 months follow-up of the ENP-DROM 2021 survey in Guadeloupe (n=361), Martinique (n=374) and Réunion (n=517). NAR_BackSleep was computed as yes/no using the child dorsal sleep position question asked at 2 months. For each DROM, adjusted prevalence ratios (PRa) of NAR_BackSleep were estimated by robust variance Poisson regressions on weighted data after imputation of missing data.

Results: The frequencies of NAR_BackSleep were 58.7%, 47.1% and 24.2% in Martinique, Guadeloupe and Réunion, respectively. Common determinants of increased PRa of NAR_BackSleep were young maternal age (in all DROM), and lack of advice received from a health practitioner on newborns' sleep position (in Martinique and Réunion). Higher PRa of NAR_BackSleep were also observed with lower maternal education and health literacy, greater precariousness and inappropriate birth weight in Guadeloupe; with having a female child and presence of maternal post-partum depression in Martinique and with maternal feeling to be at ease financially and sharing their bed with their child in Réunion.

Conclusions: High frequencies of non-application of the recommendation to put infant to sleep on their backs have been measured in French overseas departments and regions. The identification of common and specific determinants in each territory will enable us to strengthen perinatal promotion among specific populations in these territories to prevent SUDI.

Outcomes of Split-Night CPAP titration: Insights into Predictors and Challenges in Obstructive Sleep Apnea

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Introduction: A split-night study integrates diagnostic polysomnography (PSG) and continuous positive airway pressure (CPAP) titration for patients with severe sleep apnea (OSA). According to the AAST Technical Guideline (2023), planned split-night titration is recommended based on comprehensive

clinical assessments, while unplanned titration serves as an immediate safety measure for patient presenting with severe OSA. This study aims to evaluate the efficacy of split-night CPAP titration in reducing OSA severity, identify predictors of successful titration and assess their clinical implications in routine practice.

Materials and methods: We conducted a retrospective analysis of 68 patients (7.37%) who underwent split-night sleep studies from a total 923 PSG recordings at the Sleep Assessment Unit, Shatin Hospital between November 1, 2020 to March 31, 2025. The cohort included 51 males and 17 females, aged 25 to 85 years (mean age: 57.9 ± 13.6). Patients were categorized into planned ($n=40$, 58.8%) and unplanned ($n=28$, 41.2%) split-night titrations. Data were analyzed to assess the effectiveness of CPAP titration in reducing respiratory events with success defined as an apnea-hypopnea index (AHI) of less than 10 per hour or reduction of AHI by 75% from baseline (AASM, 2021) during the second half of the night.

Results: The overall success rate for split-night CPAP titration was 72.1%. Planned titrations demonstrated a significantly higher success rate of 87.5% compared to 50% for unplanned procedures ($p=0.001$). In the failure group, subjects exhibited a significantly higher arousal index (54.7 ± 27.8 vs. 39.0 ± 26.6 , $p=0.034$), AHI (60.2 ± 27.8 vs. 41.1 ± 27.3 , $p=0.012$) compared to successful counterparts, but had shorter sleep latency (10.2 ± 9.1 vs. 25.6 ± 36.6 , $p=0.008$). The central apnea-hypopnea index (CAHI) for the failure group was comparable at baseline (7.0 ± 8.5 vs. 3.3 ± 5.5 , $p>0.05$) but significantly increased to 14.0 ± 10.0 during titration ($p<0.001$). No clinically significant differences were observed in demographic characteristics, comorbidities, mood problem or insomnia symptoms. Logistic regression analysis indicated that unplanned split-night titration was more likely to have failed titration outcome (OR: 5.106, CI: 1.261 – 20.666) and was related to more severe AHI (OR: 1.055, CI: 1.026 – 1.085).

A higher prevalence of treatment-emergent central sleep apnea (TECSA) was found in the unplanned group (CAHI: 8.7 ± 9.8 vs. 2.2 ± 4.5 , $p=0.003$). TECSA was more closely associated with severe OSA, indicated by an AHI of 61.93 ± 27 for those with TECSA compared to 40.82 ± 27 for those without ($p=0.009$).

Conclusions: In conclusion, our findings indicate that treatment-emergent central sleep apnea (TECSA) is significantly more prevalent in the unplanned group, highlighting the importance of careful monitoring in these patients. While split-night CPAP titration effectively reduces AHI and improves sleep architecture, planned split-night titration is associated with a higher success rate than unplanned procedures. This suggests that a structured pre-planned approach may enhance treatment outcomes. The higher severity of OSA in the unplanned group is associated with emergence of TECSA, likely due to elevated pressures and expedited titration techniques. Future studies should focus on the mechanisms of TECSA and better identification of clinical subjects with severe AHI for planned split night studies.

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Perceptions of the causes and consequences of workplace fatigue among health leaders in Aotearoa New Zealand

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Introduction: Much of the research on workplace fatigue in healthcare has focused on frontline workers, particularly clinical staff. However, a recent nationwide survey of the New Zealand health workforce highlighted that workplace fatigue is a common experience for workers in all roles and that innovative solutions are needed to manage fatigue in health settings. Health leaders have a crucial role in championing fatigue management, as well as in developing policies and procedures to manage fatigue. Yet, little is known about their knowledge and understanding of fatigue or their perceptions of the role they play in fatigue risk management. We aimed to explore health leaders' understanding of workplace fatigue and fatigue risk management.

Materials and methods: National, clinical, health and safety and occupational health leaders at Aotearoa New Zealand's primary public-funded health organisation completed an anonymous online survey to capture their perceptions of workplace fatigue, including causes and consequences that are

supported by fatigue science. Leaders were asked to report the extent to which they perceived different factors contributed to fatigue on a 5-point scale from not at all to a great deal. Similarly, leaders were asked to rate whether they agreed that fatigue had specific consequences on a 5-point scale from strongly disagree to strongly agree.

Results: The survey was completed by 632 leaders in our target groups (national: n=89, clinical: n=523, OHS: n=20). A majority (87.5%) of leaders perceived work demands as contributing to workplace fatigue 'quite a bit' or 'a great deal'. While known physiological contributors, such as insufficient sleep, were perceived to contribute to fatigue to a similar extent by 74.8% of leaders, others were less well recognised. A notable proportion reported that circadian misalignment (21.4%) and extended wakefulness (15.4%) were 'not at all' contributors to fatigue. Similarly, 17.7% felt that work schedule design was 'not at all' a contributor. Many leaders (64.4%) felt that personal factors, such as workers' health status, home life and experience, were considerable contributors to fatigue. The overwhelming majority of leaders (97-100%) agreed or strongly agreed that workplace fatigue had consequences for patient health and safety, worker health and safety, and staff retention and turnover. Perceptions of causes or consequences of fatigue did not differ by type of leader.

Conclusions: Workplace fatigue is acknowledged as having significant consequences in the health sector in Aotearoa New Zealand. While most leaders acknowledge known contributors to fatigue, some may not be aware of relevant physiological contributors, including those associated with shift work. These perceptions may hinder leaders' understanding of fatigue-related risks and their participation in system-based approaches to manage those risks. Tailored support is needed for health leaders to increase their awareness.

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Pregnancy Sleep Dynamics: A Large-Scale Wearable Study

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Introduction: Sleep disturbances are highly prevalent in pregnancy, affecting nearly half of expectant mothers and worsening as gestation progresses. Driven by hormonal fluctuations, physical discomfort, and frequent nocturnal awakenings, these disruptions peak in the third trimester. Poor sleep has been linked to adverse maternal and fetal outcomes, including preterm birth, cesarean section and prolonged labor, and increased risk of prenatal and postpartum depression. Current understanding of sleep disturbances in pregnancy is limited by a lack of continuous, high-resolution data across gestation. Most studies rely on cross-sectional assessments or self-reported measures at isolated time points, failing to capture the dynamic, longitudinal changes in sleep patterns. This large-scale, high-density, real-world study leverages wearable technology to characterize sleep patterns from preconception to postpartum across pregnancies leading to loss, preterm, and term births, while examining the influence of maternal age and body mass index (BMI). Understanding sleep patterns and their impact on maternal health is essential for developing targeted interventions to improve pregnancy outcomes.

Materials and methods: This retrospective observational study analyzed sleep data from 10,319 Oura Ring users who self-reported pregnancy between May 2023 and November 2024. Data were collected continuously over a 64-week window, spanning 8 weeks before conception to 56 weeks postpartum. Sleep parameters, including time in bed, sleep duration, sleep stages and wake time at night, were modeled using mixed-effects linear models (MixedLM), accounting for gestational week, maternal age, and BMI.

Results: Sleep patterns shifted dynamically across pregnancy. In the first trimester, time in bed, sleep duration, and wake time peaked around week 9 (+30 min, +15 min, and +15 min, respectively), likely influenced by rising progesterone. Sleep duration returned to baseline in the second trimester, though wake time remained elevated. In the third trimester, sleep worsened, with increased wake time and reduced sleep duration possibly due to increases in physical discomfort and nocturia. Postpartum, sleep deteriorated sharply, with wake time rising ~90 min and sleep duration dropping ~70 min below pre-pregnancy levels at birth. Sleep stage analysis shows decreases in deep sleep and rapid eye movement (REM) sleep, and increases in light sleep starting early in the first trimester and persisting throughout pregnancy until birth. Pre-pregnancy age and BMI did not substantially affect sleep trajectories throughout gestation.

Conclusions: Pregnancy significantly alters sleep, with notable disruptions beginning in the first trimester, stabilizing mid-pregnancy, worsening in the third trimester, and peaking postpartum. These findings highlight the dynamic nature of maternal sleep and underscore the importance of sleep health in pregnancy care. Understanding normative sleep changes can inform targeted interventions to optimize maternal and fetal health outcomes.

Preliminary evidence about the effectiveness of a digital therapy for insomnia and remote sleep monitoring in obstructive sleep apnea treatment

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Introduction: Obstructive sleep apnea (OSA) is a prevalent sleep disorder associated with a range of health consequences. The first-line treatment for OSA is continuous positive airway pressure (CPAP), which involves the delivery of a continuous airflow to maintain airways open. Despite the well-established benefits of CPAP treatment and its high efficacy, its acceptance and compliance remain a challenge, affecting the successful treatment of OSA. Co-morbid insomnia and sleep apnea (COMISA) is a prevalent condition among patients with OSA and might lead to decreased CPAP adherence. The treatment employed in this case is an interdisciplinary approach, CPAP with cognitive behavioral therapy for insomnia (CBTi), aiming to improve insomnia symptoms and increase CPAP adherence. The objective of this study was to assess the impact of a digital CBTi platform and remote monitoring on the CPAP usage time and sleep-related outcomes.

Materials and methods:

This study evaluated CPAP usage data from 123 users of both sexes (mean age: 48.34±11.37 years) enrolled in a CBTi program combined with remote sleep monitoring (SleepUp app). Fifty-seven (46%) of the users initiated CPAP treatment in conjunction with sleep monitoring, while 66 (54%) were individuals who had been using CPAP prior to the initiation of app use. The analysis included only patients with documented CPAP usage (>0 hours) in at least 1 time point over the course of 4 epidemiological weeks of CBTi treatment. The primary outcome was the mean CPAP usage time over each epidemiological week. The secondary outcomes were self-reported sleep quality, duration, and efficiency (sleep logs).

Results:

A significant increase in the time spent using CPAP ($\chi^2=8.93$ $p=0.030$) was observed in week 4 compared to weeks 1 ($\beta=0.36$ $p=0.045$) and 3 ($\beta=0.61$ $p<0.001$). No such increase was observed in week 2 ($p=0.090$). Sleep duration was significantly higher ($\chi^2=11.45$ $p=0.010$) in week 4 than in weeks 1 ($\beta=0.64$ $p<0.001$), 2 ($\beta=0.54$ $p=0.001$), and 3 ($\beta=0.58$ $p=0.002$). No significant differences were observed in sleep quality and efficiency over the course of the 4-week CPAP treatment, neither among subjects who initiated CPAP use concomitantly with sleep monitoring or prior to it.

Conclusions: The combined use of remote sleep monitoring with OSA treatment significantly improved CPAP adherence over a 4-week interval and increased the self-reported sleep duration. The absence of a significant distinction between new and existing CPAP users indicates that digital CBTi may confer equivalent benefits to both groups. These findings underscore the potential of digital interventions to enhance compliance with CPAP therapy. However, further research is necessary to address issues related to subjective sleep perception and long-term adherence to the treatment.

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Prevalence of Dry eye and its association with sleep quality among students of Hyderabad Central University

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Introduction: Dry Eye Disease (DED) is a condition affecting the ocular surface due to tear film alterations, with risk factors including age, gender, contact lens use, smoking, low humidity, screen time, and poor sleep quality. Symptoms like grittiness, burning, pain, blurred vision, and light sensitivity can significantly reduce quality of life and productivity, leading to economic burden.

Sleep is crucial for overall health, and disturbances such as insufficient sleep, insomnia, abnormal movements while sleeping or sleep apnea can negatively impact the ocular surface. Studies have shown that poor sleep worsens dry eye symptoms, with sleep deprivation causing changes in the lacrimal gland, lipid layer, and tear secretion, contributing to shorter TBUT and increased tear hyperosmolarity.

Materials and methods: This cross-sectional study conducted in 2023 at Hyderabad Central University involved 324 students. Approved by the Institutional Ethics Committee, informed consent was obtained from all participants. A comprehensive eye evaluation was followed by dry eye assessments, including Tear Meniscus Height (TMH), Oxford stain grading, Tear Breakup Time (TBUT), Schirmer's test, and a questionnaire via Google Forms. The questionnaire included the Standard patient evaluation of eye dryness (SPEED) and Pittsburgh sleep quality index (PSQI) scales to assess dry eye symptoms and sleep quality, respectively.

Results: A sample size of 324 was taken to find the prevalence of dry eye and its association with sleep among students of Hyderabad central university. Mean age of students is 19.5 ± 0.7 years, among them 61% were males and 39% were females. 43% were emmetropes, and 57% were myopes. Myopia was the most predominant refractive error in our study.

Prevalence of evaporated dry eye is 29%, whereas aqueous deficient dry eye is 11.3%. The reported Prevalence of dry eye using standard patient evaluation of eye dryness (SPEED) questionnaire, subjectively is 72%.

The prevalence of poor sleep quality among the population of HCU was 55%. Occurrence of DED is severe in subjects with poor sleep quality as compared to subjects with good sleep quality. Multiple regression analysis was performed to see the relation between dry eye and sleep, which showed strong positive correlation of upto 80%. Spearman's correlation between SPEED and Seven components of sleep shows that there is strong positive correlation with Component 7 of PSQI which is day time dysfunction.

Conclusions: Our study found that there is prevalence of dry eye and poor sleep quality among students of Hyderabad central university was 40% and 55% and occurrence of DED was more prevalent in poor sleepers compared to good sleepers, this shows that sleep is an independent factor DED. Addressing sleep quality may play a crucial role in reducing the burden of dry eye disease among young adults. Future studies with larger and more diverse populations are recommended to confirm these findings and to explore the effectiveness of sleep improvement interventions in the management of DED.

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Prevalence of Exploding head syndrome (EHS) does not change from year to year

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Introduction: Exploding head syndrome (EHS) is a parasomnia characterized by the perception of loud noises or explosions inside the head during sleep-to-wake transition. However, the prevalence of EHS remains unclear. It is unknown whether the prevalence has changed from year to year. Therefore, we analyzed the change in prevalence of EHS over a 5-year period.

Materials and methods: As part of the Night in Japan Home Sleep Monitoring Study (NinjaSleep study), annual questionnaire survey was conducted among government employees in Koka City, Shiga Prefecture, Japan. To assess EHS, participants were queried “When dozing off or falling asleep, have you ever felt a sudden explosion in your head (e.g., bang, bang) or had the sensation that an explosion had occurred inside your skull?” from 2020 to 2024. Approval for the study protocol (R2017-111) was obtained from the Ethics Committee of the Shiga University of Medical Science.

Results: In total, 1.9% (29/1504), 1.6% (29/1832), 2.6% (48/1873), 1.6% (29/1811), and 2.0% (28/1401) of participants answered positively to the EHS screening questionnaire. No significant differences were found in the prevalence of EHS in these five years ($p=0.187$).

Conclusions: No significant differences in the prevalence of EHS were observed during the 5 years studied. Since EHS is a little-known sleep disorder, it is possible that asking this question every year would increase the percentage of positive responses; however, no obvious change in the positive response rate was observed.

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Reduction in depression outcomes following CBT for insomnia: a potential role of general and sleep-related repetitive negative thinking and behavioural activation

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Introduction: Robust evidence supports cognitive behavioural therapy for insomnia (CBT-I) as an effective treatment for individuals experiencing both insomnia and depression. However, the mechanisms by which this sleep-focused intervention exerts its antidepressant effects remain poorly understood. This study examined whether individuals participating in a CBT-I group within routine clinical settings demonstrated improvements in general repetitive negative thinking (RNT), sleep-related RNT, and behavioural activation (BA), and whether these improvements were associated with reductions in depression outcomes reflecting potential pathways through which CBT-I may alleviate depression.

Materials and methods: The study recruited 80 participants (72.5% females) aged 23 to 89 years (Mage = 56.43, SD = 15.05), of whom 41 (Mage = 47.98, SD = 14.45) were recruited from a private behavioural sleep clinic, and 39 (Mage = 65.31, SD = 9.63) from a university-based psychology clinic. All participants were received a 4 week CBT-I group program.

Results: Using latent growth modeling, we found that participants demonstrated improvements in their depression outcomes, general RNT, sleep-related RNT, and BA overtime. Furthermore, the degree of improvement in RNT differed by time of day, with participants showing greater reductions in bedtime RNT compared to daytime RNT. Our findings also revealed strong associations between the extent to which participants' bedtime and daytime sleep-related RNT improved and the extent to which their depression outcomes improved ($r = .75$, $p < .001$ and $r = .68$, $p < .001$, respectively). Due to the lack of between-person variability in improvements for general RNT and BA, our study was unable to examine their association with improvements in depression outcomes.

Conclusions: These preliminary findings suggest that sleep-related RNT may be a plausible mechanism through which CBT-I improves depressive symptoms. Our findings also supports the literature that argues insomnia-related factors, such as Sleep-related RNT, may contribute to maintenance of depression. Future studies should test the relationship between improvements in sleep-related RNT and depression outcomes using a randomised controlled trial (RCT) and employ a research design capable of determining temporal ordering.

Relationship Between Sleep Quality and Symptom Severity in Patients with Schizophrenia: A Cross-Sectional Study

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Introduction:

Sleep disturbances are common among patients with schizophrenia and may influence the severity of psychiatric symptoms. However, the relationship between sleep quality and symptom severity remains unclear. This study aimed to investigate the correlation between subjective sleep quality, assessed by the Pittsburgh Sleep Quality Index (PSQI), and the severity of schizophrenic symptoms, measured by the Positive and Negative Syndrome Scale (PANSS), in a clinical sample.

Materials and methods: A cross-sectional study was conducted on 89 patients diagnosed with schizophrenia (79 men and 10 women). Participants completed the PSQI questionnaire and were evaluated using the PANSS scale. Pearson correlation was used to assess the relationship between sleep quality and symptom severity.

Results: The mean PSQI score was 8.17 (SD = 2.11), and the mean PANSS score was 81.81 (SD = 21.49). The Pearson correlation coefficient between PSQI and PANSS scores was $r = 0.011$ ($p = 0.918$), indicating no significant linear relationship between sleep quality and severity of schizophrenic symptoms in this sample.

Conclusions: In this cohort, subjective sleep quality was not significantly associated with the severity of schizophrenia symptoms. Further research with larger samples and objective sleep assessments is warranted to explore this relationship.

Reliability and validity of the Persian version of the Chalder Fatigue Scale in Iranian populations

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Introduction: Fatigue refers to a lack of energy that makes it challenging to initiate or maintain voluntary activities. The Chalder Fatigue Scale (CFS) is a tool designed to assess the severity of fatigue. Studies indicate that it has strong validity and internal reliability, measuring both the mental and physical aspects of fatigue. We aimed to translate and assess the reliability and validity of this questionnaire in Iran.

Materials and methods: The translation process adhered to guidelines for cross-cultural adaptation of self-report measures. This cross-sectional study included 70 participants. The reliability of the CFS was evaluated through internal consistency and test-retest reliability. To determine test-retest reliability, each participant completed the scale twice, with a two-week interval between assessments. Construct validity was assessed using factor analysis and principal component analysis. For content validity, a form was completed by 15 experts to evaluate the relevance and necessity of the items, calculating both the Content Validity Index (CVI) and the Content Validity Ratio (CVR).

Results: The average age of the participants was 38 years, with a standard deviation of 8.52. Among the participants, 31.4% were male. The Cronbach's alpha coefficient for the CFS was 0.89. The Intraclass Correlation Coefficient for the CFS was 0.79 (95% confidence interval: 0.66–0.87, $P < 0.001$), reflecting good test-retest reliability. Factor analysis identified a two-factor solution. Content validity analysis yielded a CVI of 0.88, indicating acceptable relevance, and a CVR of 0.81, demonstrating good content validity.

Conclusions: The results indicate that the CFS is a reliable and valid tool for assessing fatigue, making it suitable for use in both research and clinical environments in Iran.

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Scientific and Operational Strategies to Optimize Performance through “High-Quality and Adequate-Quantity Sleep” in Elite Sport: The Italian Football Experience

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Introduction: In elite sport, optimizing recovery is as critical as training itself. Recent evidence emphasizes the pivotal role of both sleep quality and sleep duration in supporting athletic performance, cognitive function, and injury prevention. However, elite football presents unique challenges, including irregular schedules, frequent travel, and high psychological demands, which often impair sleep. This work presents a multi-level strategy developed and implemented within top-tier Italian football clubs to optimize player performance through tailored sleep science interventions, aiming to achieve both high-quality and adequate-quantity sleep.

Materials and methods:

A multidisciplinary team composed of sports scientists, sleep specialists, coaches, and medical staff collaborated to assess and improve sleep hygiene, circadian rhythm alignment, and recovery protocols. The intervention was structured according to the “**5P Method**”, a comprehensive approach to optimizing *high-quality and adequate-quantity sleep*, based on five integrated pillars:

- **Active Elements:**
 - (i) *Sleep knowledge*: structured sleep education delivered to athletes and technical staff to increase awareness and behavioral engagement;
 - (ii) *Objective data & demographic profiling*: monitoring through wearable technologies (actigraphy, HRV), sleep latency tracking, and apnea screening;
 - (iii) *Subjective data & psychographic profiling*: analysis of routines, digital behavior, anxiety levels, and individual perception of rest.
- **Passive Elements:**
 - (iv) *Sleep system*: assessment and personalization of sleep ergonomics, including mattress and pillow testing based on individual morphology and sleep patterns;
 - (v) *Sleep environment*: optimization of external conditions—light exposure, noise levels, room temperature, air quality, and reduction of electromagnetic interference (electrosmog).

Furthermore, the 5P Method was **integrated into the athletes' training and competition planning**, including:

- Sleep periodization aligned with physical and tactical workloads
- Personalized strategies for pre- and post-match recovery
- Management of jet lag and travel-related sleep disruption
- Routine screening and monitoring protocols
- Structured *power nap* strategies during training camps and competitions

These multidimensional interventions were customized to the athlete's profile and performance context, continuously monitored and refined in cooperation with club staff.

Results: Preliminary findings show significant improvements in sleep metrics, including total sleep time (+12%), sleep efficiency (+8%), and subjective sleep quality (+20%). These changes were associated with improved reaction times, reduced perceived fatigue, and a measurable decrease in injury rates. Performance data indicated a positive correlation between optimized sleep profiles and key performance indicators (KPIs) during competitive matches.

Conclusions: Implementing a structured, evidence-based sleep strategy tailored to the realities of elite football can meaningfully enhance recovery, performance, and overall player well-being. These findings support the integration of sleep science as a core component of high-performance sport programs.

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football performance. We also acknowledge the contribution of sports science and chronobiology experts who provided valuable input in designing and implementing the intervention strategies.

Sleep Disorders in a Neurological Rehabilitation Setting: Prevalence and Clinical Implications

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Introduction: Sleep disorders are common among neurological patients and can either trigger, exacerbate, or accompany neurological conditions. Examples include sleep-disordered breathing in stroke and dementia, REM sleep behavior disorder and insomnia in Parkinson's disease, and excessive daytime sleepiness and fatigue in multiple sclerosis. Despite their considerable impact on quality of life and rehabilitation success, sleep disorders are frequently underdiagnosed and seldom integrated into treatment plans within neurological rehabilitation settings.

Materials and methods: In this observational study, 202 consecutive patients (90 male, 112 female; mean age 67±13 years) undergoing neurological rehabilitation at the Center for Neurological Rehabilitation Zihlschlacht, Switzerland, were screened between May and October 2023. Sleep health was assessed using the 15-item self-reported Bernese Sleep Health Questionnaire (Vorster et al., 2024). The cohort included individuals with stroke, traumatic brain injury, Parkinson's disease, and multiple sclerosis.

Results: • Insomnia symptoms (≥3x/week) were reported by 26% of patients and were associated with poor sleep efficiency (<85%) in 25%.

- Sleep medication was used by 17%.
- Snoring was reported by 22%, while 15% exhibited a high risk for sleep apnea (abbreviated Stop-Bang score >4).
- Excessive daytime sleepiness was noted in 26%, and fatigue in 31%.
- Restless legs syndrome was indicated by 15% (Ferri et al., 2007).
- Parasomnia symptoms, including frequent nightmares (≥1x/week), were reported by 7–8% of patients.
- Overall, 34% of patients failed ≥4 out of 8 domains in the Sleep Health Score, suggesting multi-dimensional poor sleep quality.

Conclusions: Over one-third of neurological rehabilitation patients are affected by clinically significant sleep disorders requiring medical attention. Systematic screening and targeted treatment of these conditions may significantly improve both general health and rehabilitation outcomes. In light of the large number of patients with comorbid sleep disturbances and the relevance of sleep for overall prognosis, a comprehensive package of 25 measures was developed to improve this important aspect within the context of inpatient neurorehabilitation. These measures included, among others, the implementation of clinic-wide training for all staff members, as well as specialized training for a dedicated 'Sleep Nurse' who focuses specifically on issues related to sleep

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Sleep disorders in patients with low back pain and comorbid mood disorders

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Introduction: Low back pain (LBP) seriously impairs individual's quality of life and it is the leading cause of years lived with disability worldwide. LBP often accompanied by anxiety, depression, and sleep disorders. Although some previous studies have found a bidirectional relationship between pain and sleep, there may be a problem of mixed multi-site pain. Additionally, there may still lack of data on comorbid mood disorders (depression and anxiety) affecting sleep. Therefore, this study aims to systematically analyze the sleep characteristics across different types of LBP by combining subjective sleep data, and further explore the effects of depression and anxiety on sleep.

Materials and methods: This study was conducted using data from the UK Biobank. Participants were classified into three groups according to the duration of LBP: no LBP, acute LBP (<3 months), and chronic LBP (≥3 months). The subjective sleep data included sleep duration, getting up in morning easy, morning/evening person (chronotypes), nap during day, sleeplessness/insomnia, snoring, daytime dozing/sleeping. Covariates included age, sex, body mass index, smoking, drinking, depression, and anxiety. Multiple linear regression models were used to analyze the relationship between LBP types and sleep parameters. Continuous variables were represented by mean ± standard deviation, while categorical variables were represented by frequency and percentage. Group differences were analyzed by analysis of variance for continuous variables and chi-square tests for categorical variables.

Results: A total of 405,044 patients were enrolled, including 150,121, 11,187, and 14,621 patients with no pain, acute LBP, and chronic LBP, respectively. Comorbid depression and anxiety were significantly more prevalent in patients with chronic LBP than in those with acute LBP or no pain, with depression rates of 15.7%, 17.2%, and 20.3%, and anxiety rates of 17.9%, 20.5%, and 25.4%, respectively. Sleep duration was significantly reduced in the depression group (7.12 ± 1.09 hours) and the chronic LBP with depression group (7.09 ± 1.16 hours), compared to the no pain group (7.26 ± 0.95 hours). Besides, patients with chronic LBP showed more sleep disturbances, such as insomnia, sleep late, nap and daytime dozing, while patients with acute LBP showed more snoring. Patients with LBP comorbidity depression or anxiety significantly reduces sleep time, increases difficulty getting up in morning, sleep late, insomnia. Additionally, patients with chronic LBP without mood disorders have a higher rate of snoring.

Conclusions: LBP significantly affects an individual's sleep quality, and longer pain duration, comorbid depression and anxiety can exacerbate sleep disorders. These findings highlight the need for personalized, integrated interventions targeting both pain and mood disorders, which may better improve clinical outcomes and enhance the quality of life in patients with LBP.

Acknowledgments: We gratefully acknowledge the UK Biobank team for providing the data resource, and all the participants who took part in this project.

Sleep EEG Signatures of APOE4 in Older Adults with Subjective Cognitive Impairment

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Introduction: Alzheimer's disease (AD) is the leading cause of dementia and a major global health concern. The APOE4 allele is the strongest genetic risk factor for late-onset AD. Pathological changes such as amyloid-β accumulation and tau pathology begin decades before clinical symptoms, creating a critical window for early detection and intervention. Sleep—particularly non-rapid eye movement (NREM) sleep—plays a central role in glymphatic clearance and has emerged as a promising non-invasive biomarker of early AD-related change.

Subjective Cognitive Impairment (SCI), characterised by self-reported cognitive decline without objective impairment on neuropsychological testing, is increasingly viewed as a potential early manifestation of neurodegeneration. Individuals with SCI are at elevated risk for future development of dementia. However, the relationship between APOE4 status and sleep EEG features in this group remains underexplored.

Materials and methods: Participants (N = 101) were older adults with SCI enrolled in the Healthy Brain Ageing Program. All underwent overnight in-laboratory polysomnography and genotyping. EEG spectral power was calculated for NREM sleep at six standard electrodes (C3, Cz, Fz, O1, Oz, Pz).

Relative power in delta, theta, alpha, sigma, and beta bands was derived. Linear models tested the association between APOE4 carrier status and each EEG variable, adjusting for relevant demographic and clinical covariates. Results were corrected for multiple comparisons using FDR.

Results: Seven NREM EEG features significantly differed between APOE4 carriers and non-carriers. Notably, APOE4 carriers exhibited: Decreased delta power at Oz and Pz, Increased beta power at Oz and Pz, Increased sigma power at Oz, Increased alpha power at Oz, Increased theta power at O1.

These changes were most prominent in posterior electrodes. In contrast, no significant effects were observed at frontal (Fz) or central (Cz) sites, suggesting a posterior-dominant spectral profile.

Conclusions: Individuals with Subjective Cognitive Impairment who carry the APOE4 allele exhibit a distinct pattern of NREM sleep EEG alterations, characterised by reduced slow-wave activity and increased fast-frequency power in posterior regions. These findings resemble spectral changes observed in symptomatic AD but are more spatially confined. This suggests that sleep EEG may reflect early electrophysiological disruptions in at-risk individuals, supporting its role as a potential biomarker for preclinical AD.

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Sleeping while Queer: Impacts of sexual and gender identity-related concerns on sleep health in the LGBTQ+ community before and after the 2025 US presidential inauguration

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Introduction: To examine the impact of sexual and gender identity-related concerns on sleep health in the LGBTQ+ community before and after the 2025 US Presidential inauguration.

Materials and methods: LGBTQ+ adult participants completed an online survey containing questions about sexual and gender identity-related concerns and their impacts on sleep health. Pre-inauguration responses were collected June 2023 to September 2024. Post-inauguration responses were collected February to March 2025. Multivariable regression was used to assess impacts of sexual and gender identity-related concerns on sleep health pre- and post-inauguration. The survey was IRB exempt.

Results: 271 members of the LGBTQ+ community completed the survey (152 pre-inauguration, 119 post-inauguration). 74% of respondents have a diagnosed sleep disorder. 94% currently experience sleep problems, and of these, 98% reported that their sleep problems impact their physical, mental, and/or emotional well-being. 80% of respondents said concerns related to their gender and sexual identity may negatively impact their sleep.

Following the 2025 US presidential inauguration, there were significant increases in respondents' concerns about finding and maintaining friendships (OR 2.15, $p=0.007$), employment (OR 1.90 $p=0.021$), housing (OR 2.04, $p=0.043$), being safe in their homes (OR 3.39, $p=0.043$) and in public (OR 1.87, $p=0.013$), being bullied or harassed (OR 2.60, $p=0.002$), having restricted civil rights (OR 3.14, $p<0.001$), losing civil rights (OR 3.57, $p<0.001$), and accessing health care (including gender affirming care) (OR 2.36, $p=0.002$).

Transgender and nonbinary respondents were also significantly more likely to have concerns about maintaining family relationships (OR 3.64, $p<0.001$), and were significantly more likely than cisgender respondents to say their concerns have probably (OR 3.54, $p=0.003$) or definitely (OR 2.63, $p=0.02$) had a negative impact on their sleep.

Conclusions: This study finds that LGBTQ+ community members are experiencing significantly higher rates of minority stress-related sleep issues than before the 2025 US presidential inauguration. These differences may be linked to a post-inauguration increase in federal anti-LGBTQ+ policies and presidential executive orders. Overall, this study provides valuable insights into factors negatively impacting sleep health in LGBTQ+ communities following the 2025 inauguration and highlights distinct differences between the impacts on transgender and nonbinary individuals and their cisgender counterparts.

The comorbidity of ischemic heart disease requiring (IHD) revascularization significantly correlates with obstructive sleep apnea (OSA)

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Introduction:

Obstructive sleep apnea (OSA) is a chronic condition characterised by periodic stopping or shallowing of breathing during sleep due to collapse of the soft tissues of the throat. There is evidence to suggest that OSA and ischemic heart disease (IHD) may co-occur. Chronic vascular inflammation and oxidative stress, caused by episodes of hypoxia during episodes of shallowing and nocturnal apnea, have been identified as factors that predispose patients to the development of atherosclerotic cardiovascular disease (CVD). The aim of this study was to investigate the relationship between the prevalence of IHD requiring revascularisation treatment and the severity of OSA. Furthermore, the compliance of patients with mild or severe OSA with continuous positive airway pressure (CPAP) therapy was investigated.

Materials and methods: This retrospective study was conducted between 2022 and 2024, analysing data from 70 patients with different stages of OSA and varying degrees of IHD. Demographic data, respiratory parameters obtained from a sleep polygraph examination, information on comorbidities, and eligibility for continuous positive airway pressure (CPAP) treatment were analysed. Patients were divided into two groups: those without or with mild OSA and those with moderate or severe OSA.

Results: The prevalence of ischemic heart disease necessitating revascularisation therapy (by coronary artery bypass grafting or coronary artery angioplasty) was higher in patients with a greater degree of sleep apnea (41.18% in the group with severe obstructive sleep apnoea). Moreover only 14 (40%) of the patients with moderate to severe OSA who met the criteria for CPAP therapy were using this form of therapy.

Conclusions: The incidence of IHD requiring revascularisation treatment is higher in patients with severe OSA than in those with less severe forms of the condition.

The Effects of Daytime High-intensity Swimming Training in Nighttime Parasympathetic Activity for Swimmers with Different Training Status

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Introduction: Sleep involves significant fluctuations in sympathovagal balance throughout the cycles of non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Previous study demonstrated the advantage of using heart rate variability (HRV) during slow wave sleep (SWS) is that fewer external body movement or arousal which might cause abrupt HR increase and disrupt the

electrocardiography signal. The root mean square of successive normal R-R interval differences (RMSSD) was reasonably linked to vagal activity.

R-R interval and RMSSD decreased during both daytime and SWS in nighttime after supramaximal intermittent exercise in healthy individuals. Parasympathetic activity in athletes decreases during SWS but increases during wakefulness in the overload period compared to the taper period. Current studies lack objective comparisons between populations under different training conditions during sleep. Research is scarce on nighttime RMSSD performance in swimmers with varying training status under identical training volumes. This study compares sympathetic and parasympathetic activation during SWS in regular training versus recreational swimmers after five training days. We also examined psychological state and sleep architecture changes before and after training.

Materials and methods: Participants were members of the swimming team at National Cheng Kung University, Taiwan. Eligible participants were swimmers aged ≥ 20 years, free of sleep, physiological, psychological, and neurological disorders, as confirmed by a clinical physician. Exclusion criteria included late-night shift work, sports injuries within the past 6 months and long-term medication use. Participants were divided into two groups based on training load and competition participation: the recreational group (R group), consisting of swimmers from former varsity members with irregular training status (e.g. ≤ 2 days/week), and the regular training group (RT group), comprising active swimmers from varsity members with training routine of 4 or more days per week.

The study included two randomized experimental sessions, separated by at least one week: one on a training day and the other on a non-training day. HR, HRV as well as standard polysomnography (PSG) were assessed during sleep. Standard PSG was conducted for determining sleep phase while HR was measured using a wrist pulse oximeter. HR derived RR interval was further used to calculate RMSSD during N3 sleep as index of HRV.

Results: In the RT group, compared to the non-training day, REM stage, sleep efficiency, and HR in N3 increased by 3.75% ($p=0.027$), 5.89% ($p>0.05$), and 5.54 BPM ($p=0.028$), respectively, while RMSSD decreased by 16.40 ms ($p=0.028$). In the R group, REM stage, HR in N3, and RMSSD increased slightly, while sleep efficiency decreased, with no significant differences ($p>0.05$). RT group showed consistent sympathetic activation and reduced parasympathetic activity, whereas R group exhibited varied responses due to individual differences.

Conclusions: Regular trained swimmers who were capable to execute the training protocol at higher intensity demonstrated reduction in nighttime parasympathetic activity, while swimmers of recreational group showed more variability in similar measurements.

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The Influence of Short-Term and Long-Term Sleep on Postural Control and Balance

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Introduction: Sleep plays a vital role in neurophysiological processes, including synaptic plasticity, motor memory consolidation, and postural control. Disrupted or insufficient sleep impairs sensory integration and increases postural instability, elevating fall risk. While the detrimental effects of sleep deprivation are well-established, the potential of short sleep episodes (naps) to enhance postural adaptation is less understood. Additionally, the influence of long-term sleep patterns and individual chronotype on postural control remains partially underexplored. This study investigated: (a) the effect of a short nap between two postural testing blocks on postural adaptation, and (b) the relationship between sleep quantity, chronotype, and postural performance in healthy young adults.

Materials and methods: 12 participants (6 males, 6 females; aged 20–25) completed two identical experimental sessions one week apart. Each session included two blocks of 10 single-leg stabilometric trials (60 s each; 90 s rest). Between blocks, participants either napped (EEG-verified) or stayed awake (quiet seated rest) for 45 minutes; conditions were counterbalanced. Sleep parameters were also monitored via wrist actigraphy for 7 nights between sessions. Chronotype and daytime sleepiness were

assessed using the reduced Morningness–Eveningness Questionnaire (rMEQ) and Epworth Sleepiness Scale (ESS), respectively.

Results: Among the 12 participants, 2 were classified as M-type, 9 as N-type and 1 as E-type, with moderate levels of daytime sleepiness ($ESS = 7.08 \pm 2.75$). EEG monitoring during the nap showed an average total sleep time (TST) of 21 minutes and a sleep efficiency (SE) of 63%. Actigraphy data indicated a TST of 6.8 hours and SE of 79.7%.

Paired t-test revealed significant post-nap changes, whereas no significant differences were observed in the wake condition ($p > 0.05$). After the nap, participants exhibited a significant increase in postural sway variability (SD_x : $p = 0.019$; SD_y : $p = 0.001$; SD_{tot} : $p = 0.001$) and in the Area of the 95% confidence ellipse derived via Principal Component Analysis ($p = 0.001$). Concurrently, there was a significant decrease in Entropy along both x ($p = 0.035$) and y axes ($p = 0.004$), suggesting a reduction in postural control complexity.

Correlation analyses showed that greater post-nap increases in sway amplitude and area were associated with higher subjective fatigue ($p < 0.05$), but not with chronotype or sleepiness. Although overall EEG-based regression models were not significant, N2 duration emerged as a predictor for some postural parameters. In contrast, actigraphy-based models revealed that actigraphic TST significantly predicted pre–post nap difference in SD_y , SD_{2D} , and Area (all $p < 0.001$, all r negative). Mixed-effects models confirmed a significant main effect of the interaction between condition (Sleep/Wake) and time (Pre/Post) for most stabilometric variables. Notably, entropy showed an opposite pattern of change compared to sway-related variables, suggesting distinct underlying mechanisms in postural control responses to sleep. A trial effect suggested potential learning across repetitions.

Conclusions: Sleep produces measurable alterations in postural control, increasing sway magnitude and reducing signal complexity. These changes appear influenced more by long-term sleep quantity than by nap-specific sleep architecture. These findings are preliminary, and further analyses are underway to validate and expand upon these initial results.

The Sleep and Wearables Operational Research for Readiness and Deployment (SWORD) Lab: A Program to Study Sleep and Circadian Science in the U.S. Military

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Introduction: Insomnia is a common sleep disorder that is 2-3 times more prevalent in military/veteran United States (U.S.) Service Members (SMs) than civilians. Moreover, over half of U.S. SMs sleep less than six hours a night. Sleep deficits decrease performance, attention, and information processing, and increase risk of injury, suicidality, and chronic diseases. Sleep physiology is complex, remains poorly understood, and interventions, especially those that are noninvasive, are limited. This multi-pronged program uses wearables to capture longitudinal autonomic data, studies glymphatic correlates, seeks to further understand biomarkers and cognitive function related to sleep, investigates biofeedback-based interventions, and utilizes retrospective/large sample datasets to inform measurements. The program also aims to understand the impact of unique U.S. military exposures on sleep, such as repeated low-level blast exposure experienced during training, and also to understand novel phenomena such as local sleep in wake.

Materials and methods: Our program includes six components focused on non-invasively characterizing and modulating sleep physiology in U.S. SMs, veterans, and their families:

1. Glymphatics physiology measuring brain interstitial fluid, cerebrospinal fluid, and cerebral blood flow changes during wake and sleep via ultra-high-performance magnetic resonance imaging (MRI) and wearable functional near-infrared spectroscopy (fNIRS) headband.
2. Autonomics functioning and circadian rhythm modeling measurements via multimodal wearables worn longitudinally, with a focus on gold-standard validation.
3. Sham-controlled wearable interventions, including: a) wearable transcranial electrical stimulation headband, b) smartwatch haptic biofeedback, c) whole-body and transcranial photobiomodulation, and d) low-intensity focused ultrasound.
4. Biospecimen measurements from high sensitivity assays via blood, sweat, saliva, and microbiome.

5. Cognitive testing via high-specificity customized tasks.

6. Retrospective/large sample polysomnogram analysis to uncover novel biomarkers.

Approximately 750 participants are projected to be enrolled. To date, over 60 participants are enrolled across projects. The program includes five (5) study enrollment sites.

Results: We will present multimodal pipeline designs for review. Preliminary results will include sleep correlates with blood biomarkers, cognition, wearables, and fNIRS data. Initial assessment of wearable devices will be presented. Early validation efforts of commercial and non-commercial devices for sleep monitoring will be presented.

Conclusions: Sleep physiology remains inadequately characterized and treated, especially in far-reaching environments such as those experienced in military operations. Modulation techniques for sleep quality, or targeting specific sleep features, remain limited and often include pharmacological approaches. Our program embarks on an exciting multimodal approach to better characterize sleep physiology and even deliver therapy longitudinally in a noninvasive manner.

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Tired and Wired: Sleep Deprivation Prevents Affective Renormalisation During Exposure to Ambiguous Threat

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Introduction: Sleep deprivation amplifies next-day state anxiety and impairs threat-related information processing, but little is known about how sleep loss affects the evolution of anxiety over the course of a threatening experience. Reciprocally, sleep slow wave activity (SWA) has been shown to reduce next-day state anxiety, but whether SWA influences the evolution of threat-related anxiety remains to be established. In the current study, we combined immersive virtual reality (VR) and psychophysiology to test two hypotheses: 1) sleep deprivation amplifies in-the-moment arousal responses to prolonged threats, and 2) SWA supports the resolution of anxiety during exposure to prolonged threat.

Materials and methods: Following a night of polysomnographically-monitored sleep or total sleep deprivation, N = 54 adults (mean [SD] age = 20.30 [2.27] years, 33 females) entered an immersive VR world that cycled between threatening and non-threatening environments, during which their skin conductance level (SCL) and heart rate (HR) were monitored. Participants then watched a replay of their VR experience and retrospectively rated their subjective arousal at each moment. Physiological (SCL and HR) and subjective arousal measures were averaged across the various threatening and non-threatening environments and applied to a 2 (Environment: Threatening/Non-Threatening) X 2 (Group: Restful Sleep/Sleep Deprivation) mixed ANOVA.

Results: We replicated previous studies demonstrating that self-reported state anxiety significantly increased overnight in sleep-deprived participants, while it significantly declined in those who were well-rested. Physiological arousal (based on SCL) remained elevated across the threatening parts of the VR world after sleep deprivation but not after restful sleep (where instead arousal declined over time; interaction: $p = .030$), supporting our first hypothesis. No such effect was observed in the HR data or for subjective arousal. Correlational analyses indicated that SWA was not associated with the sleep-related decline of threat-related physiological arousal, contrary to our second hypothesis.

Conclusions: Our findings indicate that a restful sleep promotes the resolution of anxiety when engaging in threatening environments for prolonged periods of time. However, this anxiolytic benefit of sleep does not appear to be dependent on SWA. More broadly, this work provides novel insight into the mechanisms through which our brains navigate threats and uncertainties in our everyday lives.

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Updated Atlas and Scoring Rules for the Cyclic Alternating Pattern (CAP): A Consensus Report by the ESRS Taskforce

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Introduction: The cyclic alternating pattern (CAP) is a hallmark of NREM sleep microstructure and a recognized biomarker of sleep instability. Since the 2001 CAP rules, advancements in EEG analysis, pediatric neurophysiology, and REM sleep understanding have highlighted the need for updated and standardized scoring criteria. This project, commissioned by the European Sleep Research Society, aimed to develop a revised CAP scoring framework compatible with modern standards and clinical applicability.

Materials and methods: An expert Taskforce systematically reviewed the original CAP scoring system, integrating updated AASM guidelines, newly validated EEG patterns, and structured input from pediatric and REM sleep research. Consensus-derived rules were formulated through iterative discussion and literature synthesis.

Results: Key innovations include:

- Dual amplitude and frequency criteria for defining phase A onset and offset, with $\geq 60\%$ lead concordance.
- Expanded EEG event catalog for phase A (e.g., high-amplitude slow transients, mixed-frequency transients, beta bursts).
- Formalized subtype classification with clear decision rules.
- Comprehensive pediatric adaptations, including age-specific EEG norms and developmental thresholds.
- Optional CAP scoring guidelines for REM sleep in pathological contexts (e.g., RBD, REM OSA).
- Standardized metrics for CAP quantification (e.g., CAP rate, subtype distribution, sequence characteristics).

Conclusions: The updated CAP Atlas provides a rigorous, developmentally sensitive, and clinically translatable scoring system. It enables accurate assessment of sleep instability across populations and conditions, fostering harmonized CAP use in research and clinical practice.

Parasomnia

Enhanced Phase-Amplitude Coupling Prior to Dream-Enactment Behaviors in isolated REM Sleep Behavior Disorder: A Video-Polysomnography Study

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Introduction: REM sleep behavior disorder (RBD) is characterized by dream-enactment behaviors (DEBs), often involving motor activities and vocalizations that are sometimes violent. However, the neurophysiological mechanisms underlying these behaviors remain poorly understood. Previous studies on NREM parasomnia have suggested that mixed features of sleep and wakefulness may contribute to the occurrence of abnormal behaviors. Although similar dissociation of arousability between brain regions may be implicated in RBD, the neural information processing underlying subsequent episodic behaviors remains poorly understood. Our previous study demonstrated increased functional connectivity in the beta frequency range preceding DEBs in patients with isolated RBD (iRBD). However, no study has yet investigated cross-frequency interactions, such as phase-amplitude coupling

(PAC), leading to DEBs. In this study, we analyzed polysomnographic (PSG) data from patients with iRBD to investigate changes in PAC preceding DEBs.

Materials and methods: We analyzed EEG recordings from 30 patients with iRBD (24 males; mean age: 69.7 years) with intense, complex movements confirmed by video-PSG at Shiga University of Medical Science Hospital. EEG was recorded using six scalp electrodes (F3, F4, C3, C4, O1, and O2). Ethical approval and informed consent were obtained from all patients. The EEG data were re-referenced using the M1-M2 average before the analysis. For each patient, we compared two 60-second artifact-free REM sleep periods: (1) pre-DEB periods immediately preceding DEB onset and (2) non-DEB periods without DEBs and with minimal submental EMG activity.

PAC was computed using the Kullback-Leibler modulation index (phase: 0.5–8.0 Hz with 0.5 Hz-bin; amplitude: 10–50 Hz with 1-Hz bin). We first analyzed PAC across the average of the six electrodes to identify significant PAC clusters. Using a one-tailed cluster-based permutation test (10,000 permutations; $p < 0.05$), we identified significant PAC frequency pairs ($p < 0.005$). Frequency clusters for further analysis were defined based on the significant clusters. Subsequently, PAC was evaluated at each individual electrode to investigate topographical characteristics.

Results: We first identified increased PAC clusters in the pre-DEB periods compared to the non-DEB periods using cluster-based permutation testing across averaged electrodes. Based on their spectral features, we defined two broader clusters: low-delta (0.5–1.5 Hz)-gamma (30–50 Hz) and theta (4–8 Hz)-gamma frequency range. Next, PAC analysis at individual electrodes revealed similar patterns between left (F3, C3, O1) and right (F4, C4, O2) sites. The frontal and occipital electrodes showed comparable PAC enhancement, whereas the central electrodes exhibited fewer increases and a distinct pattern. Region-specific modulation was also observed: gamma-band amplitude was modulated by slow-wave phases in the frontal region, while beta-band amplitude was modulated in the occipital region.

Conclusions: We found significant PAC increases in low-delta-gamma and theta-gamma frequencies during the pre-DEB periods compared to the non-DEB periods. PAC enhancement may reflect activation or suppression related to visuomotor control, potentially associated with dream experiences leading to DEBs. These findings provide new insights into the neurophysiological processes preceding DEBs. Future longitudinal studies are needed to examine whether PAC changes before DEBs evolve over time and predict phenoconversion.

High-Frequency Oscillations Across Wakefulness and Sleep in NREM Parasomnia and Sleep-Related Hypermotor Epilepsy

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Introduction: High-frequency oscillations (HFOs) have recently been defined in patients with epilepsy as electrophysiological markers of the neuronal hyperexcitability. HFOS have become increasingly prominent in epilepsy research as their role in the pathophysiology of epilepsy has been well-established in recent years. Based on the anatomo-patho-physiological interconnections between non-rapid eye movement (NREM) arousal parasomnias and sleep-related epilepsies, we hypothesized that HFOs, namely ripples and fast ripples, may also be detected in these patients, reflecting an increased excitability in cortical-subcortical networks.

Materials and methods: Sixteen patients with NREM arousal parasomnias, fourteen patients with non-refractory SHE, and ten age- and sex-matched healthy controls were prospectively included. HFO analysis was performed in 16-channel electroencephalography in three-minute periods from wakefulness before sleep, N2, N3 and REM sleep stages in the first (first 4 hours) and second half of the night, and wakefulness after sleep.

Results: A total of 16 patients with NREM-related parasomnia, 14 patients with SHE and 10 patients in the control group were included in our study. The ripple and/or fast ripple activities were detected in 50% of the patients with NREM parasomnias, in 71.4% of the patients with SHE, and in 30% of the healthy controls ($p=0.039$). While the total numbers of ripples and fast ripples in sleep and wakefulness were significantly higher in patients with epilepsy in compared to the patients with NREM parasomnias and controls, the comparison of data obtained from the patients with NREM-related parasomnia and

control group showed that the total number of ripples was higher in patients with NP ($p=0.048$). The total number of fast ripples occurring in the second half of sleep ($p=0.061$), the total number of fast ripples occurring during the whole sleep ($p=0.049$) and the total number of fast ripples ($p=0.044$) were also significantly higher in the parasomnia group. In patients with NP, the numbers of ripple and fast ripple activities were higher in wakefulness (than those in sleep), in temporal cortical regions (than those in frontal regions), and on right-side (than those on left side) ($p<0.05$). It was observed that the patients with SHE of frontal origin was associated with higher numbers of ripples during sleep in frontal cortical areas at seizure side, while fast ripples were increased in both wakefulness but predominantly in sleep in patients with SHE of temporal origin ($p<0.001$). In control group, the overall numbers of HFOs were scarce, being higher in sleep (than those in wakefulness), in frontal cortical regions (than those in temporal regions), and on right-side (than those on left side).

Conclusions: Our study demonstrated that high-frequency oscillations can be detected in patients with NREM arousal parasomnias. It may be suggested that HFOs, which may represent physiological elements, could similarly be disrupted in pathological states, like in parasomnias and epilepsy, as evidenced by the observed differences between normal conditions. To our knowledge, this is the first study demonstrating the presence of increased HFOs in patients with NREM arousal parasomnias, and encouraging further research to better explore the role of HFOs in the pathophysiology of NREM-related parasomnias.

Knowledge and prevalence of sleep paralysis in medical students from two Latin American universities: UDES Colombia and ULA Venezuela

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Introduction: Sleep paralysis is a state of consciousness and unconsciousness that occurs during sleep, characterized by people being able to open their eyes, but cannot move or speak. They usually experience symptoms such as shortness of breath, chest pressure, and hallucinations. Sleep deprivation resulting from long hours of study in medical students can increase the prevalence of these seizures. The objective of this study was to determine the prevalence of sleep paralysis in a group of students from two Latin American universities and their knowledge about this point.

Materials and methods: Observational, descriptive, cross-sectional study. All first- to third-year medical students from the University of the Andes (ULA) in San Cristóbal, Venezuela and the University of Santander (UDES) in Cúcuta, Colombia, were invited to participate. After signing the informed consent, a questionnaire was applied on the main symptoms of sleep paralysis and another on knowledge about the subject. Statistical analysis was performed with SPSS 22 and significance was considered less than 0.05. For categorical variables, Chi-square was used. The study was approved by the Ethics Committee of the Universidad de Los Andes.

Results: A total of 147 students were included (34.69% UDES and 65.31% ULA). The average age was 21.52 years for UDES (SD: 3.17; min: 17 and max: 35), and 25.38 years for ULA (SD: 2.71; min: 23 and max: 34) ($p<0.05$). The female sex predominated (68.63% UDES and 65.63% ULA) ($p=n.s.$). For the questions regarding knowledge of sleep paralysis, some of the answers were as follows: 1. Yes, I know what sleep paralysis is (86.36% UDES Vs 98.96% ULA) ($p=0.0051^*$). 2. It is a sleep disorder (86.27% UDES Vs 95.79% ULA) ($p=0.045^*$). For the prevalence questions, some of the answers were: 1. Have you ever felt awake while sleeping, but unable to articulate words, scream, and/or move (60.78% UDES Vs 52.08% ULA) ($p=n.s.$). 2. After a long and stressful study day, upon going to bed, have you experienced some of the sensations described above (37.25% UDES Vs 37.50% ULA) ($p=n.s.$).

Conclusions: The prevalence of sleep paralysis tends to be the same in medical students from both countries, however, students from the ULA in Venezuela have a greater knowledge about the pathology than those from the UDES in Colombia. This may be because the lead author of this study is a professor of psychiatry at that school, and he devotes several classes to sleep disorders, which goes a long way toward promoting sleep medicine education at universities.

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Mental Experiences in Disorders of Arousal: Findings from a Two-Week Prospective Diary Study

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Introduction: For decades, episodes associated with disorders of arousal (DOA) were believed to occur in the absence of mental experiences. However, recent retrospective and serial awakenings studies have challenged this view, suggesting that vivid, emotionally charged mental content may be present during these episodes. However, these findings are vulnerable to recall bias and may overrepresent atypically intense episodes. Starting from these premises, we aimed to investigate mental contents associated with parasomnia episodes using a prospective, longitudinal paradigm.

Materials and methods: To investigate mental experiences during parasomnia episodes prospectively, we developed a dedicated Event Diary, which participants were instructed to complete within 15 minutes upon awakening for 14 days. This tool was designed to systematically record the occurrence of DOA episodes and to assess the associated mental contents. Specifically, we investigated their characteristics from multiple perspectives, including perceptual, emotional, sensorimotor, and contextual aspects, as well as specific elements present within the experience. Patients also completed a battery of questionnaires, including the Paris Arousal Disorders Severity Scale (PADSS) and the Sleep Condition Indicator (SCI) to assess perceived sleep disturbances severity.

Results: 11 DOA patients (age: 29.45 ± 7.28 ; M/F: 6/5), diagnosed by a neurologist expert in sleep medicine, were enrolled, two out of them did not report any episode. The mean PADSS score was 18.44 ± 10.47 while the mean SCI score was 17.00 ± 5.07 , with the 44.44% of the sample reporting the presence of insomnia symptoms. Across 152 diary entries, 64 DOA episodes were reported.

Remarkably, over 65% of these episodes involved recollections of mental content, often described as highly realistic and emotionally intense. Higher emotional intensity was significantly associated with stronger perceived realism of the experience ($r = 0.50$, $p = 0.005$). Fear, threat, worry, and surprise emerged as the most common emotions, underscoring the disturbing nature of these experiences. Moreover, the fear intensity score positively correlated with disease severity measure by PADSS global score ($r = 0.78$; $p = 0.015$) and PADSS subscale A ($r = 0.82$, $p = 0.013$).

Furthermore, episodes involving greater sensory details and perceptions of movements were linked to stronger emotional intensity, in particular fear ($r = 0.58$; $p = 0.004$), heightened realism ($r = 0.42$; $p = 0.036$), and increased feelings of threat ($r = 0.49$; $p = 0.014$).

Contrarily to what has been reported in the literature, rarely the experience was settled in their actual sleep environment, and even more rarely they included in the scenario people, animals or objects that were really present in the room.

Conclusions: Previous retrospective studies suggested that emotional and perceptual rich mental experiences are a frequent feature of DOA episodes. However, these studies faced criticism due to potential memory and selection biases. Our daily assessment provides stronger, methodologically sound evidence supporting these findings, confirming conscious and vivid experiences during DOA episodes. Furthermore, our results highlight the clinical relevance of assessing mental content for a more comprehensive understanding of disease severity and for guiding future targeted therapeutic interventions.

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Non-Rapid Eye Movement Parasomnias and Their Impact on Academic Performance in Medical University Students: A Cross-Sectional Study

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Introduction: Parasomnias are undesirable events or experiences that occur during sleep transitions, classified into rapid eye movement (REM) and non-rapid eye movement (NREM) types. NREM parasomnias (arousal disorders) include confusional arousals, sleepwalking, and sleep terrors. Despite knowing that parasomnias can negatively impact, there is a noticeable paucity of studies on parasomnias among university students. This study is the first one in Pakistan to explore the prevalence of arousal disorders, their association with sleep quality, and their impact on the academic performance of university students.

Materials and methods: University students were sampled as part of a cross-sectional investigation. The Arousal Disorder questionnaire was used to evaluate features of NREM parasomnias among the participants, and the Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality and its characteristics. All descriptive and inferential statistical tests were conducted on IBM SPSS 26, and a $p < 0.05$ was considered statistically significant for all applied measures.

Results: The sample consisted of 319 participants of age ranging from 18-25 years [1.46 ± 0.499]. NREM parasomnias were prevalent among $n=211$ (66.1%) female participants as compared to male one $n=108$ (33.9%). Out of all, the prevalence of NREM Parasomnias included confusional arousals (49.2%), sleepwalking (15.4%), and sleep terrors (38.9%). The mean PSQI scores of the participants were 7.94 ± 3.55 , indicating an overall poor sleep quality. Sleep quality was significantly associated with prevalence of confusional arousals ($p < 0.001$), sleep walking ($p = 0.004$), and sleep terrors ($p < 0.001$). Additionally, participants' age was also significantly associated with the prevalence of confusional arousals ($p = 0.012$), with confusional arousals being more common in older age groups. Sleep quality was significantly associated with prevalence of confusional arousals ($p < 0.001$), sleepwalking ($p = 0.013$, $p = 0.004$), sleep terror ($p < 0.001$, $p = 0.001$), respectively. Sleep quality had no significant effect on students' academic performance ($p = 0.382$).

Conclusions: NREM parasomnias were fairly prevalent among university students. Poor sleep quality is strongly linked to a greater frequency of NREM parasomnias. This study focuses on NREM parasomnias among university students, which limits generalizability to non-student populations. Larger-scale studies encompassing a diverse population are warranted to ascertain the relationship between NREM parasomnias and sleep quality.

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Parasomnias and Associated Factors Among University Students: A Cross-Sectional Study in Saudi Arabia

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Introduction: Parasomnias are a group of sleep-related movements or emotions like sleepwalking, sleep talking, teeth grinding (Bruxism), nocturnal enuresis (sleep enuresis), sleep terrors (night terrors), sleep-related eating disorder (SRED), nightmare disorder, REM Sleep Behavior Disorder (RBD), and confusional arousals. Parasomnias are more common in children than in adults. This study aimed to estimate the prevalence of different parasomnias among university students in Saudi Arabia. Additionally, it aimed to study the relationship between different parasomnias and gender-associated sleep disorders, mental disorders, and other medical diseases, stress, substance use, and medications.

Materials and methods: This study is a descriptive cross-sectional survey-based study. The target population for this study is university students from different regions of Saudi Arabia. Parasomnia was defined as having at least one of

the 11 disorders (over the past six months). Data was collected through an online survey. The survey was distributed on different online platforms to collect data from other regions of Saudi Arabia. The study took place between August and November 2022.

Results: Among 1,296 participants, 934 (72.1%) were female, and 1,071 (82.6%) were aged 19-24 years. A total of 1054 (81, 3%) participants reported having at least one parasomnia disorder. The most prevalent parasomnias were sleep talking 656 (50.6%), nightmares 650 (50.2%), and confusional arousals 524 (40.4%). The least prevalent parasomnia was sleep-related eating disorder 98 (7.6%). Among participants, 580 (44.8%) had a family history of parasomnia, 439 (33.9%) were diagnosed with sleep disorders, 296 (22.8%) were diagnosed with mental illnesses, and 92 (7.1%) had other medical diseases.

Conclusions: Parasomnias are prevalent among university students in Saudi Arabia. Parasomnias were higher in female students and in students with a family history of parasomnia. Parasomnias in adults might be a chronic or recurrent disorder. Parasomnias are significantly associated with psychological stress, depression, and anxiety disorders.

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Reliability and diagnostic accuracy of home video recording in differentiating Sleep-related Hypermotor Epilepsy from Disorders of Arousal

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Introduction: Video-polysomnography is the gold standard for diagnosing Sleep-related Hypermotor Epilepsy (SHE) and confirming Disorders of Arousal (DoA), but it is expensive and may not always capture relevant events. Home video has emerged as a cost-effective alternative for detecting sleep-related behavioral episodes, though its diagnostic reliability remains under debate. This study aims to evaluate the inter-rater reliability (IR) and diagnostic accuracy of home video in differentiating SHE from DoA among neurologists with varying expertise levels. It also examines learning effects in non-experts and identifies key diagnostic features and confounding elements

Materials and methods: Twenty-four home videos from 12 patients with confirmed SHE and 12 with DoA were selected, each showing a representative sleep-related event. A group of 18 experts in epilepsy and/or sleep medicine and 12 general neurologists/residents reviewed the videos in a full-day session, classifying each as "SHE", "DoA", or "unknown" based solely on event semiology. Inter-rater agreement was assessed using Kappa statistics before and after expert discussion. Learning effects among non-experts were evaluated using McNemar's test. Thematic analysis of participant comments was conducted to identify key diagnostic features and confounding factors

Results: Overall agreement reached 75%, with a “moderate” IR (Kappa = 0.56). Among experts, agreement was 79% with “substantial” IR (Kappa = 0.62). In general neurologists, agreement increased from 70% to 82% after training, improving IR from “moderate” (Kappa = 0.47) to “substantial” (Kappa = 0.65). Misclassification was more common in DoA cases. Thematic analysis identified abrupt onset, short episode duration, ambulatory behavior, and irregular breathing as the main confounders

Conclusions: Home video is a valid and practical tool for distinguishing SHE from DoA. Its diagnostic accuracy is high among specialists and can significantly improve in non-experts following brief training. Home video can thus serve as a valuable diagnostic aid, especially in settings with limited access to advanced neurophysiological testing, and may support both initial diagnosis and long-term monitoring

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Sexomnia in a Young Adult Male. A complex case of Non-REM Parasomnia with Diagnostic and Therapeutic Challenges

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Introduction: Sexsomnia, a distinct non-rapid eye movement (NREM) parasomnia, involves involuntary sexual behaviors during sleep. Although more than 100 cases have been documented in the literature, underreporting and misdiagnosis remain prevalent. Factors such as anxiety, insomnia, and other parasomnias (e.g., sleepwalking, sleep terrors) may predispose individuals to sexsomnia. Despite emerging insights, treatment options remain largely empirical and range from pharmacotherapies to behavioral interventions, including hypnosis.

Materials and methods: Materials and Methods

We present the case of a 29-year-old male with a two-year history of aberrant sexual behaviors during sleep, initially occurring daily and later reducing to three times per week. The patient underwent in-laboratory video-polysomnography, including a comprehensive electroencephalogram (EEG) and electromyogram (EMG) assessment, as well as standard cardiopulmonary monitoring. An extensive clinical evaluation was performed, including sleep questionnaires (Epworth Sleepiness Scale, STOP-BANG), MRI of the brain, and a review of psychiatric and family history. Therapeutic interventions trialed included fluoxetine, melatonin, and valerian root.

Results:

Diagnostic findings revealed normal EEG and MRI, with an apnea-hypopnea index of 2.3 events/hour and a REM respiratory disturbance index of 15.5. The patient's Epworth Sleepiness Scale score was 5, and STOP-BANG was 2, indicating no significant risk of obstructive sleep apnea. The sexsomnia episodes were exacerbated by anxiety and insomnia. Pharmacotherapy attempts (fluoxetine, melatonin) did not alleviate symptoms, whereas self-initiated valerian root supplementation resulted in a 90% reduction in episode frequency.

Conclusions: This case illustrates the multifaceted nature of sexsomnia and highlights the importance of a comprehensive, multidisciplinary approach involving sleep specialists, psychiatrists, and primary care providers. While first-line pharmacological options may be beneficial for some, nonpharmacological interventions, such as valerian root and possibly hypnosis, can offer substantial improvements. Further research is warranted to develop evidence-based guidelines, as most current management strategies rely on case reports and small

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Transgender Identity Moderates the Association Between Nightmare Frequency and Suicidal Ideation

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Introduction: Frequent nightmares are known risk factors for suicidal ideation. Nightmares and suicide are both relatively understudied within minority populations. Transgender individuals experience disproportionately higher rates of sleep disturbances and suicidality, potentially due to the minority stress of transgender identity. Despite this, the intersection of transgender identity, nightmares, and suicidality has not been adequately investigated. To address this gap, we investigated the potential moderating relationship that transgender identity may play in the association between weekly nightmare frequency and suicidal ideation severity.

Materials and methods: We used the Assessing Nocturnal Sleep/Wake Effects on Risk of Suicide (ANSWERS) data set (N = 971), accessed through the National Sleep Research Resource. Nightmare frequency was measured using the 5-item Disturbing Dream and Nightmare Severity Index (DDNSI). The 25-item Columbia Suicide Severity Ratings Scale (CSSRS) was used to assess lifetime suicidal ideation severity. Linear regression was used to determine the association between nightmare frequency and suicidal ideation while controlling for both age and race. Transgender identity was then included as an interaction term.

Results: Weekly nightmare frequency was independently associated with lifetime suicidal ideation severity ($\beta = 0.14$, 95% CI: [0.09, 0.19], $p < 0.001$). Further, transgender identity moderated the relationship between weekly nightmare frequency and lifetime suicidal ideation severity ($\beta = 0.28$, 95% CI: [0.02, 0.54], $p = 0.035$).

Conclusions: Transgender individuals with higher weekly nightmare frequency appeared to be more likely than non-transgender to have higher lifetime suicidal ideation. This finding highlights a unique mental health disparity within the transgender population, emphasizing the importance of addressing sleep disturbances and their potential contribution to suicidality. Future research should explore the role of intersecting factors, such as minority stress, using larger and more diverse samples. These findings may help prioritize targeted care for transgender individuals experiencing frequent nightmares and suicidal ideation.

Pediatric

Achieving recommended sleep duration and abdominal fat deposition: a sex-specific relationship in 10-year-old children

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Introduction: Sleep deprivation and obesity has been extensively studied but there is limited literature examining the link between sleep duration and abdominal adipose tissue volumes in children.

Abdominal adiposity is more closely linked to obesity-related morbidity and mortality than total body fat in adults. Additionally, within the abdominal areas, subcutaneous and visceral adipose tissues have different associations with cardiometabolic outcomes. Moreover, hormonal differences can lead to differential fat deposition in boys and girls. This study aimed to study the sex-stratified associations between attaining recommended sleep duration and abdominal fat volumes.

Materials and methods: Sleep duration (weekday and weekend) of 10-year-old children ($n=638$, 51% boys, mean age 10.2 ± 0.2 years) was caregiver reported in the GUSTO study with a subset having additional actigraphy data ($n=491$). Recommended total sleep duration was defined as ≥ 9 hours per day, as per National Sleep Foundation recommendation. Total fat mass was quantified by quantitative magnetic resonance ($n=528$). Abdominal adipose tissue volumes [superficial subcutaneous adipose tissue (SSAT), deep subcutaneous adipose tissue (DSAT) and visceral adipose tissue (VAT)] were quantified by magnetic resonance imaging ($N=377$) (mean age 10.7 ± 0.2 years). Multivariable linear regression was used with adjustment for ethnicity and maternal education.

Results: Boys whose caregiver reported sleep duration met recommendation on weekdays and weekends ($n=111$), had lower body mass index z score (BMIz) (0.34 ± 0.16 vs 0.98 ± 0.12) ($P=0.001$), lower total fat mass ($8.77 \pm 0.69\text{kg}$ vs $11.31 \pm 0.51\text{kg}$) ($P=0.002$) lower SSAT ($651 \pm 85\text{ml}$ vs $888 \pm 55\text{ml}$) ($P=0.013$), DSAT ($492 \pm 86\text{ml}$ vs $729 \pm 56\text{ml}$) ($P=0.014$) and VAT volumes ($415 \pm 51\text{ml}$ vs $557 \pm 33\text{ml}$) ($P=0.013$). Boys whose actigraphy recorded sleep duration met recommendation, had lower DSAT ($454 \pm 119\text{ml}$ vs $685 \pm 59\text{ml}$) ($P=0.077$) and VAT volumes ($352 \pm 71\text{ml}$ vs $535 \pm 35\text{ml}$) ($P=0.019$). Only boys who met sleep duration recommendation for both weekdays and weekends had significantly lower BMIz, DSAT and VAT volumes compared to boys who did not meet sleep duration recommendation all week (weekdays and weekends). Boys who met sleep duration recommendation on either weekdays or weekends ($n=142$), did not differ on BMIz, total fat mass and abdominal fat volumes, compared to those who did not meet sleep duration recommendation all week (weekdays and weekends). No significant differences were observed in BMIz, total fat mass and abdominal fat volumes in girls.

Conclusions: Boys, but not girls, who achieved the recommended sleep duration for both weekdays and weekends, have lower BMIz, total fat mass and abdominal fat volumes. Interventions to help children attain the recommended sleep duration for both weekdays and weekends may help reduce abdominal and total adiposity, especially in boys.

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Altered Sleep Oscillation Dynamics: Enhanced Slow Oscillation–Spindle Coupling in Children with Dyslexia

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Introduction: Dyslexia is a neurodevelopmental disorder characterized by difficulties in reading and language processing, often accompanied by distinctive neurophysiological patterns. Previous research has shown that children with dyslexia (DS) display atypical electroencephalographic (EEG) activity during sleep, particularly in the architecture and density of sleep spindles—brief bursts of oscillatory brain activity critical for cognitive functioning and learning. The interaction, or coupling, between sleep spindles and slow oscillations (SO)—large-amplitude, low-frequency waves prominent in non-REM sleep—has been identified as a key mechanism underlying memory consolidation and learning. However, the precise nature of SO-spindle coupling in dyslexia remains insufficiently understood. This study aims to address this gap by systematically examining SO-spindle coupling during non-REM sleep stages N2 and N3 in children with dyslexia compared to typically developing, normally reading children (NC).

Materials and methods: We recruited 10 children diagnosed with dyslexia (3 males, mean age 11.22 ± 1.30 years) and 11 age-matched, normally reading controls (6 males, mean age 11.83 ± 1.70 years). All participants underwent comprehensive overnight polysomnographic recordings to capture detailed sleep EEG data. We quantified the density of fast spindles (FS, 12–15 Hz), slow spindles (SS, 9–12 Hz), and slow oscillations (SO, ~ 1 Hz) in both fronto-central and occipital EEG derivations. Additionally, we calculated the percentage of SO-spindle coupling events, representing the proportion of spindles temporally aligned with SOs. Custom MATLAB scripts were used for signal processing and event detection. Statistical analyses included mixed ANOVA for group comparisons of spindle and SO densities, and Dirichlet regression for analyzing coupling percentages, all conducted using R.

Results: Our analyses revealed that both FS and SS densities were significantly reduced in the N2 sleep stage of dyslexic children compared to controls (adjusted $p < 0.05$). SO density was also lower in DS relative to NC, with significant differences observed in central and frontal regions during N2 (adjusted $p < 0.05$) and across all derivations during N3 (adjusted $p < 0.001$). Intriguingly, despite these reductions in absolute densities, the percentage of SO-spindle coupling was significantly higher in DS than in NC for both FS and SS during N2 and N3 ($p < 0.001$). This indicates that, although fewer spindles and SOs occur overall in DS, a greater proportion of the remaining spindles are temporally aligned with SOs.

Conclusions: The reduction in spindle and SO densities we observed aligns with previous reports linking impaired sleep oscillatory activity to deficits in cognitive and learning processes. However, the increased SO-spindle coupling percentage in DS suggests a compensatory or maladaptive reorganization of sleep dynamics. This heightened coupling may reflect an attempt by the dyslexic brain to enhance memory consolidation processes, but it could also indicate inefficient or aberrant neural mechanisms underlying sleep-dependent learning. Overall, our results provide novel insights into the sleep microstructure of dyslexia, suggesting that altered SO-spindle coupling could serve as a biomarker for disrupted cognitive processing during sleep in this population. Further research is warranted to clarify the functional implications of these findings and their potential translational value for interventions targeting sleep in dyslexia.

A novel machine learning algorithm for predicting sleep apnoea in children using oximetry

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Introduction: Polysomnography (PSG) is the gold standard test for diagnosing obstructive sleep apnoea in children, but resource-intensiveness limits availability. Although oximetry testing is widely available, manual scoring methodologies such as McGill oximetry scoring (MOS) have poor sensitivity (17-43%), are subject to inter-observer variation, and have decreased positive predictive value (52-71%) when applied to those with complex medical comorbidities. We hypothesised that a computerised approach to oximetry analysis could overcome these limitations. We aimed to develop and test the performance of a *novel support vector classifier (SVC) machine learning algorithm with a component for discarding of likely movement/wake artefact* that classifies the overnight oximetry as being either low risk (predicted apnoea hypopnoea index $< 5/\text{hour}$) or high risk ($\geq 5/\text{hour}$).

Materials and methods: Oxygen saturation (SpO₂) and pulse rate (PR) data were extracted and down-sampled to 0.5Hz from 3476 diagnostic PSGs performed at Queensland Children's Hospital (QCH). Children aged 2-18 years regardless of underlying comorbidity were included. 3114 (90%) PSGs were selected for model training with ten-fold cross-validation, with the remainder held out for final testing. Extracted SpO₂ and PR data were subjected to a rules-based filter, with periods of oxygen saturation $< 60\%$ or PR > 225 or < 40 discarded as likely wake/movement artefact. Additionally, all data from PSGs $< 6\text{hrs}$ in length was discarded. Thirteen SpO₂ and PR-related features were used for SVC model training using the non-discarded data. These features were a combination of desaturation measures (e.g. ODI3, D90, CT95), central tendency measures, entropy measures (e.g. PR and SpO₂ Shannon entropy), and Lempel-Ziv SpO₂ complexity. Model training was performed in MATLAB R2024a using the fitcsvm function, and optimal gamma and c hyperparameter selection using Bayesian optimisation. Model performance was then evaluated on held-out data from QCH and other PSG datasets.

Results: Testing of the SVC using data from 344 held-out PSGs performed at QCH showed a positive predictive value of 93%, negative predictive value of 90%, specificity of 99%, sensitivity of 65% and weighted F1 score of 90%. When tested on similarly extracted SpO2 and PR data from PSGs within the Childhood Adenotonsillectomy Trial (CHAT), Paediatric Adenotonsillectomy Trial for Snoring (PATS) and clinical British Columbia Children's Hospital datasets (n=1215, n=721 and n=2895 respectively) the performance of the QCH model showed specificities of 99%, 98% and 84% respectively, with sensitivities of 35%, 57% and 62% respectively.

Conclusions: A SVC machine learning algorithm can be used to predict with a high degree of overall accuracy AHI <5 or ≥5 using oximetry data obtained from children both with and without a diverse range of comorbidities. The consistently high specificity across multiple datasets suggests a strong potential for this SVC approach to identify children at high risk of obstructive sleep apnoea, supporting use in home oximetry for triaging PSG waitlists or fast-tracking likely moderate-to-severe cases for surgical intervention when timely PSG access is limited. Alternatively, a modified version of the SVC with costs/penalties applied in training in order to increase sensitivity to >90% (at the expense of specificity) has the potential to be used as a screening test.

Application of the Das-Naglieri Cognitive Assessment System in Children with Sleep-Disordered Breathing

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Introduction: This study focuses on the application of the Das-Naglieri Cognitive Assessment System (DN-CAS) in a specific pediatric population: children with sleep breathing disorders (SDB). Although the DN-CAS has been extensively used to assess cognitive functions in children with Attention Deficit Hyperactivity Disorder (ADHD), there is limited research on its application in children with SDB. The similarities in behavioral characteristics between SDB and ADHD, such as hyperactivity, impulsivity, and learning difficulties, suggest that they may share underlying cognitive impairments. Therefore, this study aims to explore the applicability and effectiveness of the DN-CAS in children with SDB, aiming to provide guidance for their treatment.

Materials and methods: Study Participants: Children aged 6 to 12 years with SDB who were treated in our department between July 2021 and December 2022 were included in this study. Based on polysomnography results, participants were divided into mild (n=32) and severe groups (n=24). Additionally, children with severe obstructive sleep apnea syndrome (OSAS) (n=8) who underwent continuous positive airway pressure (CPAP) treatment were prospectively analyzed with a follow-up period of 2 months.

Study Design: A cross-sectional analysis and a prospective study design were adopted. All participating children underwent polysomnography and DN-CAS assessments for attention and planning functions. The applicability and effectiveness of the DN-CAS were assessed by comparing sleep parameters and cognitive functions between the mild and severe groups, as well as changes in cognitive functions in children with SDB before and after CPAP treatment.

Assessment Tool: The Das-Naglieri Cognitive Assessment System, which is based on the PASS theory and focuses on assessing individuals' abilities in planning, attention, simultaneous processing, and successive processing.

Results: Cross-Sectional Study Results: In terms of cognitive functions, although there were no significant differences in scores for attention and planning functions between the two groups, children in the severe group performed slightly worse on certain cognitive tasks.

Prospective Study Results: CPAP treatment significantly improved sleep parameters such as obstructive apnea-hypopnea index and lowest oxygen saturation in children with severe OSAS. Additionally, CPAP treatment significantly improved cognitive functions, particularly attention functions, in these children. This suggests that CPAP treatment may have potential value in improving cognitive functions in children with SDB.

Multiple Linear Regression Analysis Results: N3 sleep stage was one of the factors influencing attention and planning functions in children with SDB. Other sleep parameters, such as sleep efficiency and wake time after sleep onset, also had a certain impact on cognitive functions, but the impact was relatively small.

Conclusions: This study explored the application effect of the Das-Naglieri Cognitive Assessment System in children with SDB through cross-sectional analysis and prospective study design. The results indicate that the DN-CAS can be used to assess cognitive functions in children with SDB and help reveal the impact of SDB on their cognitive functions. Furthermore, CPAP treatment significantly improves sleep parameters and cognitive functions in children with SDB, providing strong evidence support for clinical interventions. In summary, the Das-Naglieri Cognitive Assessment System has potential application value in children with SDB and deserves further research and promotion.

Association Between Behavioral Problems and Vigilant Attention in Japanese High-School Students

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Introduction: Behavioral problems among high school students often occur alongside inattentive or risky behavior, which can affect safe school life. These problems can be assessed using the Strengths and Difficulties Questionnaire (SDQ), which is a subjective measure. An objective measure is the three-minute Brief Psychomotor Vigilance Test (PVT-B). While higher SDQ scores have been shown to increase the number of delayed responses on the PVT-B in elementary school students, this relationship has not yet been examined in high school students. In the present study, we examined the relationship between the five SDQ domains and vigilance attention in Japanese high school students.

Materials and methods: We studied 417 students (ages 15–17, 47% male) from two public high schools in Tokyo. During one class period, the students completed the Japanese SDQ, followed by a three-minute PVT-B on laptops. The following indicators were derived from the PVT-B: Lapse355 (The number of reaction times ≥ 355 ms) were counted and grouped into quartiles: Q1: 0–2; Q2: 3–5; Q3: 6–7; and Q4: ≥ 8 . For each SDQ domain (emotional symptoms, conduct problems, hyperactivity/inattention, peer problems, and prosocial behavior) the top 20% of scores defined a high-risk group. Multivariable logistic regression was used to compare Q1 with Q2–Q4 and test for trends, adjusting for age, BMI, sleep duration, caffeine intake, and time from awakening to PVT (two-sided $p < 0.05$).

Results: Impaired vigilant attention (Q4) was associated with high-risk conduct problems (adjusted odds ratio [aOR], 3.93; 95% confidence interval [CI], 1.63–9.44; P-trend, 0.024) and low prosocial behavior (aOR, 2.51; 95% CI, 1.19–5.29; P-trend, 0.028). However, emotional symptoms, hyperactivity/inattention, and peer problems were not significant (all $p > 0.20$).

Conclusions: High school students with impaired vigilant attention showed more conduct problems and lower prosocial behavior. The PVT-B could provide schools with a rapid, objective screening tool for identifying students at risk for externalizing behavior. Longitudinal studies should determine whether improving sleep or vigilant attention ameliorates these behavioral problems.

ASSOCIATION BETWEEN PARASOMNIAS AND CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CROSS-SECTIONAL STUDY IN VIETNAM

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Introduction: Attention deficit hyperactivity disorder (ADHD) is frequently associated with sleep disturbances, including parasomnias, which may worsen ADHD symptoms. However, the relationship between ADHD and parasomnias remains underexplored, particularly in newly diagnosed pediatric populations. This study aimed to determine the prevalence of parasomnias and identify associated factors in children with ADHD.

Materials and methods: A cross-sectional study was conducted on 629 children aged 6 – 12 years newly diagnosed with ADHD according to DSM-5 criteria at Vietnam National Children's Hospital. Parasomnias were classified using the ICSD-3, and data on comorbidities and sleep behaviors were collected through structured interviews and sleep diaries. Univariate and multivariate logistic regression analyses were performed to determine significant associations.

Results: Parasomnias were identified in 27.8% of children with ADHD, with NREM-related parasomnias being the most prevalent. The presence of comorbid psychiatric disorders, particularly tic disorders,

anxiety–depression, learning disorders, and intellectual disability, significantly increased parasomnia risk (OR 2.49 – 4.29, $p < 0.001$). Sleep talking was the strongest independent predictor (OR = 5.74, $p < 0.001$). ADHD clinical subtypes were not significantly associated with parasomnias.

Conclusions: Parasomnias are common in children with ADHD and are strongly linked to comorbid conditions and sleep-related behaviors. These findings emphasize the need for routine sleep assessments in ADHD management. Future studies should incorporate longitudinal designs and objective sleep assessments to better understand underlying mechanisms and intervention strategies.

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Association Between Spindle Wave Activity and Subjective Sleep Evaluation in Drug-Naïve Adolescents With ADHD and Sleep Complaints

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Introduction: Sleep disorders are frequently observed in neurodevelopmental conditions, and approximately 50% of individuals with attention-deficit/hyperactivity disorder (ADHD) are reported to experience some form of sleep disturbance (Cortese S. et al., *Journal of the American Academy of Child & Adolescent Psychiatry*, 2009). Several studies have examined abnormalities in sleep architecture and sleep-related cognitions in ADHD. However, these studies are often limited by factors such as insufficient control groups, heterogeneity in the diagnostic criteria for ADHD, failure to exclude comorbid psychiatric condition, and potential confounding effects of medication. (Bertisch S.M., *Sleep*, 2014).

Our previous research suggested a paradoxical dissociation between subjective and objective sleep assessments in individuals with ADHD from childhood to adulthood (Kato T. et al., *Journal of Attention Disorders*, 2023). However, the underlying mechanisms of this dissociation remain unclear. Recent studies have suggested a potential association between cognitive functioning and spindle wave (SW) activity during sleep. This study investigated the relationship between SW parameters and subjective sleep perception in drug-naïve adolescents with and without ADHD who underwent clinical polysomnography for sleep-related complaints.

Materials and methods: We retrospectively analyzed data from patients under the age of 18 ($n = 70$) who presented with sleep disturbances at the Department of Psychiatry and Sleep Medicine at Kurume University Hospital between April 2015 and March 2020. ADHD was diagnosed based on DSM-5 criteria. Patients with comorbid conditions known to affect sleep structure—narcolepsy (NL), idiopathic hypersomnia (IH), obstructive sleep apnea (OSA; $AHI \geq 5$), restless legs syndrome (RLS), or periodic limb movement disorder (PLMD)—were excluded. After applying these criteria, the final sample comprised 40 patients. Spindle wave parameters obtained from polysomnography (PSG) were compared between the ADHD and non-ADHD groups. Subjective sleep quality was assessed using the Japanese version of the Epworth Sleepiness Scale (JESS) and the Pittsburgh Sleep Quality Index (PSQI). This study was approved by the Ethics Committee of Kurume University.

Results:

1. The ADHD group showed significantly higher scores on the JESS (15.9 ± 4.4 vs. 11.3 ± 5.3 ; $p = 0.0342$) and the PSQI (8.8 ± 2.7 vs. 5.8 ± 2.4 ; $p = 0.0124$) compared to the non-ADHD group.
2. PSG analysis revealed significantly higher SW counts (112 ± 10.2 vs. 24 ± 4.8 ; $p = 0.0361$) and SW frequency per hour (93.5 ± 10.3 vs. 23 ± 4.6 ; $p = 0.0272$) in the ADHD group, particularly in the slow spindle frequency range.
3. In the ADHD group, the number of slow SW events was positively correlated with the PSQI sleep duration component (C3) ($r = 0.8452$, $p = 0.0341$) and negatively correlated with the subjective sleep duration reported immediately after PSG ($r = -0.7516$, $p = 0.0315$).

Conclusions: These findings suggest that increased spindle activity—particularly within the slow spindle range—may influence the process of subjective sleep evaluation in drug-naïve adolescents with ADHD, independent of comorbid sleep or psychiatric disorders and pharmacological influences.

Association of Outdoor Artificial Light at Night with Sleep Duration and Social Jetlag Among Preschool-aged Children

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Introduction: Recent studies have increasingly focused on the influence of outdoor artificial light at night (ALAN) on children's sleep patterns. However, its specific impact on sleep duration and social jetlag in this population remains underexplored. In densely populated urban centers such as Hong Kong, children are increasingly exposed to elevated levels of nighttime illumination. Our previous research demonstrated the detrimental effects of electronic screen use on children's sleep. The present study aimed to examine the association between outdoor ALAN exposure and both sleep duration and social jetlag among preschool-aged children in Hong Kong. The findings are expected to provide important insights into the impact of light pollution on pediatric sleep health and support the development of preventive strategies.

Materials and methods: This study included 3,686 preschool children recruited from kindergartens across four geographical regions in Hong Kong. Parent-completed questionnaires provided information on socioeconomic status (SES), as well as children's and parents' sleep-wake patterns. Outdoor ALAN exposure was assessed within a 1,000-meter radius of each participant's kindergarten address using satellite imagery data, with a spatial resolution of approximately 1,000 meters. To estimate the associations between ALAN exposure and children's sleep duration and social jetlag, a Generalized Linear Mixed Model (GLMM) was employed, with geographical region included as a random effect. Social jetlag misalignment was defined as a difference greater than one hour between weekday and weekend midsleep time, corresponding to the 75th percentile of the distribution in our sample. Bedtime screen exposure was defined as the use of electronic screens within one hour before bedtime.

Results: The mean age of the participants was 3.85 ± 0.99 years, with 52.85% being girls. The average sleep duration was 626.6 ± 60.2 minutes per day. ALAN exposure ranged from 10.18 to 84.28 nW/cm²/sr. A significant negative association was observed between ALAN exposure and children's sleep duration, with each unit increase in ALAN corresponding to an estimated decrease of approximately 0.198 minutes in sleep duration ($P = 0.003$). After adjusting for age, sex, family income, parental education level, and bedtime screen exposure, the association became marginal ($\beta = -0.11$, $P = 0.070$). A significant interaction was identified between ALAN exposure and bedtime screen exposure ($P_{\text{interaction}} = 0.043$), indicating that children exposed to screens at bedtime were more susceptible to ALAN-related reductions in sleep duration ($\beta = -0.21$, $P < 0.001$). We further examined the relationship between ALAN exposure and social jetlag. Children in the highest quartile of ALAN exposure had a significantly higher risk of social jetlag misalignment (OR = 1.131, 95% CI: 1.03–1.68; $P_{\text{trend}} = 0.009$), based on multivariable-adjusted models.

Conclusions: This study found that higher levels of outdoor ALAN were associated with shorter sleep duration and a greater risk of circadian disruption among preschool-aged children. Future research aiming to address the adverse effects of ALAN on children's sleep should also account for indoor light exposure, particularly from electronic screens, to inform the development of more targeted and effective interventions.

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Associations between household passive smoke exposure and sleep health in Chinese primary school students: a pilot study

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Introduction: Sleep is a critical determinant of physical, cognitive, and emotional development in children. However, sleep health is increasingly disrupted by environmental factors, including exposure to environmental tobacco smoke (ETS). While the adverse effects of ETS on respiratory health are well-documented, its potential consequences for paediatric sleep health remain underexplored. This study examines the associations between household ETS exposure and sleep duration and quality in primary school-aged children in China.

Materials and methods: This ongoing study is being conducted at the physical examination clinic of the affiliated hospital of Hangzhou Normal University, China. Data on household ETS exposure and children's demographic characteristics were collected through parent-reported questionnaires. Household ETS exposure was defined as daily exposure to tobacco smoke from family members residing in the same household. Sleep health was assessed using the Children's Sleep Habits Questionnaire (CSHQ), a validated instrument for evaluating paediatric sleep duration and quality. Regression models, adjusted for age and gender, were employed to analyze the associations between household ETS exposure, average sleep duration, and sleep quality indicators, including symptoms such as bruxism and snoring.

Results: A total of 50 children (mean age: 7.9 ± 2.1 years; males: 62.0%) were included in the analysis. The prevalence of daily household ETS exposure was 44.0%, with paternal smoking as the primary source (38%), followed by maternal smoking (4%) and smoking by other household members (2%). The average sleep duration during weekdays was 8.9 ± 0.7 hours, increasing to 9.5 ± 0.9 hours on weekends, with a weekly average of 9.1 ± 0.6 hours. Sleep disorder symptoms were reported in a substantial proportion of children, with 24% exhibiting weekly bruxism and 30% experiencing weekly snoring. Regression analysis indicated that daily household ETS exposure was significantly associated with reduced average sleep duration ($\beta = -0.30$, $p = 0.05$) after adjusting for age and gender. However, no statistically significant associations were observed between ETS exposure and poor sleep quality in the current pilot analysis.

Conclusions: These findings suggest that household ETS exposure may adversely affect sleep duration in primary school-aged children. Although no significant associations with overall sleep quality were identified in this pilot analysis, the high prevalence of sleep-related symptoms highlights the need for further investigation into the broader impacts of ETS exposure on paediatric sleep health. Future large-scale studies are necessary to confirm these findings and elucidate the underlying mechanisms linking ETS exposure to disrupted sleep. Interventions aimed at reducing household smoking may represent an important strategy for improving sleep health in children.

Associations Between Nocturnal Autonomic Activity in Infancy and Later Neurocognitive Development: The AuBE Cohort Study

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Introduction: The autonomic nervous system (ANS) reflects central nervous system (CNS) function and can be assessed non-invasively using heart rate variability (HRV). However, most studies assess HRV over 24 hours, mixing wake and sleep periods, limiting insights into sleep-specific ANS activities. Understanding how ANS activity during distinct sleep stages relates to neurocognitive outcomes is essential, given the critical role of sleep in early life for shaping brain development. This study aimed to:

(1) compare ANS activity between active sleep (AS) and quiet sleep (QS) at birth (M0) and at six months (M6); (2) evaluate ANS maturation during sleep from birth to six months; and (3) investigate associations between ANS activity during sleep in early infancy and neurocognitive performance at three years of age.

Materials and methods: Participants were part of the French AuBE birth cohort. Inclusion criteria for this analysis were availability of overnight polysomnography (PSG; 8 pm–8 am) at birth (M0) and cognitive assessment at three years using the Wechsler Preschool and Primary Scale of Intelligence-III (WPPSI-III). A subset of infants also underwent PSG at six months (M6).

Electrocardiogram (ECG) data were extracted to compute HRV indices in both time and frequency domains: mean heart rate (HR), SDNN, and low-frequency power (LF) as markers of sympathetic activity; pNN50, RMSSD, and high-frequency power (HF) as markers of parasympathetic activity; and the LF/HF ratio to evaluate sympathovagal balance. HRV parameters were compared between AS and QS at both M0 and M6, and changes from M0 to M6 were analyzed according to sleep stage.

Associations between HRV indices and WPPSI-III scores (Verbal IQ, Performance IQ, Total IQ) were assessed using correlations.

Results: A total of 56 full-term infants were included at M0 (48% girls), among which 34 had follow-up data at M6. HRV parameters did not differ by sex. Significant differences in ANS activity were observed between sleep stages at both M0 and M6. AS was characterized by higher sympathetic activity (elevated HR, SDNN, LFnu, and LF/HF ratio), while QS showed increased parasympathetic activity (higher RR intervals, pNN50, RMSSD, HFnu).

Between M0 and M6, ANS maturation was evident during QS, with an increase in RR intervals and HFnu, and a decrease in HR, LFnu, and LF/HF ratio, indicating an increase in parasympathetic regulation and a decrease in sympathetic dominance. No significant maturation was observed during AS. Importantly, higher total power during QS at M0 correlated positively with Performance IQ at three years ($r = 0.31$, $p < 0.05$).

Conclusions: This study demonstrates that ANS activity in infants varies significantly according to sleep stage, with QS favoring parasympathetic predominance. ANS maturation primarily occurs during QS within the first six months of life. Furthermore, ANS function during QS at birth, as reflected by total power, is associated with later cognitive outcomes. These findings suggest that early sleep-specific ANS markers could serve as indicators of neurodevelopmental trajectories.

Association with severity obstructive apnea (OSA) with elevated blood pressure amongst the pediatrics population

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Introduction: The prevalence of pediatric hypertension has risen from 1.1% in 2004 to 6% in 2019, driven largely by increasing childhood obesity. As obesity is a key risk factor for obstructive sleep apnea (OSA), we hypothesize that OSA in children is associated with elevated blood pressure in a pediatric sleep clinic population.

Materials and methods: Retrospective chart review of pediatric patients who underwent polysomnography and evaluation at Rady Children's Hospital between January 2019 and December 2024. Demographic data included sex, age, BMI, ethnicity, and systolic (SBP) and diastolic (DBP) blood pressure percentiles(%). Polysomnography determined the obstructive apnea-hypopnea index (OAHI), with OSA severity classified as follows: no OSA (OAHI <1/hour), mild OSA (OAHI 1–5/hour), moderate OSA (OAHI 5–10/hour), and severe OSA (OAHI >10/hour). Exclusion criteria included craniofacial, cardiac, pulmonary, and neuromuscular abnormalities. Blood pressure percentiles were calculated based on NHLBI pediatric blood pressure guidelines, with hypertension defined as SBP or DBP at or above the 95th percentile for age, sex, and height.

Results: 484 pediatric subjects (mean age:10.8±4.3 years, 37.6% female) were evaluated. Ethnicity distribution included 214(44.3%) non-Hispanic and 261(53.9%) Hispanic. Mean±SD SBP% and DBP% by OSA severity were as follows: no OSA(n=45): 0.786±0.236/0.677±0.225; mild OSA(n=229): 0.792±0.232/0.700±0.214; moderate OSA(n=106): 0.801±0.208/0.725±0.222; and severe

OSA(n=104): $0.893 \pm 0.151 / 0.772 \pm 0.222$. SBP% was significantly higher in severe OSA compared to all other severities ($p < 0.05$), while DBP% was significantly higher in severe OSA compared to mild OSA ($p < 0.05$) and borderline compared to no OSA ($p = 0.07$). Only SBP% significantly correlated with OAH1 ($p < 0.05$). The OAH1 trended higher in children with hypertensive BP measurements compared to those without (8.89 ± 15.5 vs. 5.96 ± 10.6 , $p = 0.063$). Multivariate regression analysis, adjusted for age and BMI, revealed that OAH1 was not significantly associated with either SBP% or DBP%.

Conclusions: The findings demonstrate that BP increases with OSA severity in a pediatric sleep clinic population. While the association between OAH1 and BP was not independent of age and BMI, children with severe OSA are more likely to have elevated BP and a trend toward hypertension, emphasizing the need for targeted BP screening and management in children with greater OSA severity.

A Study on Sleep Status and Its Relationship with Quality of Life in Children with Chronic Diseases

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Introduction: To examine the current sleep status of children with chronic illnesses and explore its association with health-related quality of life, in order to provide evidence for developing targeted interventions to support self-management in this population.

Materials and methods: A convenience sampling method was used in this study. Data were collected using a general information questionnaire, the Physical Activity Questionnaire for Children (PAQ-C), the Children's Sleep Habits Questionnaire (CSHQ), and the Patient-Reported Outcomes Measurement Information System (PROMIS-25). A total of 230 hospitalized children from the departments of rheumatology and immunology, gastroenterology and nephrology, cardiology, and cardiac surgery at a pediatric medical center were surveyed to assess their sleep status and analyze its association with quality of life.

Results: The average PAQ-C score among the 230 children with chronic illnesses was 1.85 ± 0.81 . The average CSHQ score was 46.82 ± 7.88 , with notable disturbances observed in the dimensions of parasomnias and daytime sleepiness. The average daily sedentary time over the past week was 11.43 ± 3.17 hours, significantly exceeding the 2-hour limit recommended by the *Chinese Guidelines for Physical Activity for Children and Adolescents*. In the PROMIS-25, the average scores for depression, fatigue, pain, and anxiety were all below 45, indicating normal levels. However, the mean score for physical function-mobility was 23.66 ± 4.62 , suggesting functional limitation. Mediation analysis showed that the total effect of CSHQ on PROMIS-25 was significant (path c, $\beta = -0.35$, $p < 0.001$). CSHQ significantly affected PAQ-C (path a, $\beta = -0.28$, $p < 0.01$), and PAQ-C significantly affected PROMIS-25 (path b, $\beta = 0.42$, $p < 0.001$). After controlling for PAQ-C, the direct effect of CSHQ on PROMIS-25 remained significant (path c', $\beta = -0.20$, $p < 0.05$). The bootstrap confidence interval for the indirect effect was $[-0.15, -0.05]$, excluding zero, indicating a significant mediating effect. These findings suggest that physical activity level partially mediates the relationship between children's sleep habits and health-related quality of life.

Conclusions: Sleep disturbances are prevalent among children with chronic illnesses and may adversely affect their health-related quality of life. Sleep habits appear to influence quality of life in part through their impact on physical activity levels. These findings underscore the need for healthcare professionals to recognize and address sleep and activity-related challenges in this population through the development of targeted, evidence-based interventions aimed at promoting both physical and psychological well-being.

Autism, Sleep, and Medicinal Cannabis: Evaluating 18-Month Efficacy and Safety Outcomes

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Introduction: Sleep disturbances are common in children with Autism Spectrum Disorder (ASD), affecting up to 80% of this population. Poor sleep onset, frequent awakenings, and reduced sleep quality contribute to behavioral challenges, impaired cognition, and increased caregiver stress. Standard

treatments like melatonin or sedatives offer limited relief, making medicinal cannabis a promising alternative. Cannabis-based therapies with cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) in tailored ratios have shown encouraging short-term results for sleep improvement in ASD. This study evaluates the long-term efficacy and safety of medicinal cannabis for sleep management over 18 months, focusing on sustained outcomes and side effects.

Materials and methods: This longitudinal observational study enrolled 120 pediatric patients (ages 3-17 years) with a confirmed diagnosis of ASD who experienced chronic sleep disturbances. Patients were treated with medicinal cannabis formulations containing varying ratios of CBD and THC, customized based on individual tolerance and therapeutic response.

Baseline data were collected three months prior to initiating cannabis treatment, including metrics on sleep onset latency, sleep maintenance, and overall sleep quality, as reported by caregivers and validated sleep assessment tools. Follow-up assessments were conducted three months post-treatment initiation and at 18 months to evaluate long-term efficacy and safety. Primary endpoints included improvements in sleep parameters (sleep onset latency, sleep maintenance, and overall sleep quality) and caregiver-reported quality of life. Secondary endpoints included the identification of adverse effects and the development of treatment tolerance. Data were analyzed using paired t-tests and repeated measures ANOVA for longitudinal comparisons.

Results: Initial results demonstrated significant improvements in sleep onset latency, maintenance, and quality within the first three months of treatment, with over 80% of patients showing measurable benefits. At the 18-month follow-up, 68% of patients sustained their sleep improvements without requiring substantial dosage adjustments.

Adverse effects were minimal, with increased appetite and agitation reported in less than 10% of patients, primarily during the initial adjustment phase. No severe adverse events were recorded. A small subset of patients (12%) showed signs of developing tolerance, necessitating dosage increases to maintain efficacy. Overall, caregiver-reported quality of life improved in parallel with sleep improvements, highlighting the positive impact of treatment on both patients and their families.

Conclusions: This 18-month observational study highlights the long-term efficacy and safety of medicinal cannabis for managing sleep disturbances in ASD. Tailored treatments sustained sleep improvements with minimal side effects, making this a viable option for a challenging population. While tolerance development is a concern for some, the overall safety profile and lasting benefits support medicinal cannabis as part of a comprehensive sleep management strategy. Future studies should refine dosing regimens, including terpene and flavonoid profiles, to establish standardized therapeutic guidelines.

Acknowledgments: The authors acknowledge the patients and caregivers for their participation and trust throughout this study. This research was conducted independently without external funding. Data were derived from patients receiving care at a neurology sleep clinic, where progress was monitored as part of routine care. Gratitude is extended to the clinic staff for supporting data collection and patient management. Their dedication made this study possible.

Behavioral and Parental Predictors of Sleep Problems in Primary School Children: A Cross-Sectional Study

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Introduction: Sleep problems are highly prevalent in school-aged children and are known to adversely affect cognitive and emotional development. Previous research suggests that both child behavioral difficulties and familial factors, such as parental sleep quality and socioeconomic conditions, may contribute to sleep disturbances. However, integrated models that consider both child and parent-level predictors in community samples remain limited. This study aimed to examine the behavioral and parental predictors of sleep problems in Turkish primary school children using standardized tools and multivariable modeling.

Materials and methods: A cross-sectional study was conducted with 332 children aged 7–11 years (mean age = 8.3 ± 1.2 years; 50.9% boys) recruited from public primary schools in a city district of Istanbul. Child sleep problems were assessed using the Child Sleep Habits Questionnaire (CSHQ), and

behavioral difficulties were measured via the Strengths and Difficulties Questionnaire (SDQ), which includes subscales for emotional problems, conduct problems, hyperactivity, peer problems, and prosocial behavior. Parental sleep quality was evaluated using the *Pittsburgh Sleep Quality Index* (PSQI). Children were categorized as having sleep problems based on CSHQ scores >41 . Nonparametric group comparisons were performed due to non-normal distributions. Multiple linear regression was used to identify independent predictors of sleep problems. Predictors included SDQ subscale scores, parental PSQI score, child sex, age, and perceived socioeconomic status. Given the low rate of missing data (4.8%), listwise deletion was applied, resulting in a regression sample of 316 children.

Results: Overall, 66.6% of children ($n = 221$) met the threshold for significant sleep problems. Children with sleep problems had significantly higher scores in emotional problems, conduct problems, hyperactivity, peer difficulties, and total difficulties and lower scores in prosocial behaviour (*all* $p < .001$). They also had significantly poorer parental sleep quality (PSQI median: 5 [IQR 4–7] vs. 3 [2–6], $p < .001$). Screen exposure in the hour before bedtime ($p < .001$), and the presence of a tablet or smartphone in the bedroom ($p = .048$) were more common in children with sleep problems and parents of children with sleep problems reported lower perceived socioeconomic status ($p = .018$). The full regression model was statistically significant ($F(9, 306) = 16.48$, $p < .001$) and explained 30.7% of the variance in child sleep scores. The significant predictors for child sleep problems were emotional difficulties ($\beta = .301$, $p < .001$) and parental PSQI score ($\beta = .229$, $p < .001$).

Conclusions: This study highlights the importance of the family sleep environment and child emotional regulation in the sleep health of school-aged children. Both emotional difficulties and parental sleep quality independently predict child sleep problems. These findings underscore the need to integrate child behavioral screening with family-level assessments in pediatric sleep evaluations. Intervention strategies targeting shared family dynamics—including evening screen use and household sleep routines—may provide effective targets for improving family sleep health.

Beyond the recommendations: A bioecological analysis of pre-bedtime screen use, moderate-to-vigorous physical activity and food intake in family contexts

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Introduction: Current guidelines suggest youth limit screen use, physical activity, and the consumption of food in the hour before bed. However, whether these sleep hygiene strategies actually influence sleep, or how worthwhile and practical they are for youth and families in real-life is uncertain. This study draws on Bronfenbrenner's Bioecological Model of Human Development to explore and analyze pre-bedtime screen use, moderate-to-vigorous physical activity (MVPA) and food intake within family contexts.

Materials and methods: We conducted a qualitative study nested within the randomized crossover Helpful Activities Before It is Time to Sleep (HABITS) trial. HABITS experimentally investigates whether restricting pre-bedtime screen use, MVPA and food intake in the hour before bed impact sleep quantity and quality in youth. Sixteen youth (19% indigenous Māori, 6% Pacific, 6% Asian, 50% female) aged 10 to 14 years and their parents were interviewed upon completion of HABITS. Semi-structured interviews explored youth and families' experiences of adhering to current sleep hygiene recommendations—avoiding screen use, MVPA and food intake in the hour before bed—and their implementation of each behavior. Interviews were recorded, transcribed, and analyzed using reflective thematic analysis.

Results: Four key themes were identified: 1) tensions arise from the misalignment between recommendations to limit these behaviors and established family routines; 2) pre-bedtime screen use, MVPA and food intake are viewed as purposeful family practices; 3) families negotiate between ideal recommendations and practical realities; 4) youth and family expressed uncertainty about the actual impact of these sleep hygiene behaviors on sleep. Most youth and families perceived complete bans on pre-bedtime screen use, MVPA and food intake as unrealistic and unsustainable. When examined through a bioecological lens, these behaviors emerged as contextually negotiated practices shaped by broader family systems.

Conclusions: Sleep hygiene recommendations should acknowledge and reflect developmentally grounded, socio-cultural, and context-specific practices that align with the realities of family-based sleep routines.

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Breastfeeding and Neonatal Sleep: The Circadian Rhythms of the Breast Milk Microbiome and Metabolome and Their Impact on Global Infant Health

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Introduction: To investigate the relationship of breastfeeding ways and neonatal sleep, and explore whether the components of human milk exhibit circadian rhythms in terms of microbiome and metabolome profiles.

Materials and methods: A cross-sectional study was implemented to investigate the basic characteristics, feeding practices of 89 mother-infant dyads, and neonatal sleep patterns, utilizing Questionnaire Star for data collection. A total of 42 breast milk samples were obtained from 21 lactating women at noon and midnight. The melatonin concentration in milk samples was quantified via enzyme-linked immunosorbent assay (ELISA). Metagenomic sequencing was performed on the milk samples to ascertain the microbial composition, while metabolites in the milk were identified through liquid chromatography-mass spectrometry (LC-MS).

Results: Neonates who were exclusively formula-fed exhibited longer durations of both nocturnal and daytime sleep, and more frequent nighttime awakenings, compared to those who were exclusively breastfed. Neonates in the mixed feeding group were reported to experience more sleep-related issues than those in the exclusive breastfeeding group. Melatonin concentration was significantly higher in the midnight samples compared to the noon samples. A total of 335651 differential microbiome were found and 20 bacterial genera and 20 microbial taxa in noon and midnight human breast milk reveals significant differences exist between the microbial populations. Such as *cognataguiflexum*, *segnochrobacterium*, *aquabacterium* were significantly more abundant in milk from the midnight group ($P < 0.05$). Metabolic pathway analysis of the different metabolites revealed that the following were enriched in both groups: lipid metabolism pathways, amino acid metabolism pathways.

Conclusions: Breastfeeding styles influence the neonatal sleep patterns, and the composition of breast milk varies according to the maternal circadian rhythm. In the NICU, matching the feeding times of neonates with the breast milk or donor milk collection times may facilitate the development and maturation of sleep/wake cycles in newborns and preterm infants.

Building Predictive Models for Hypoventilation in Children with Neuromuscular Disorders

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Introduction: Children with neuromuscular disorders are at risk of hypoventilation. The ability to predict or screen for hypoventilation could inform when diagnostic polysomnography, a limited resource, was warranted.

Materials and methods: Children with neuromuscular disorders from three sites had laboratory polysomnography to identify hypoventilation ($pCO_2 > 50\text{mmHg}$ for $\geq 25\%$ total sleep time). The associations between hypoventilation and demographic factors, anthropometrics, clinical factors, motor function, pulmonary function tests and patient and parent-reported outcome measures were determined. Patient-reported outcome measures were collected for participants aged eight and older. Significant factors were examined with Binary Logistic Regression to construct predictive models.

Model predictive power was assessed by using the generated predictive probabilities to construct Receiver Operator Characteristic curves and calculating the area under the curve (AUC).

Results: Hypoventilation was present in 16% of the 64 participants. Significant associations with hypoventilation were a diagnosis of congenital myopathy/congenital muscular dystrophy, BMI z-score, higher parent and self-reported hypoventilation symptom score, higher self-reported hyperactivity and externalising behaviours score with the Strengths and Difficulties (SDQ) questionnaire and lower self-reported Peds QL™ Neuromuscular module health and total score. The predictive model with the highest AUC combined self-reported hypoventilation symptom score, SDQ hyperactivity score and Peds QL™ Neuromuscular module health score (AUC 0.975, $p < 0.001$). For children aged less than eight, a diagnosis of congenital muscular dystrophy/congenital myopathy and BMI z-score resulted in an AUC of 0.872 ($p < 0.001$). Regression coefficients were used to construct predictive equations for the probability of hypoventilation.

Conclusions: The predictive models that were developed performed well and could be used as screening tools for hypoventilation in children with neuromuscular disorders to determine when polysomnography is warranted. Patient-reported outcome measures resulted in the model with the highest predictive power.

Can sleep spindle characteristics distinguish children with narcolepsy from those with idiopathic hypersomnia and subjective sleepiness?

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Introduction: Central disorders of hypersomnolence are characterised by excessive daytime sleepiness (EDS) that is unexplained by insufficient sleep or other underlying medical conditions. Included in this poorly understood category of sleep disorders are narcolepsy and idiopathic hypersomnia (IH). There has been growing interest in analysing sleep micro-architecture, to further understand how sleep is affected by different conditions. Sleep spindles are a hallmark electroencephalogram (EEG) waveform of N2 sleep with a characteristic frequency in the sigma range of 11-16 Hz. We aimed to investigate if sleep spindle activity differed between children with narcolepsy, IH, and subjectively sleepy children with a non-diagnostic multiple sleep latency test (MSLT), and matched controls.

Materials and methods: 28 children with narcolepsy, 11 with IH and 26 with subjective sleepiness were included and individually matched for age and sex with a control. All children underwent overnight polysomnography. Fast (>13 -16 Hz) or Slow (9- <13 Hz) sleep spindles were identified manually during N2/N3 sleep. Spindle activity was characterised as spindle number, density (number of spindles/h) and intensity (density x average duration) of right central (C4) and frontal (F4) EEG electrodes across the sleep period and also when separated into NREM sleep periods (NREMP) across the night. Groups were compared with one-way ANOVA.

Results: Spindle duration was longer for F4 and C4 Slow, C4 Fast and F4 and C4 Fast&Slow spindles in the children with narcolepsy compared to the children with subjective sleepiness ($p < 0.05$ for all) and compared to the narcolepsy controls ($p < 0.05$ for all). There were no differences in spindle duration between the children with IH or subjective sleepiness and their controls. In the children with narcolepsy and subjective sleepiness spindle intensity of C4 Slow and C4 Fast&Slow spindles was greater ($p < 0.05$ for all) compared to controls. When spindle number was compared across the night in each NREM period, in both the children with narcolepsy and subjective sleepiness there were more F4 Fast&Slow spindles in the 3rd NREMP and 4th NREMP ($p < 0.001$ for all) compared to controls. Spindle density and intensity of C4 Fast&Slow spindles were lower in the 1st NREMP compared to the 4th NREMP ($p < 0.05$) in the children with narcolepsy and lower in the 1st NREMP compared to both the 3rd NREMP and 4th NREMP ($p < 0.05$ for both) in the children with subjective sleepiness.

Conclusions: Our study identified sleep spindles are longer in children with narcolepsy compared to children with subjective sleepiness or their controls. In addition, sleep spindles are more concentrated at the end of the night compared to the beginning of the night in both children with narcolepsy and subjective sleepiness compared to controls. Children with IH did not demonstrate these spindle findings, supporting a different disease entity. Understanding the microstructure of sleep in combination with clinical history may aid in being able to distinguish between groups of children

referred for assessment of EDS, particularly those who do not meet strict diagnostic criteria for a primary disorder of hypersomnolence but did have abnormal MSLT results (our subjectively sleepy group).

CBT-I Teen: An Adapted CBT-I Protocol Developed for and with Adolescents and Other Stakeholders

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Introduction: Cognitive-Behavioral Therapy for Insomnia (CBT-I) is a highly efficacious treatment in adults. However, adolescents have unique sleep physiology, lifestyles, and cognitive styles that may warrant CBT-I adaptation to meet their developmental needs. Further, some recommendations in standard CBT-I protocols (e.g., waking at the same time 7 days per week; avoiding screens before bed) have limited acceptability in adolescents. Thus, the objective of this study was to engage adolescents and other stakeholders in: 1) identifying aspects of standard CBT-I that may require adaptation; and 2) evaluating an adapted CBT-I protocol (CBT-I Teen) for efficacy and acceptability in a RCT compared to a waitlist control.

Materials and methods: Ten focus groups were conducted with adolescents with insomnia (n=76; 57% White, 23% Black, 20% Asian; 12% Hispanic), six focus groups with parents of adolescents with insomnia (n=51; 55% mothers), and two focus groups with clinicians (n=18) who provide treatment for insomnia in adolescents. In the first phase of focus groups, stakeholders identified adaptation needs and proposed solutions. In the second phase of focus groups, stakeholders provided feedback and anonymous ratings on the acceptability, feasibility, appropriateness, likely effectiveness, and fidelity of the adapted protocol.

Results: Themes from focus groups were identified for treatment process and content domains. Treatment process themes included the perception of sleep logs as stressful, a desire for personalized and interactive psychoeducation, and heterogeneity regarding if and how parents should be involved in treatment. Treatment content themes included the importance of the bed as a place of relaxation, preference for distraction over active relaxation strategies, low acceptability and feasibility of a consistent waketime across weekdays and weekends, and heterogeneity of screen use and impact.

An adapted protocol incorporated components such as alternative approaches to sleep tracking[LM1], adolescent choice about parental involvement, more flexible stimulus control recommendations, a naturalistic sleep restriction approach, and a harm reduction strategy for screen use. Stakeholders rated the adapted protocol highly (1-5 scale; 5 indicates high appropriateness, feasibility, etc): adolescents perceived the treatment as likely to be effective (M=4.7; SD=0.5), acceptable (M=4.2; SD=0.7), feasible (M=4.1; SD=0.8) and understandable (M=4.3; SD=0.6); parents perceived the treatment as likely to be effective (M= 4.6; SD=0.5) and acceptable[LM2] (M=4.2; SD=1.3); and clinicians rated the intervention as likely to be effective (M=4.3; SD=0.6), acceptable to teens (M=4.4; SD=0.5), appropriate (M=4.6; SD=0.6), and with strong fidelity to CBT-I mechanisms (M=4.6; SD=0.5).

Conclusions: An adapted CBT-I protocol (CBT-I Teen) is acceptable and feasible for adolescents with insomnia. More work is needed to evaluate the efficacy of the adapted protocol in reducing insomnia symptoms in adolescents.

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Change in AHI and effects of sleep health on weight loss trajectory in adolescents undergoing metabolic and bariatric surgery

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Introduction: Metabolic and bariatric surgery (MBS) is emerging as a treatment option for the rapidly rising rates of severe obesity and associated morbidities such as obstructive sleep apnea (OSA) in children. In adults, MBS significantly improves BMI and apnea-hypopnea index (AHI), but little research has been conducted in children. MBS results in steep weight loss in the 12 months after surgery followed by slower weight regain over the subsequent years. Patients experience varying amounts of weight regain following MBS, but the impact of factors such as sleep health on weight regain is unknown. The aim of the current study was to examine change in AHI following MBS and to examine associations between sleep health and weight loss/regain following MBS in a clinical sample of youth with severe obesity.

Materials and methods: A retrospective chart review was conducted for patients who underwent MBS at Children's Hospital Colorado between 2017 and 2022. Inclusion criteria for this analysis was completion of both pre- and post-surgery polysomnography (PSG). Patient demographics, weight data, and self-reported sleep health and behaviors were derived from bariatric clinic visits at time of surgery and up to 3-years post-surgery. PSG data and Epworth Sleepiness Scale (ESS) total scores were collected from the sleep study reports. Descriptive statistics are reported as median (Q1, Q3) or frequency (%). Change in AHI from pre- to post- surgery were evaluated using paired Wilcoxon and McNemar's tests. Group-based trajectory models (GBTM) were used to identify trajectory groups based on percent weight change post-surgery using SAS PROC TRAJ. GBTM identified two trajectory groups, one with high weight loss and another with significant weight regain. Comparisons between groups were made with Wilcoxon, chi-squared, or Fisher's exact tests.

Results: Patients were a median age of 17.0 years at time of MBS (N=52). Nearly all patients (98%) underwent gastric sleeve MBS; 1 patient underwent gastric band. Patients were majority female (51.9%) and Hispanic/Latino (59.6%). Median AHI was 17.2 events/hour pre-surgery and this significantly reduced to 2.0 events/hour post-surgery ($p<0.001$). Prior to surgery 90.4% of participants had an AHI >5 , while only 26.9% of participants had an AHI >5 post-surgery. There was no significant component of central sleep apnea in this population. Prior to MBS, 42.6% of participants had an ESS score >10 compared to 12.8% after MBS ($p<0.05$).

50% of participants were in the weight regain trajectory group and 50% of participants were in the weight loss group. There were no significant difference in demographics between groups. Significantly more patients in the weight regain group had pre-surgery ESS >10 (58.3%, compared to only 25% in the high weight loss group; $p<0.05$). There were no significant difference in self-report sleep duration or timing, insomnia symptoms, electronics use at bedtime, or pre- or post-surgery AHI between trajectory groups.

Conclusions: MBS dramatically improves sleep apnea and excessive daytime sleepiness in adolescents with obesity. Participants with weight regain post-surgery were more likely to report clinically significant daytime sleepiness prior to surgery. Future research is needed to better understand the impact of daytime sleepiness on weight regain in youth undergoing MBS.

Characterization of children with specific learning disabilities and sleep complaints

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Introduction: Specific learning disabilities (SLD) are reported in 8% to 10% of the general population. They are often associated with Attention Deficit Disorder with or without Hyperactivity (ADHD) (33-70%). These neurodevelopmental disorders are generally associated with various comorbidities such as anxiety-depressive disorders. Previous studies, based on questionnaires, have shown more sleep disorders in this population compared to control children, particularly in children with both pathologies. The aim of this study is to assess sleep characteristics in SLD children with or without ADHD associated with sleep complaints.

Materials and methods: One hundred and seventy-six children (66 girls) were included in this retrospective study, median age 11.4 years (range 6.9 to 17.8 years). Patients were divided into 3 according to their disorders: SLD (n = 76), ADHD (n = 36) and SLD -ADHD (n = 66). For each patient, medical history, sleep disorders, Epworth sleepiness score and polysomnographic results were

collected. Non-parametric comparisons were made between our groups (Kruskal Wallis, Wilcoxon and Chi²).

Results: SLD -ADHD had a higher frequency of Multi- SLD disorder (60.9% vs. 40.8% without ADHD). Children with ADHD had a higher frequency of respiratory and mood disorders. At polysomnography, the main sleep disorders observed were respiratory problems, generally mild OSA and UARS (82.9%), sleep fragmentation (pathological AI, 54%), as well as a higher percentage of NREM 1 for our groups with SLD. Comparisons revealed differences based on psychostimulant treatment, with lower levels of sleepiness and an increase in treatment-associated insomnia.

Conclusions: This study highlights a high proportion of comorbidities in SLD children, with a possible impact on sleep. Frequent complaints of somnolence and insomnia are present, with a difference in the type of complaint depending on the presence or absence of stimulant treatment. These results underline the importance of taking into account associated comorbidities in children with SLD with or without ADHD.

Clinician Perceptions Around Management of Sleep Problems in Children with Neurodisability

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Introduction: Children with neurodisability experience sleep problems at significantly higher rate than typically developing children. These sleep problems are multifactorial, often involving both disease-specific and environmental factors and include sleep disordered breathing alongside non-respiratory sleep problems. As children with neurodisability frequently receive care from multiple specialist services, sleep concerns are commonly raised by caregivers and encountered by clinicians across various disciplines. However, the perspectives of non-sleep specialists on managing these problems remain understudied. This study aims to evaluate how clinicians from diverse paediatric disciplines perceive their role in the assessment and management of sleep difficulties in children with ND.

Materials and methods: A cross-sectional survey was conducted across three tertiary children's hospital in Australia. Participants included medical staff (consultants, registrars, fellows and paediatric advanced trainees) and senior nursing staff (clinical nurse consultants, clinical nurses and nurse practitioners) working in paediatric specialties other than sleep medicine. The survey included free text responses, multiple choice questions and case studies. Data analysis included descriptive statistics and thematic analysis of free text responses.

Results: Ninety-five non-sleep specialised clinicians participated. Eighty percent of clinicians reported sleep was a significant problem for this group of children, stating that sleep problems are regularly raised by families in routine check-ups and acute presentations in emergency departments. Most participants (70%) relied on informal methods to assess sleep, with limited use of validated screening tools. Uncertainty around the prescription and use of sleep medications was evident, with clinicians expressing both perceived benefits and discomfort with prescribing due to not always fully understanding the underlying aetiology of a child's sleep difficulties. Eighty nine percent of medical specialists (n=47) reported regularly offering advice and support to caregivers around sleep but also described limited training in this field and low confidence in their skills. Clinicians outlined limited time to address sleep problems as a considerable barrier to care and expressed a desire for national guidelines to provide a more supported and consistent approach to sleep assessment and management in children with ND.

Conclusions: Non-sleep specialist clinicians acknowledge the high prevalence of sleep disorders in children with ND but in general reported feeling ill-equipped to initiate management when encountered in their day-to-day clinical practice. This highlights the need to prioritise further training and education on sleep problems and management in this group of children for non-sleep specialised clinicians. Furthermore, prioritising the development of national guidelines to standardise the assessment and management of sleep problems could improve patient care.

Comparison of Treatment Efficacy Between Rapid Maxillary Expansion and Adenotonsillectomy in Children With Obstructive Sleep Apnea: An RCT

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Introduction: Adenotonsillectomy (AT) is usually recommended as the first-line therapy for pediatric obstructive sleep apnea (POSA). While AT treats soft tissue obstruction, it does not address the underlying skeletal abnormalities, such as maxillary constriction. Despite growing evidence supporting RME as a treatment option for POSA, a significant research gap remains. Therefore, we conducted a randomized controlled trial (RCT) to compare treatment efficacy between RME and AT.

Materials and methods: This study recruited 24 children diagnosed with POSA and presented with concurrent significant adenotonsillar hypertrophy and transverse maxillary deficiency. Participants were randomly assigned to either AT or RME for treatment. All participants underwent Type I PSG at baseline and 6 months post-treatment. Additional assessments included dental and cephalometric analyses, the pediatric sleep questionnaire (PSQ), and the OSA-18 questionnaire. Baseline and endpoint comparisons between the two treatment groups were performed.

Results: There was no significant difference between treatment groups in all parameters at baseline. The comparisons between pre- and post-treatment results showed significant improvements across multiple parameters, including AHI for both AT and RME. There was no significant difference in PSG parameters (AHI, LSAT, MSAT, and REM sleep time) and cure rate between RME and AT. However, PSQ and OSA-18 scores were significantly higher for the RME group.

Conclusions: RME and AT significantly improved sleep-related respiratory parameters in patients with POSA. RME demonstrated comparable efficacy to AT in reducing AHI and improving LAST, MSAT, and REM sleep time. However, AT provided significantly better improvement in clinical symptoms and QOL.

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Correlation between morning serum melatonin/ferritin levels and sleep problems in Japanese 5-year-old children with ASD

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Introduction: The prevalence of sleep problems is high in children with autism spectrum disorder (ASD). Melatonin and ferritin supplementation are helpful for sleep, but few studies have investigated the relationship between blood melatonin/ferritin levels and sleep problems in children. The objective of this study was to determine the correlation between sleep problems and morning serum melatonin/ferritin levels, and the differences in serum melatonin/ferritin levels between children with ASD and without ASD.

Materials and methods: Four years of data from population-based 5-year-old checkups were referenced. Fifty-five children were divided into the ASD group (N=45) (Who were positive in the first check-up, which is a screening for risk for neurodevelopmental disorders, and diagnosed with ASD by the DSM-5 and classified as "autism" or "autism spectrum" by the ADOS-2 in the second check-up) and the non-ASD group (N=10) (Who were negative in the first check-up, but whose caregivers requested assessments, and who were not diagnosed in the second check-up with ASD, Attention Deficit Hyperactivity Disorder, or Intellectual Disability). Blood samples were collected from fasted children at 8:30 a.m. The Japanese Sleep Questionnaire for Preschoolers (JSQP), a Japanese culture-based sleep

caregiver observation-based questionnaire was used to assess sleep problems. Statistical analysis was the Mann-Whitney U test and partial regression analysis with forced entry method.

Results: In partial regression analysis, in the ASD group, the JSQP V: Insomnia or circadian rhythm disorder was significantly correlated with the serum melatonin level (standardized $\beta=0.501$, $p<0.05$). There were no significant differences in morning serum melatonin levels between the two groups. In children with ASD, high morning serum melatonin levels suggest problems with difficulty getting to sleep and circadian sleep rhythm. Children with high morning serum melatonin levels may have delayed melatonin increase/decrease phase.

In partial regression analysis, in the ASD group, the JSQP IX: sleep habit score was significantly correlated with the serum ferritin level (standardized $\beta=0.559$, $p<0.01$). In children with ASD, the higher the morning serum ferritin levels suggest difficulty getting sleep spontaneously. There may be a direct or indirect association between higher serum ferritin levels and difficulty getting sleep spontaneously in children with ASD. The morning serum ferritin level in the ASD group (23.48 ± 9.14 ng/mL) was significantly higher than that in the non-ASD group (14.84 ± 7.09 ng/mL) ($p<0.05$), but the WHO defines serum ferritin <15 $\mu\text{g/L}$ as iron deficiency, and it should be noted that serum ferritin levels were low in both the ASD and non-ASD groups in this study.

Conclusions: In children with ASD, problems with difficulty getting to sleep and circadian sleep rhythm was correlated with the high serum melatonin level. Appropriate reduction of morning serum melatonin concentration may lead to a decrease in difficulty getting to sleep and sleep rhythm problems (e.g., morning light exposure, nighttime melatonin administration to regulate increase/decrease rhythm, etc.). The possibility that measuring melatonin levels one time in the morning may be meaningful in diagnosing sleep problems and selecting treatment in children.

Correlation of Transcutaneous Carbon Dioxide with Sleep-Disordered Breathing Severity in Indian Children: A Preliminary Observational Study

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Introduction: Sleep-disordered breathing (SDB) in children can present as obstructive apneas, hypopneas, and chronic alveolar hypoventilation. Transcutaneous carbon dioxide (TcCO_2) monitoring offers a non-invasive, continuous measure of ventilatory function during sleep studies. Despite its growing use, there is limited data from India, particularly in children with underlying neurological and neuromuscular disorders. This study aims to evaluate the correlation between TcCO_2 levels and polysomnographic indices such as apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) in a pediatric Indian cohort.

Materials and methods: This retrospective observational study was conducted at a tertiary pediatric center in India, including all children who underwent polysomnography (PSG) between October 2021 and February 2025. Demographic and clinical data, sleep indices, and hourly TcCO_2 values were extracted from PSG reports. A mean TcCO_2 value was computed for each study. The AHI and ODI were recorded as per standard PSG scoring based on AASM. Spearman correlation was used to assess relationships between TcCO_2 and both AHI and ODI.

Indications for PSG were categorized into clinical subgroups. Neuromuscular disorders accounted for 42% of cases, including spinal muscular atrophy types 1 and 2, Duchenne muscular dystrophy, and congenital myopathies. Central nervous system conditions (e.g., cerebral palsy and leukodystrophies) represented 18%, craniofacial syndromes 9%, and idiopathic SDB or obesity-related indications made up 22%. Remaining studies were performed for other miscellaneous indications.

Results: A total of 156 pediatric patients had transcutaneous CO_2 data available and were included. The median age was 8.3 years (range: 1 month to 18 years). Among these, 118 were diagnostic studies, and 38 were titration studies.

TcCO_2 was measured across multiple time points during each study and averaged to yield a single mean value per patient. Correlation analysis showed that AHI did not significantly correlate with TcCO_2 ($r = 0.06$, $p = 0.4194$). In contrast, a statistically significant positive correlation was observed between ODI and TcCO_2 ($r = 0.16$, $p = 0.0415$), suggesting that children with frequent oxygen desaturations may also have elevated transcutaneous CO_2 levels, indicative of nocturnal hypoventilation.

Conclusions: This is the first dataset reporting TcCO₂ monitoring during pediatric sleep studies from India. While AHI did not correlate with TcCO₂, a weak but significant association with ODI was identified, supporting the potential role of TcCO₂ in identifying ventilatory defects among children with SDB. The predominance of neuromuscular disorders in this cohort underscores the relevance of TcCO₂ in these high-risk populations. Further studies with prospective design and inclusion of follow-up TcCO₂ data post-intervention (such as BIPAP initiation) are warranted to validate TcCO₂ as a tool for longitudinal assessment and therapy response monitoring.

Current status and perspectives of research on postoperative sleep health in pediatric liver transplant recipients

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Introduction: To summarize the current research status of sleep health in children after liver transplantation, to analyze the characteristics, influencing factors, and evaluation methods of postoperative sleep disorders, to explore nursing intervention measures, and to provide proof for optimizing clinical management.

Materials and methods: We searched PubMed, Web of Science, Embase, Cochrane Library, CINAHL, CNKI, and Wan Fang databases to screen for relevant studies on sleep disorders in children after liver transplantation. The included literature includes studies on sleep quality, influencing factors, evaluation tools, and nursing interventions after liver transplantation in children. Ultimately, 18 eligible articles were included for review and analysis.

Results: Research has shown that sleep disorders in children after liver transplantation mainly manifest as difficulty in falling asleep, increased awakenings, and sleep breathing disorders. The main influencing factors include postoperative pain, incomplete liver function recovery, infection, use of immunosuppressants, hospitalization environment, and psychological factors. The commonly used assessment tools currently include the Pittsburgh Sleep Quality Index (PSQI), the Obstructive Sleep Apnea Specific Quality of Life Questionnaire for Children (OSA-18), and the Multi Lead Sleep Recorder (PSG). Nursing intervention measures involve optimizing ward environment, strengthening family and social support, individualized psychological intervention, and adjusting sleep behavior. However, there are still problems in current nursing practice such as insufficient standardization of intervention measures and lack of long-term follow-up data.

Conclusions: Sleep disorders after liver transplantation in children have a significant impact on their growth, development, and quality of life. Systematic evaluation should be strengthened, individualized nursing plans should be optimized, and environmental regulation, psychological support, and behavioral intervention strategies should be comprehensively used to improve postoperative sleep health. Large-scale, multi center research is needed to verify the effectiveness of nursing interventions and promote the clinical translation of personalized and multidimensional nursing models.

Developing A Tailored Behavioural Sleep Program for Children with Neurodisability Through Consumer and Stakeholder consultation

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Introduction: Sleep disorders are highly prevalent in children with neurodisability (ND), affecting up to 75% of children in this group. Sleep disorders often have a multifactorial aetiology with concurrent sleep disordered breathing and non-respiratory sleep difficulties. Difficulty initiating and maintaining sleep, anxiety around nighttime, reduced sleep duration and restless sleep are commonly reported by families of children with ND. In most cases the approach to management involves using behavioural sleep interventions that have been extrapolated from those designed for typically developing children.

Whilst effective for some, interventions do not incorporate the needs of all children with ND conditions. Currently, there are no existing guidelines to support a standardised management approach for children with ND. In this study we develop a tailored behavioural sleep intervention program and describe how this has been guided and informed by the perspectives of consumers and stakeholders.

Materials and methods: A collaborative research framework was utilised to develop a behavioural sleep intervention, co-designed with input from both caregivers of children with ND and multidisciplinary healthcare professionals. A consumer advisory group, comprising 4 parents of children with a ND under the care of a tertiary sleep clinic, participated in three discussions to inform and develop the program's structure and content. Simultaneously, consultations were conducted with key stakeholders comprising of health practitioners.

Results: *Consumer results:*

Consumers highlighted the need for a parent directed intervention that delivered accessible and digestible information. Consumers commented on clear, concise communication in the intervention, acknowledging parental fatigue and lowered capacity. A group-based format was proposed to promote peer validation and shared experiences, with caregivers highlighting its value. Additionally, communication barriers between children and caregivers on essential needs (such as toileting needs, pain) were identified as a critical factor contributing to sleep interferences and requiring specific support for management. As a result, communication tools, practical and easy to follow strategies and tailored advice around extra considerations at bedtime were developed to align with parental priorities.

Stakeholder results:

Stakeholders' input provided discipline-specific recommendations. Speech pathologists recommended the use of social stories and visual aids to accommodate communication difficulties and reviewed developed resources. Physiotherapists emphasised the impact of pain on sleep and provided insights to sleep positioning for children with physical impairments. Occupational therapists addressed the negative impact of stress-inducing activities in the hours prior to sleep, sensory processing considerations, environmental considerations, and the importance of promoting child autonomy in bedtime routines. Sleep specialised nurses discussed monitoring and managing nighttime medical events and the dietary influences on sleep. Respiratory and sleep physicians contributed insights into medical comorbidities and medication use that impact sleep, and strategies for managing sleep regressions.

Conclusions: This research demonstrates the importance of consumer and stakeholder engagement when developing a tailored behavioural sleep intervention for children with ND, highlighting the priorities these groups identified to ensure an effective program that meets the need of the target population. Evaluation of the effectiveness of this intervention is now underway as part of a large, multi-centre Australian randomised controlled trial.

Developmental trajectories of sleep regularity during early childhood are related to somatic complaints and thought problems at school age

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Introduction: In recent years, sleep regularity across nights has been recognized as an important dimension of sleep health that is associated with diverse health outcomes. In the first few years of life, children's sleep-wake rhythms become less irregular as their nocturnal sleep lengthens and becomes more consolidated, and their daytime naps decrease in frequency and duration. These developmental changes in sleep regularity vary widely across individuals, and their implications on emotional and behavioural outcomes are not known. This study aimed to examine whether different sleep regularity trajectories during early childhood are associated with emotional and behavioral difficulties at school age.

Materials and methods: Data were drawn from 372 children (48.9% boys) from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort born between November 2009 and May 2011. These children had at least 6 consecutive days of sleep diary data at minimally 2 of 5 time points (6, 18, 24, 36, and 54 months), and data from the parent-reported Child Behavior Checklist (CBCL) at age 7 years. We computed the Sleep Regularity Index (SRI) using the sleep diary data. Latent class models, including group-based trajectory model (GBTM), latent class growth analysis (LCGA), and growth mixture model (GMM), were used to identify distinct SRI trajectories, following the Guidelines for Reporting on Latent Trajectory Studies. CBCL outcomes were compared across trajectory groups using ANCOVA to control for the effects of sex, ethnicity, maternal educational level, parental stress level at age 7 years, and total sleep duration across 24 h averaged across usable time points.

Results: SRI increased during early childhood (mean $\pm$ SD at 6 months: 45.7 ± 13.7 ; 18 months: 69.7 ± 13.4 ; 24 months: 76.0 ± 12.2 ; 36 months: 80.4 ± 10.4 ; 54 months: 83.5 ± 8.7). Compared to other latent class models, LCGA with error variance different for time points but same for classes performed best, and thus, was chosen to fit SRI trajectory. Two trajectory groups – the persistently less regular group ($n = 61$, 16.4%) and the persistently more regular group ($n = 311$, 83.6%) – were distinguished. Compared to the persistently more regular group, the persistently less regular group had more somatic complaints (mean $\pm$ SD: 56.6 ± 5.9 vs 54.4 ± 5.8 , $p = .030$) and thought problems (56.1 ± 5.9 vs 54.1 ± 6.0 , $p = .026$) at 7 years old after adjusting for covariates. The two groups did not differ in aggressive behavior, anxious/depressed problems, attention problems, rule-breaking behavior, social problems, withdrawn/depressed problems, internalizing problems, externalizing problems, and total problems ($p > .181$).

Conclusions: Sleep regularity early in life may contribute to certain domains of children's well-being at school age. Behavioural sleep interventions, such as sleep education, should emphasise the importance of sleep regularity and be targeted at parents with young children to optimise developmental outcomes.

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Diagnostic Accuracy of a Contactless Sleep Mat; “The Sonomat®” compared to Level 1 Polysomnography in Children with Neurodisability – Findings from an Australian Multi-Centre Trial

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Introduction: Sleep disordered breathing (SDB) is highly prevalent in children with neurodisability (ND), with prevalence estimates as high as 80%. In Australia, at present, PSG or polysomnography (level 1

sleep study) remains the standard of care for diagnosis and quantification of SDB in children with ND. However, PSG is often challenging in children with ND due to the intensive monitoring applied. In our previous research, children with ND were >3 times more likely to experience problems tolerating any PSG study leads than neurotypical children. This highlights the importance of developing alternative measures for evaluating SDB in this population. The Sonomat® is a contactless device that non-invasively monitors movement and sound through a mattress placed under the bed sheet. It has been shown to accurately diagnose SDB in neurotypical children and in a small pilot study of children with Trisomy 21. In this study we report findings from a large multi-centre Australian trial of children with ND in which the diagnostic accuracy of the Sonomat® sleep mat system for SDB, was directly compared to PSG.

Materials and methods: This prospective study involved children with ND under the care of one of three Australian tertiary sleep centres. Participants were those aged 2-18yrs, who had been deemed to require a PSG by a sleep physician for assessment of SDB. The Sonomat® was used concurrently to level 1 diagnostic PSG monitoring on the night of the child's scheduled sleep study. Sonomat® and PSG studies were scored independently by a trained scorer and results compared. Agreement for sleep and respiratory parameters was assessed using concordance correlation coefficients (CCC), while detection and classification of SDB were assessed using indicators such as sensitivity, specificity, likelihood ratios and receiver operator characteristic curves.

Results: Preliminary analysis is available from 159 children with ND (88 male, median Age 9.41yrs, IQR 5.36-13.85). 59% of participants had a genetic syndrome, 21% had a diagnosis of ASD and/or ADHD, 12% an underlying neurological condition and 8% with "another" ND condition. The CCC for the apnoea hypopnoea index (AHI) was 0.91 (CI 0.88-0.94) indicating moderate agreement between Sonomat® and PSG. For obstructive apnoea hypopnoea index (OAHI) CCC was 0.63 (CI 0.56-0.71) and for central apnoea hypopnoea index (CAHI) CCC was 0.87 (CI 0.84-0.90). For predicting moderate to severe SDB (AHI³5) the sensitivity, specificity, positive and negative predictive values for the Sonomat® were 61%, 94%, 74% and 89% respectively.

Conclusions: Preliminary findings from this study demonstrate good agreement between AHI derived from the Sonomat® and that derived from PSG. Obstructive hypopnoeas were the least concordant parameter. The high specificity and negative predictive value confirm that the Sonomat® is a suitable tool for screening of SDB in children with ND. This may be a more attractive option for children with ND compared to other current screening tools such as oximetry, due to its contactless application. Further analysis including a larger sample is still underway to determine the diagnostic potential of the Sonomat® an alternative to PSG for children with ND.

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Differences in parent-reported sleep patterns in toddlers sleeping in cribs versus beds

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Introduction:

Extensive literature has shown the importance of environmental factors for optimal sleep in early childhood, including levels of noise, light and temperature. Less attention has been devoted to the type of sleep space. We examined the prevalence of crib versus bed sleeping among toddlers and whether it was associated with differences in toddler sleep.

Materials and methods: We recruited 1167 parents of toddlers 18-48 months old (58% female; 24.3±6.2 months; 98% of parents college educated) from the Nanit user base in the United States. Parents completed the BISQ-R, which provided information on sleeping location and sleep patterns. We performed linear regressions with sleep space as a predictor, parent-reported toddler sleep metrics as outcomes, sex as covariate and stratification by the following child's age groups: 18-23 months, 24-30 months, 31-36 months, 37-48 months.

Results:

Crib-sleeping rates decreased with age: 89% of toddlers aged 18–23 months, 71.5% of those aged 24–30 months, 47% of those aged 31–36 months, and 25% of those aged 37–48 months were reported to sleep in a crib. Among those who had made the transition to a bed, 63% did it by 24 months of age. Parents reported safety concerns (44%) and age appropriateness (56%) as the main reasons for transitioning to a bed.

Compared to crib-sleeping, bed-sleeping was significantly associated with later bedtimes at 18-23 months (23.4 ± 5.4 minutes, $p < 0.001$), longer sleep onset latency at 18-23 months (3.8 ± 1.5 minutes, $p = 0.01$) and 24-30 months (7.2 ± 2.0 minutes, $p < 0.001$); more night awakenings at 18-23 months (0.54 ± 0.10 awakenings, $p < 0.001$), 24-30 months (0.37 ± 0.15 awakenings, $p = 0.01$), 31-36 months (0.7 ± 0.3 awakenings, $p = 0.02$); and shorter nighttime sleep duration at 18-23 months (-23.4 ± 9 minutes, $p = 0.01$), 24-30 months (-25.8 ± 9 minutes, $p = 0.004$) and 37-48 months (-33 ± 15.6 minutes, $p = 0.04$). In addition, sleep of the child was reported to be perceived as a problem more for children sleeping in a bed compared to a crib at 18-23 months ($\beta = 0.2 \pm 0.08$, $p = 0.04$), 24-30 months ($\beta = 0.35 \pm 0.1$, $p < 0.001$) and 31-36 months ($\beta = 0.34 \pm 0.17$, $p = 0.05$). Lastly, children who slept in cribs were less likely to require an adult's presence to fall asleep at 18-23 months ($OR = 11.9, CI: 6.3-22.3$), 24-30 months ($OR = 3.7, CI: 1.7-7.8$), and 31-36 months ($OR = 3.7, CI: 1.03-12.9$).

Conclusions: Based on these findings, crib-sleeping was associated with better sleep patterns compared to bed-sleeping, for children particularly up to 36 months of age; however, due to the cross-sectional design of the study, causality cannot be implied. In addition, generalizability of these findings is limited due to a sample representing only parents in the US and from a higher socio-economic background. Thus, these findings offer additional information for parents and healthcare providers regarding recommendations for toddler transition to bed, in addition to those based on height by the AAP. Nonetheless, more research is needed to understand the effect of transitioning from crib to bed, utilizing objective and prospective sleep data.

Disparities in Maternal Knowledge and Practices on Sleep Training: A Cross-Sectional Analysis of Urban VS Rural Areas

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Introduction: Quality sleep is crucial for the growth and development of children. Sleep training is an effective method to improve the sleep quality of young children. This study aims to identify the knowledge and practices of mothers regarding sleep training for young children in Indonesia.

Materials and methods: This cross-sectional study involved 417 mothers with young children aged 3-36 months in urban and rural areas of Indonesia. Data on socio-demographic characteristics, maternal knowledge, and maternal practices related to sleep training were collected between March and June 2024. Data were collected using forms and questionnaires completed by the participants. Univariate and bivariate analyses were conducted, and comparative analysis between groups was done using the Chi-square and Fisher's exact test.

Results: The Fisher's exact test indicated that mothers in urban areas, with higher education, working in informal sectors, and having a higher economic status had significantly better knowledge of sleep training ($p < 0.05$). No significant association was found between maternal age, residential area, educational background, occupation, economic status, and maternal behavior related to sleep training. Additionally, no significant association was found between maternal knowledge and behavior related to sleep training.

Conclusions: Conclusion

Mothers living in urban areas with higher education, working in informal sectors, and having a higher economic status have significantly better knowledge of sleep training. However, this knowledge is not significantly associated with their behavior in implementing sleep training practices. Further research is necessary to explore the complexities of the relationship between maternal knowledge and behavior in sleep training.

Effectiveness of a nurse-led community-based infant sleep intervention programme: The Sleep Easy Programme (SleEP), Singapore

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Introduction: Sleep plays a vital role in infant development, ensuring optimal brain function and overall health. However, infant sleep problems are common, affecting up to 25% of infants who experience difficulties with sleep onset and problematic night wakings. Early intervention is crucial, but effective community-based programmes are limited. This study aimed to describe and explore the implementation and preliminary outcomes of a nurse-led, community-based intervention programme designed to identify and address early sleep disturbances in infants.

Materials and methods: The Sleep Easy Programme (SleEP) is a nurse-led, community-based programme implemented across multiple primary care centres in Singapore, targeting mainly infants aged 0-6 months. It consists of a three-tiered intervention approach. In Tier 1, parents complete a 22-item questionnaire adapted from the Brief Infant Sleep Questionnaire (BISQ) during routine well-baby visits at four different timepoints and receive anticipatory guidance on age-specific sleep management. Infants identified with sleep concerns (questionnaire score > 5) proceed to Tier 2, where they are referred to a National University Hospital sleep nurse for individualized teleconsultation and education on sleep interventions. Tier 3 involves referral to a sleep psychologist for infants with persistent sleep problems requiring further intervention. Descriptive statistics were used to analyse trends in referral rates, and parents' confidence levels in managing their infants' sleep and perception of the usefulness of the teleconsultation.

Results: Between November 2024 and June 2025, a total of 1,375 questionnaires were completed. The scores for 344 (25.0%) of these were greater than 5, suggesting sleep concerns in the infants and necessitating referral to Tier 2 for further intervention.

Among 163 infants screened at multiple timepoints, 32 (19.6%) were referred to Tier 2 at their first screening. During their second screening, 23 (71.9%) of these infants showed improvement and did not meet the referral threshold again, indicating positive sleep behaviour changes following the interventions. For the remaining 131 infants who were not referred initially, only 15 (11.6%) crossed the referral threshold upon subsequent assessments, suggesting sustained sleep health in the majority.

Overall, the Tier 2 referral rate among infants who were screened at multiple timepoints decreased from 19.6% at the first screening to 14.7% at the second, suggesting a trend towards improved sleep patterns following nurse-led education and intervention. 100% of parents reported increased confidence in managing their infants' sleep post-teleconsultation and/ or usefulness of the teleconsultation.

Conclusions: Preliminary findings from SleEP highlight the impact of structured, nurse-delivered sleep education and teleconsultation support in reducing sleep-related concerns within the first 6 months of life. The integration of sleep health into routine nursing assessments reinforces the expanded role of community nurses in early childhood development. Further research with a control group would be needed to establish effectiveness conclusively.

Acknowledgments: My gratitude goes to the NUP nurses for their role in screening and educating the families. I would also like to thank the NUH Evidence-Based Nursing Unit for their guidance as well.

Effect of caregivers' perception on short-term adherence of children with OSAHS treated with CPAP

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Introduction: to explore the effect of caregivers' perception on short-term adherence of children with OSAHS treated with CPAP.

Materials and methods: 72 children with OSAHS who were treated with CPAP in our department from 2018 to 2020 were retrospectively analyzed. First, according to the difference of caregivers' perception on OSAHS and CPAP treatment, the patients were divided into two groups: group I (n = 27) for CPAP treatment and group II (n = 45) for operation. The related parameters of the two groups were

compared. Then, the children in group II are divided into good adherence group ($n = 18$) and poor adherence group ($n = 27$) according to the standard that the AHI decreased by more than 50% after 2 months, which the above parameters are compared. Finally, the trend of day1 and day 2 among group I, good and poor adherence group are analyzed.

Results: the average time of use(h) of group I is more than group II ($p=0.046$). the AHI of good adherence group in group II is severer than poor adherence group ($p=0.046$). in the trend chart, the day1(h) and day2(h) of group I remain ahead, while day1(h) of good adherence group falls behind the poor adherence's, but exceeds it in the day2(h).

Conclusions: The short-term adherence of CPAP treatment can be improved by sufficient education of caregivers. It is suggested that the education of preoperative CPAP treatment should be carried out in outpatient department for the children with severe OSAHS. In addition, improving the short-term adherence of CPAP treatment in children with severe OSAHS can promote the implementation of long-term adherence, especially in the first two days of CPAP treatment.

Effects of Ambient Temperature and Pollen Exposure on Sleep, Respiratory Events, and Apnea-Specific Pulse Rate Response in Children with Sleep Disordered Breathing

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Introduction: Increased nasal resistance is a recognized risk factor for pediatric sleep-disordered breathing (SDB). Ambient temperature variations and elevated pollen concentrations might modulate upper airway inflammation and obstruction, which may potentially alter sleep architecture, SDB severity and autonomic function in children.

Materials and methods: A retrospective analysis of in-laboratory diagnostic polysomnography (PSG) data in 690 Chinese children (median age 6.0 years [IQR: 4.0-9.0]) was conducted. The children were present with habitual snoring or witnessed apneas between January 2017 and December 2024. Daily ambient temperature records and pollen counts (expressed as pollen grains per cubic meter of air, grains/m³) were obtained from official sources. High pollen days were defined as calendar days with ≥ 100 grains/m³ atmospheric pollen concentration. Δ HR was defined as the difference between the maximum and minimum heart rates within an event-related window around each respiratory event, calculated directly from the continuous heart rate recordings. This metric quantitatively reflects sympathetic activation during sleep apnea events. Associations between pollen concentration, ambient temperature and PSG parameters were analyzed.

Results: Participants exhibited a median age of 6.0 years (interquartile range [IQR]: 4.0–9.0). PSG-confirmed OSA was present in 302 children (43.7%), with a median obstructive apnea-hypopnea index (OAHI) of 3.9 events/hour (IQR 1.8–10.7).

Lower minimum, mean, and maximum ambient temperatures were significantly associated with greater proportion of NREM stage 3 ($p = -0.130$, $p = 0.001$; $p = -0.124$, $p = 0.001$; $p = -0.113$, $p = 0.003$). And ambient temperatures demonstrated positive correlations with proportion of NREM stage 2 ($p = 0.134$, $p < 0.001$; $p = 0.122$, $p = 0.001$; $p = 0.126$, $p = 0.001$). No significant associations were observed between ambient temperatures and OAHI, SpO₂, WASO, sleep latency, or sleep efficiency.

Children monitored on days with higher ambient pollen levels (≥ 100 grains/m³, median 210 [IQR 160–358]) exhibited significantly lower nadir oxygen saturation (91% [88–93] vs. 92% [89–95], $p = 0.014$) and less Δ HR (36.9 [29.3–44.8] vs. 39.4 [31.4–47.3] bpm, $p = 0.029$) compared to those monitored during low-pollen exposure periods. Notably, no significant differences were observed in OAHI, arousal index, sleep latency, or sleep efficiency (all $p > 0.05$), indicating that the observed effects are independent of conventional sleep-disordered breathing metrics.

Conclusions: These findings suggest that elevated environmental pollen concentrations might exert subtle but measurable effects on sleep architecture, nocturnal oxygenation and autonomic regulation. Ambient factors might be considered as effect modifiers when evaluating sleep apnea-induced pathophysiological consequences in children with sleep disordered breathing.

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Emotional and Behavioral Difficulties Partially Mediate Sleep Problems in Children With and Without Chronic Illness: A Cross-Sectional Analysis

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Introduction: Children with chronic illnesses are often thought to be at greater risk for sleep disturbances due to physical and psychological stressors. However, the interplay between chronic disease, emotional/behavioral difficulties, and sleep problems remains unclear. In children with chronic kidney disease (CKD), disease-related factors such as uremia, edema, acidosis, or anemia have been implicated in the pathogenesis of sleep disorders, however, the effect of behavioral problems in the development of sleep disorders is understudied. This study aimed to investigate the interplay between emotional/behavioral difficulties and sleep problems in children with CKD and healthy children.

Materials and methods: This cross-sectional study included 152 children aged 6 to 16 years (11.8 ± 2.8), 49 with CKD and 103 healthy controls. Parents completed the Sleep Disturbance Scale for Children (SDSC) and the Strengths and Difficulties Questionnaire (SDQ). Group comparisons were conducted using t-tests, followed by linear regression and mediation analyses using PROCESS (Model 4, 5,000 bootstrapped samples). All continuous variables were mean-centered for interpretability.

Results: Children with CKD had similar levels of sleep problems as healthy controls (34.9 ± 11.8 vs 35.7 ± 6.9 , $p = 0.63$) based on SDSC scores. However, they showed higher total difficulties score in SDQ compared to healthy controls (9.9 ± 4.0 vs 6.7 ± 4.5 ; $t(150) = -4.15$, $p < 0.001$). Regression analysis revealed that higher total difficulties scores predicted more sleep problems ($\beta = .44$, $p < .001$), while group status independently predicted fewer sleep problems, with children in CKD group showing lower SDSC scores when controlling for SDQ ($\beta = -.22$, $p = 0.007$). An interaction term between group and total difficulties scores was added to test whether the association between SDQ and sleep problems differed by health status. The interaction was not statistically significant ($p = 0.304$), indicating that SDQ difficulties predicted sleep problems similarly in both healthy children and children with CKD. Mediation analysis revealed that total difficulties score partially mediated the relationship between group and sleep problems, with a significant indirect effect ($B = 2.95$, 95% CI [1.33, 5.75]). The direct effect of group status on sleep remained significant ($B = -3.67$, $p = 0.011$), indicating partial mediation, meaning that children with CKD have fewer sleep problems, even after adjusting for SDQ. A reverse mediation model testing sleep as mediator between group and SDQ was not significant (indirect effect = -0.17 , 95% CI [-1.22, 0.63]).

Conclusions: Despite comparable levels of sleep disturbance, children with CKD showed more emotional and behavioral difficulties, which partially mediated their sleep outcomes. Structured routines and close parental monitoring, necessary for disease management in CKD, may be improving sleep in children with CKD. Besides, emotional/behavioral difficulties may be more apparent than sleep problems, which might not always translate into measurable sleep disturbance, resulting in underreporting by parents. These findings suggest that while chronic illness may not directly worsen sleep, its emotional burden plays a critical role, warranting integrated psychosocial and sleep-focused care. The emotional/behavioral difficulties are important predictors of sleep disturbances both in healthy children and those with CKD, underscoring the importance of psychosocial health in evaluating sleep health across pediatric populations.

Enhancing Parental Knowledge of Sleep through Bibliotherapy: A path to improve pre-schoolers sleep

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Introduction: Healthy and adequate sleep is essential for neurodevelopment, especially during early childhood at preschool level. Children's sleep health relies on parents' understanding of their developmental sleep needs. Therefore, bibliotherapy, which is typically delivered by the parents through storytelling and book reading for younger children, may serve as a promising intervention to

improve sleep in children. However, there is a lack of sufficient evidence to support the effectiveness of bibliotherapy in improving parent's sleep knowledge and children's sleep practice.

Materials and methods: This was a pilot randomized controlled trial conducted in pre-schoolers with short sleep duration and their parents. Eligible participants were randomly assigned to 4 weeks bedtime bibliotherapy intervention group or wait-list control group at 1:1 ratio. Assessments for parents' sleep knowledge, children's sleep hygiene practices and parent-child relationship were conducted at baseline, post-intervention and 2-month follow-ups.

Results: A total of 30 pre-school aged children and their parents were enrolled in this pilot study. Three parent-child pairs dropped out after the randomization, leaving 27 (intervention group: $n = 13$; control group: $n = 14$; 46% girls; mean age $\pm$ SD: 3.6 ± 0.8 years) included in the final analysis. Most the parents who involved in the study were mothers ($n = 26$, 96%) At post-intervention, the intervention group had a nonsignificant increase in parents' sleep knowledge compared to baseline ($4.7 [-0.1 \text{ to } 10.3]$, $p = 0.10$), albeit there was no significant interaction effect between the two groups across the two follow-up timepoints after the intervention ($p = 0.33$). Similarly, a nonsignificant reduction in children's maladaptive sleep hygiene practices were also observed in the intervention group at post-intervention relative to baseline ($-3.2 [-7.8 \text{ to } 1.5]$, $p = 0.18$) but not in the control groups. In addition, a marginally significant improvement in the parent-children relationship was noticed in the intervention at both post-intervention ($1.7 [-0.2 \text{ to } 3.7]$, $p = 0.08$) and 2-month follow-ups ($1.9 [-0.1 \text{ to } 3.9]$, $p = 0.057$) compared to baseline, while the control group have similar scores over all the assessment timepoints.

Conclusions: In this pilot study, bibliotherapy intervention is a feasible intervention tool that is welcomed by the participating parents according to the feedback from parents after the intervention. The pilot findings found non-significant increase in parents' sleep knowledge and apparent improvement in the parent-children relationship in the intervention group. Further study with larger scale RCT with adequate statistical power is needed to determine whether the use of bibliotherapy will be able to enhance parent's sleep knowledge, children's sleep practice and parent-child relationship.

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Establishing Consensus Guidelines for the Assessment and Management of Sleep-Disordered Breathing and Behavioural Sleep Disturbance in Children with Neurodisability: A Delphi Study

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Introduction: Children with neurodisability (ND) exhibit disproportionately higher rates of sleep-disordered breathing (SDB) and behavioural sleep problems, compared to their peers. Sleep disorders have a profound developmental impact on the child, affecting physical and psychological wellbeing. To date there are no evidence-based guidelines, specifically developed for the management of sleep problems in children with neurodisability. This study describes the preliminary findings from a modified Delphi process underway in Australia and New Zealand, aiming to develop consensus recommendations to inform management of sleep disorders in children with Neurodisability.

Materials and methods: A modified e-Delphi methodology was employed to achieve expert consensus on the management of sleep problems in children with neurodisability. Accredited paediatric sleep medicine specialists in Australia and New Zealand, were invited to participate in 2 iterative rounds of online surveys and a virtual round table discussion with key stakeholders, including consumers, other specialists caring for children with ND, psychologists, sleep nurses and pharmacists. Questions in round 1 included those designed to understand the current interventions and management practices used in routine practice, including pharmacotherapy, medical and behavioural sleep interventions. Consensus was defined as $\geq 80\%$ agreement on items.

Results: Thirty participants completed round 1 of the Delphi survey, the majority of whom were senior medical staff (87% with 50% >15yrs experience) working in public hospitals (67%) with on-site sleep laboratories (97%). While 73% of consultants felt confident managing sleep problems in children with

neurodisability (ND), only a third agreed they had received sufficient training in this area. Clinicians estimated that over half of children with ND experience sleep problems, with many estimating that 25–75% of their sleep clinic population had a neurodisability. Almost half of the participating clinicians expressed a desire for more evidence-based resources, with a third acknowledging the gap in this area. Assessment of sleep varied, with 80% routinely evaluating a broad range of parent concerns, including disordered breathing, behavioural sleep problems, impact on daytime functioning and family wellbeing. 80% of clinicians reported “rarely” using validated sleep screening measures in their assessment.

For sleep-disordered breathing (SDB), Level 1 polysomnography was the most common investigation (93%), with home oximetry (80%) and parent-recorded videos (50%) also used. Half of the clinicians surveyed, reported modifying their standard approach for managing SBD when caring for children with ND.

For non-respiratory sleep problems, 50% reported using modified behavioural sleep interventions, and 40% initiated medications earlier in children with ND when compared to NT children. Other tools used included paper sleep diaries, videos and actigraphy.

Analysis of subsequent rounds of the Delphi process are underway.

Conclusions: Using a Delphi approach provides a methodologically robust pathway for developing the 1st consensus statement for the management of sleep problems in children with ND. Preliminary data from this study suggests that many specialists modify their standard approach to sleep disorders for children with ND and practices vary. Subsequent rounds of this study will determine final recommendations for optimal management of sleep disorders in children with ND, aiming to improve outcomes for this population by modifying sleep.

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Estimated prevalence of sleep problems in 3-year-old children and the relationship between sleep problems and development - Report from a population-based study of 3-year-old health check-ups

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Introduction: Children's sleep problems affect cognitive ability, psychosocial health, obesity, and problem behaviors. The prevalence of sleep problems in young children has been reported to be high, but the prevalence by age has not been clarified. In 2024, we reported a prevalence of preschool sleep problems of 18% in a population-based study at a 5-year-old health check-up, but it is expected that children's sleep problems begin at an earlier age. This study aimed to estimate the prevalence of sleep problems in 3-year-old children and to clarify the relationship between sleep problems and development, with the aim of realizing sleep intervention at 3-year-old health check-ups.

Materials and methods: The study subjects were 1,300 children who participated in a 3-year-old health checkup in a medium-sized city in northern Japan from December 2023 to March 2025, and 1,268 children (97.5%) (644 boys and 622 girls, mean age 41.6 months) who agreed to participate in a contracted developmental study were included. Sleep problems were evaluated using the Japan Sleep Questionnaire for Preschoolers (JSQP), and a total score of 86 or more was defined as having a sleep problem. 1) Sociality was evaluated using the 14-item Screening for Social Development (SSD14), 2) stuttering, tics, reading, writing, and motor development was evaluated using the Check List of Obscure Disabilities in Preschoolers 3-year-old version (CLASP-3y), and 3) behavior was evaluated using the Child Behavior Check List (CBCL). Statistical analysis was performed using t-tests, multiple regression analysis, and partial regression analysis with forced entry method to identify items with strong associations. This study was approved by the Ethics Committee of the Graduate School of Health Sciences, Hirosaki University.

Results: The proportion of subjects with sleep problems (JSQP $\geq$ 86) was 24.8%. Multiple regression analysis showed a significant correlation between the JSQP total score and the sub-items of SSD14 ($R^2 = .201$, $p < .001$), CLASP-3y ($R^2 = .204$, $p < .001$), and CBCL ($R^2 = .429$, $p < .001$). Partial correlation analysis showed that 1) in SSD14, the JSQP total score was significantly correlated with peer relationships, hyperactivity, social awareness, social communication, social motivation, and repetitive/restrictive behavior. 2) in CLASP-3y, the JSQP total score was significantly correlated with

stuttering and simple vocal tics. In terms of reading and writing skills, there was a significant correlation between phonological representation/phonological discrimination and auditory discrimination, and in terms of motor skills, there was a significant correlation between motor execution, accuracy, and posture maintenance. 3) In the CBCL, there was a significant correlation between the JSQP total score and somatic complaints, withdrawal, sleep problems, attention problems, and aggressive behavior.

Conclusions: The estimated prevalence of sleep disorders in 3-year-olds (24.8%) was slightly higher than the prevalence in 5-year-olds (18%). It was also suggested that sleep problems may co-occur with developmental and behavioral problems. Cohort studies in other countries have reported that sleep problems in infancy are related to the emergence of later mental disorders and behavioral characteristics. It is desirable to actively investigate sleep in infant health checkups and aim to improve sleep problems as early as possible.

Exploring the Impact of Technology Use in Children with and without Neurodisabilities. Findings from a Cross-Sectional Study

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Introduction: In clinical practice, parents of children with neurodisabilities (ND) sometimes report that technology use helps their children settle down before bedtime, despite the general advice to avoid screen use prior to bed. There is limited research focusing on bedtime technology use and its impact on sleep in children with ND. This cross-sectional comparative study examined sleep patterns and technology use in children with ND by comparing them to a cohort of neurotypical (NT) peers to inform tailored sleep management guidance for children with ND.

Materials and methods: The primary prospective study was conducted across three Australian paediatric hospital sites where parents or caregivers of children aged 2–18 years with a diagnosed ND condition and referred for diagnostic polysomnography (PSG) were recruited. A smaller group of NT children undergoing a clinical PSG study were recruited from one clinical site for comparison. Caregivers completed a study-designed questionnaire which examined device type, frequency of use, duration, reported helpfulness and data regarding any sleep problems in the participant. Comparison of groups was performed using chi-square tests. Qualitative thematic analysis of caregiver free text responses was also undertaken.

Results: There were 192 participants in the ND group (53.1% male, mean age 10.1) and 35 participants in the NT group (48.6% male, mean age 10.1). Frequency of “everyday” device use was generally high in both groups but was 10% higher in the ND group. Older children with ND showed a statistically significant higher frequency of device use than younger children ($p=0.002$). Caregiver report of sleep symptoms in their child was higher amongst participants in the ND group compared to those in the NT group (53% and 29% respectively). Amongst participants in the ND group, 18% reported sleep symptoms when device use was low (“never/little”) whereas 42% reported sleep symptoms when device use was described as high (“more than 1-2 days per week”). 40% of caregivers in the ND group reported technology use at bedtime to be “somewhat” helpful compared to 14% of participants in the NT group. Differences between device use within different ND condition subtypes as well as qualitative analysis of free text responses from caregivers were also evaluated in this study.

Conclusions: There was a high prevalence of technology use at bedtime in all children, with those with ND reported to have overall higher use. This study strongly suggests an association between bedtime technology use and a higher report of sleep symptoms in children with ND. Despite this finding, just under half of the caregivers in the ND group indicated some perceived benefit of technology use at bedtime for their child, suggesting that the relationship between sleep and screen time is complex in this population. Our findings highlight the importance of not only providing guidance to families about the potential negative impact of technology use around bedtime for their child's sleep but also a need to consider modified advice for children with ND, to balance potential benefits from technology use that may be key to assisting parents with implementing day to day routines

Feasibility and clinical utility of daytime polysomnography performed in NICU to diagnose sleep disordered breathing in infants

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Introduction: Sleep disordered breathing (SDB) is widely prevalent in infants. Early diagnosis and treatment of SDB improves feeding, growth, and neurodevelopment in affected infants. Polysomnography (PSG) is vital for early diagnosis and treatment of SDB in infants; but often difficult to obtain. Our aim was to assess the feasibility and clinical utility of daytime PSGs conducted in neonatal intensive care unit (NICU) to diagnose SDB when compared with the existing practice of overnight PSGs performed in sleep laboratory in infants <3 months age.

Materials and methods: We commenced a pilot project of conducting daytime PSGs in our centre in May 2021. PSG results were collated prospectively for infants less <3 months of age, between 1st May 2021 and 31st May 2024. Comparison was made between results for daytime PSG in the NICU and overnight PSG in the sleep laboratory. Primary outcomes were successfully completed PSGs (feasibility) and clinical utility. The primary outcome to assess clinical utility was percent sleep efficiency. The secondary outcomes were percent REM sleep, REM sleep latency, sleep latency, and other indices (per hour of sleep) spontaneous arousals, Obstructive apnea hypopnea index (OAHI) and Apnea hypopnea index (AHI).

Results: Of 60 PSGs, 28 were daytime and 32 were overnight. Daytimes studies had younger age (median 18 vs 55 days, $p < 0.001$), and shorter median recording time (8.2 vs 10.4 hrs, $p < 0.001$). Feasibility showed that all daytime PSGs were successful. For clinical utility, after adjusting for age (at PSG) and total recording time, percent sleep efficiency was equivalent in the two groups (95% CI -12.4, 5.7; $p 0.456$). For secondary outcomes, daytime PSGs had a higher % REM sleep by 9.9% points (95% CI 1.1, 18.8; $p 0.028$) compared to overnight PSG. Parameters that were not different included: frequency of spontaneous arousals, REM latency, sleep latency, apnoea-hypopnea index, and obstructive apnoea-hypopnea index. A decline in requests for overnight PSGs and corresponding increase in daytime PSGs over the course of the study was observed.

Conclusions: This is the first prospective study to report that standard PSGs can be performed during the daytime in NICU for infants <3 month of age and can provide reliable results. Despite being performed outside the sleep laboratory, daytime PSGs were universally successful (feasible) and captured similar percent sleep efficiency (clinically useful) with 9.9% higher percent of REM sleep. Other sleep and respiratory parameters comparable to studies of infants conducted overnight. Notably, we were able to perform daytime PSGs at a younger age indicating reduced wait times. Daytime PSGs model may facilitate earlier access to PSGs, improve patient safety by bringing the diagnostic service to the bedside of the infant in NICU and expanded resource capacity with potential for cost-savings.

Acknowledgments: We would like to acknowledge Perth Children's Hospital Foundation for funding the equipment and implementation of the daytime bedside polysomnography at Perth Children's Hospital.

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Impact of Adolescent Sleep Restriction on Self-Report Hunger and Macronutrient Intake at the First Meal of the Day

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Introduction: Pediatric obesity rates are rising and are associated with both negative physical and psychosocial health outcomes. Poor sleep is tied to pediatric obesity and changes in composite 24-hour macronutrient consumption. However, the impact of poor sleep on macronutrient intake at specific timepoints across subsequent day is largely unknown. This study evaluated the roles of sleep duration, sex, and BMI in predicting adolescent macronutrient consumption during the first meal of the day and time-matched self-reported hunger variables. This information will support targeted behavioral intervention at key timepoints in a 24-hour period.

Materials and methods: Sleep (actigraphy), macronutrient consumption (24-hour food logs), and BMI were assessed at baseline. Adolescents (N=61) completed two sleep conditions in a randomized order, each preceded by a washout period of 3 nights of adequate sleep (~9 hours of sleep per night) and followed by a laboratory visit. The conditions included 1) restricted sleep (~4 hours of sleep for 1 night) and 2) adequate sleep (~9 hours of sleep for 1 night). Participants tracked food consumption via 24-hour self-report food logs before each follow-up appointment and began fasting 12 hours prior to each follow-up appointment. At their follow-up appointments, participants reported hunger, fullness, and ability and desire to eat, and were provided with a self-serve buffet for their first meal of the day. Buffet items were weighed before and after the meal to determine the amount consumed and macronutrient consumption was determined via the Nutrition Data System for Research.

Results: Restricted sleep ($M_{\text{Duration}}=4$ hours 12 minutes, $SD_{\text{Duration}}=50.7$ minutes) was associated with reduced consumption of calories, fat, protein, and saturated fatty acids ($ps<.05$; $\eta_p^2=.08-.12$). BMI and sex did not significantly influence this association. However, restricted sleep was associated with self-reported reductions in hunger and desire to eat among female adolescents ($M_{\text{Duration}}=8$ hours 54 minutes, $SD_{\text{Duration}}=58.0$ minutes) and increased self-reported hunger in male adolescents ($ps<.05$; $\eta_p^2=.09-.15$).

Conclusions: Restricted sleep is associated with reduced macronutrient intake at adolescent's first meal of the day. Given previous research documenting overall increases in adolescent 24-hour macronutrient consumption following sleep restriction, it is possible that decreased morning consumption leads to increased consumption and binge like behaviors later in the day. Targeting key moments, such as breakfast, in timed behavioral interventions may optimize patient outcomes.

Improving Children's Sleep: The Importance of Parental Sleep Beliefs and Practices

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Introduction: Improving children's sleep is crucial for their development, as sleep difficulties in early childhood can have lasting effects on both children and their families. Parental sleep beliefs and practices play a key role in shaping children's sleep behaviors, yet their distinct contributions to sleep remain unclear. This study examined whether improvement in parental sleep-related beliefs and practices following a short sleep intervention predicted improvements in children's sleep.

Materials and methods: 74 families, including one or both parents and their 3 to 5-year-old child, participated in a two-hour group intervention focused on improving children's sleep. During the intervention, parents received guidance on beliefs and practices related to child sleep while children engaged in sleep-related educational activities in a separate room. A follow-up session took place two weeks later with the parents, during which they could receive additional support. Parents completed the Children's Sleep Habits Questionnaire (CSHQ), the Parent-Child Sleep Interaction Scale (PSIS), and the Maternal Cognitions about Infant Sleep Questionnaire (MCISQ) before the intervention (T1) and approximately two months later (T2). Three paired sample t-tests were conducted to assess changes, comparing T1 and T2 scores. Additionally, hierarchical linear regression was performed to examine whether changes in parental practices (PSIS) and sleep-related cognitions (MCISQ) predicted changes in children's sleep difficulties (CSHQ scores) at T2. In the first model, T1 scores for CSHQ, PSIS, and MCISQ were entered, and in the second model, T2 scores for PSIS and MCISQ were added.

Results: Results showed significant reduction after two months in child sleep difficulties ($M = 54.08 \pm 8.01$ vs $M = 48.09 \pm 7.46$, $t(73) = 7.68$, $p < .001$). Results also showed significant improvement in parental practices ($M = 12.64 \pm 5.53$ vs $M = 9.12 \pm 5.48$, $t(73) = 6.31$, $p < .001$); and parental beliefs about children's sleep ($M = 29.65 \pm 6.80$ vs $M = 25.85 \pm 6.20$, $t(73) = 6.07$, $p < .001$). Results from the

hierarchical regression analysis showed that the first model was significant ($F(3, 70) = 15.03, p < .001$) and explained 36.6% of the variance in T2 child's sleep difficulties. T1 child's sleep difficulties was the only significant predictor of T2 child's sleep quality ($B = .58, p < .001$). When T2 parental practices and parental beliefs about children's sleep were added to the model, they accounted for an additional 5.6% of the variance. This change in R^2 was significant ($F(2, 68) = 4.39, p = .016$), with the final model explaining 42.2% of the variance. T1 child's sleep difficulties ($B = .63, p < .001$) and T2 parental practices ($B = .46, p = .005$) were significant predictors of child sleep difficulties at T2.

Conclusions: These findings suggest that enhancing parental practices seems to be essential for improving children's sleep. However, as parental beliefs often shape these practices, future research employing advanced analyses could uncover a more nuanced relationship between parental sleep beliefs, parenting practices, and children's sleep.

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Infant sleep patterns are related to specific temperamental traits

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Introduction:

Adequate sleep is crucial for children's physical health, cognitive development, and emotional regulation. Previous studies have shown that a difficult temperament is related to more sleep awakenings and sleep problems in general. This study aims to explore the intricate relationship between sleep patterns and temperament in a large sample of infants.

Materials and methods:

Caregivers of 623 infants aged 9-13 mos ($M=10.3 \text{ mos} \pm 1.1$, 52.0% females) were recruited among users of Nanit baby-monitor in the United States and reported on their baby's temperament by completing the Infant Behavior Questionnaire (IBQ-R). The IBQ-R assesses three scales: 1) Positive Affectivity/Surgency (PAS): Relates to positive affect, approach tendencies, smiling, laughter, activity, and enthusiasm, similar to adult extroversion. 2) Negative Emotionality (NEG): Associated with distress to limitations, fear, sadness, and difficult recovery from arousal, comparable to adult Neuroticism. 3) Orienting/Regulatory Capacity (ORC): Encompasses attention-based regulatory skills and enjoyment of calm activities. Objective infant sleep metrics (night sleep time duration, number of night wakings, sleep efficiency, bedtime, wake up time, time awake at night and parent interventions) were obtained from the Nanit camera (1 week of data averaged). A cluster analysis was conducted to group infants based on sleep metrics. The between-cluster comparison for IBQ-R temperament scores was performed using one-way analysis of variance (ANOVA). Post hoc tests were performed.

Results: Three reproducible and stable sleep groups were identified: Long Sleepers (LS, n.338), Interrupted Sleepers (IS, n.130) and Short Sleepers (SS, n.155). All sleep metrics were statistically significantly different in the three groups: LS were characterized by long nighttime sleep duration, SS presented later bedtime and earlier wake up time, IS presented more night wakings. When comparing IBQ-R scoring between the three groups, IS and SS showed higher scores in the NEG scale than LS, with a statistically significant difference (respectively $0.36 \pm 0.09, p < .001$ and $0.39 \pm 0.09, p < .001$), thus showing greater sadness and fear, lower tolerance to limitations and more difficulty recovering from distress.

Conclusions:

Our findings support previous research highlighting that poor sleep in infancy is associated with negative affectivity. Ensuring adequate sleep may serve as a preventive measure against temperament-related issues, contributing to the overall health.

Insufficient Weekday Sleep Predicts Emotional Distress in Adolescents: A Study of Sleep Patterns in Taiwan

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Introduction: Adolescents experience dramatic shifts in sleep chronotype during puberty, often resulting in chronic sleep deprivation during school weeks due to early school start times. This insufficient sleep has been linked to a range of biopsychosocial impairments. Previous research has identified sleep disturbances as a significant risk factor for suicidal behavior among adolescents. Given the rising suicide rates among Taiwanese adolescents in recent years, this study aimed to investigate the extent of sleep deprivation in this population and to further examine the relationship between weekday sleep duration, emotional distress, and executive function. The findings may inform future interventions targeting severe psychological distress and suicidal ideation.

Materials and methods: A total of 548 adolescents aged 13–18 participated in the study. Participants completed a battery of assessments, including: (1) a demographic, sleep, and lifestyle questionnaire; (2) the Chinese version of the Beck Youth Inventories – Second Edition (for junior high school students), the Beck Depression Inventory-II and the Beck Anxiety Inventory (for high school students); and (3) the computerized Wisconsin Card Sorting Test (WCST) to assess executive function. Data were analyzed using SPSS version 29.0.

Results: The average weekday sleep duration among Taiwanese adolescents was 6.63 ± 1.1 hours, compared to 8.85 ± 1.5 hours on weekends. Notably, 89.6% of adolescents reported sleeping less than 8 hours on weekdays, indicating widespread weekday sleep insufficiency and significant discrepancies between weekday and weekend sleep patterns. Correlational analyses revealed that shorter weekday sleep duration was significantly associated with higher anxiety ($r = -.138$, $p = .001$) and depression levels ($r = -.226$, $p < .001$). However, no significant relationships were found between weekday sleep duration and executive functioning as measured by WCST indicators. Regression analyses further showed that shorter weekday sleep duration significantly predicted higher levels of anxiety ($\beta = -.138$) and depression ($\beta = -.226$).

Conclusions: This study provides updated data on adolescent sleep patterns in Taiwan, revealing a high prevalence of weekday sleep deprivation and a tendency toward weekend "catch-up sleep." Importantly, insufficient weekday sleep was found to be a significant predictor of emotional distress among adolescents. These findings highlight the mismatch between adolescents' biological sleep needs and the structural demands of school schedules, which may chronically impair emotional regulation. Notably, even with the implementation of delayed school start times in some schools, insufficient sleep remains prevalent among adolescents. This underscores the importance of comprehensive sleep hygiene education and targeted psychological interventions to effectively promote mental well-being and address suicide-related concerns in this population.

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Integrated metagenomic and metabolomic analysis reveal distinctive gut microbiota-derived metabolites in pediatric obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is one of the common sleep disordered breathing diseases which could affect growth and development in children. However, the unique molecular signatures and multi-omics profiles in pediatric OSA remain unclear. Here, we aimed to characterize the signatures of gut microbiome, plasma and fecal metabolites in pediatric OSA.

Materials and methods: We recruited 51 patients with pediatric OSA and 30 controls for conducting an integrated analysis by shotgun fecal metagenomics, plasma metabolomics and fecal metabolomics.

Results: We identified 37 bacterial species were significantly different between pediatric OSA and controls, as evidenced by increased abundance of *Bacteroides_nordii* and decreased abundance of *Bifidobacterium_bifidum*, and *Veillonella_dispar* in pediatric OSA group. Besides, we identified that short-

chain fatty acids (SCFA) in plasma could significantly discriminate pediatric OSA from controls. Notably, co-occurrence network analysis revealed that *Bifidobacterium_bifidum* and *Veillonella_dispar* had strongly positive relationships with SCFA, suggesting that disturbed gut microbiome might mediate depletion in SCFA in pediatric OSA. Furthermore, we identified a combinatorial marker panel that could distinguish pediatric OSA from controls with high accuracy.

Conclusions: Altered microbiome-metabolomics interactions help to explain the pathophysiologic process induced by pediatric OSA. Additionally, this study offers a unique SCFA-related signatures in pediatric OSA which will open new potential avenues for preventive and therapeutic approaches for impairment induced by pediatric OSA.

Inter-Scorer Concordance and Method Agreement in Paediatric Sonomat® Scoring for Sleep Disordered Breathing

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Introduction: The Sonomat® is a contactless sleep monitoring device comprising a mattress overlay embedded with polyvinylidene fluoride (PVDF) sensors and microphones. It records thoracoabdominal movement and acoustic breath sounds, providing indirect surrogates for respiratory effort and airflow. While validation studies have shown promising agreement with PSG in detecting sleep disordered breathing (SDB), the absence of standardised paediatric scoring rules has limited uptake. Recently developed Sonomat-specific paediatric scoring criteria (unpublished) aim to address this gap. This study evaluated inter-scorer concordance using these new rules and assessed agreement between Sonomat and PSG across key respiratory event indices.

Materials and methods: Five trained sleep scientists independently scored 10 sonomat studies using the Sonomat Replay software (© Sonomedical, Balmain, Australia) and following formalised paediatric scoring rules. Scoring outputs included standard respiratory indices: Apnoea Index (AI), Hypopnoea Index (HI), Apnoea-Hypopnoea Index (AHI), Central Event Index (CEI), and Obstructive Event Index (OEI). Each study also had gold-standard Sonomat scoring from a reference expert (AC). Intraclass correlation coefficients (ICC[2,1]) were calculated to quantify inter-scorer reliability for each Sonomat index. Bland-Altman and mean difference analyses were performed to compare Sonomat scores with paired PSG data.

Results: Inter-scorer agreement using the newly developed paediatric Sonomat scoring rules was highest for AI (ICC=0.95), CEI (ICC=0.90), and AHI (ICC=0.85), reflecting excellent reliability between trained scorers. Agreement was lower for OEI (ICC=0.57) and poor for HI (ICC=0.31), indicating inconsistency in the identification of hypopnoeas.

When comparing individual Sonomat scores from the reference scorer (AC) to PSG, Bland-Altman analysis showed the narrowest limits of agreement for OEI (-1.17 to +0.82 events/hour) and AI (-3.71 to +3.00), with the widest limits observed for CEI (-5.11 to +6.45). Mean differences were generally small across all indices, with AHI and CEI showing slight overestimation compared to PSG.

A group mean analysis was also performed, comparing the average Sonomat scores across all five scorers to the PSG reference. Agreement remained strongest for apnoea-based indices (AI, AHI), while greater variability was observed for CEI and HI. The group-level differences were consistent with individual scorer comparisons, supporting the robustness of scoring across the trained cohort.

Conclusions: The use of standardised scoring rules for Sonomat studies in children demonstrated excellent inter-scorer reliability for apnoea-based metrics, supporting its potential clinical utility as a screening tool for SDB in settings where PSG is poorly tolerated or unavailable. The strongest agreement was seen for AI and AHI, both within and across scorers, with acceptable limits of agreement relative to PSG. However, reduced agreement for hypopnoeas and obstructive events highlights the need for ongoing scorer training and refinement of visual interpretation strategies. Notably, hypopnoea scoring is known to exhibit lower inter-scorer concordance even within standard PSG, suggesting that the variability observed with Sonomat is consistent with broader challenges in

respiratory event classification. This study reinforces the importance of structured scorer education when implementing new technologies in paediatric sleep diagnostics and provides a foundation for future work using the Sonomat in broader clinical and home-based settings.

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Learning from parents about the prevalence of SDB in children with neurodevelopmental disorders and their preferences for diagnostic testing

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Introduction: Existing literature demonstrates a high prevalence of sleep disordered breathing (SDB) in children with specific neurodevelopmental disorders (ND). However, no large studies have evaluated prevalence of SDB in a broad population of children with ND (CWND). Additionally, whilst it's recognised that undertaking gold standard monitoring with polysomnography (PSG) is more difficult in children with ND, few studies have explored perspectives of primary caregivers. Here, we describe parent reports of SDB symptoms in a large multicentre sample of CWND and detail their experiences and views regarding diagnostic testing.

Materials and methods: Data were combined from two Australian multicentre studies undertaken to evaluate sleep in a diverse sample of CWND. Primary caregivers of children 0-18 years with a ND condition (ICD-11) completed a survey that included the Paediatric Sleep Questionnaire (PSQ) to determine parent reported prevalence of SDB. Participants were recruited from: (i) a tertiary sleep clinic and (ii) a community sample recruited through community organisations that support CWND. A cut-off value of 0.33 on the PSQ was regarded as indicative of SDB risk. In addition, primary caregivers of a second cohort of CWND (0-18 years) who were undergoing PSG for evaluation of SDB at the same centres completed a customised survey regarding feedback on their experiences of PSG and hypothetical preference between in-lab PSG or an in-home mat-based sleep test.

Results: PSQ data was available from 226 participants (56% male, 54% 5-12yrs). 37% had autism spectrum disorder (ASD) and/or attention deficit hyperactivity disorder (ADHD), 35% a genetic syndrome, 16% a neurological disorder and 12% another ND condition. The mean PSQ total score was 0.46 and 75% had a PSQ score >0.33. There was no significant difference in mean total PSQ score between different NDD categories and no difference in the proportion of children with a PSQ >0.33 when comparing the sleep clinic and community sub-groups.

143 primary caregivers of CWND undergoing PSG completed a customised survey regarding PSG experiences. "Worry levels" for undergoing PSG were reported as "moderate" for children and lower for parents, with the highest worry levels in children with ASD and neuromuscular diagnoses. The option for at home testing with a mat-based option was preferable to parents, with 57% indicating a preference for this if available compared to 7% preferring an in-laboratory PSG.

Conclusions: Discussion: Combined data from a large sample of Australian CWND demonstrates (1) a high prevalence of parent reported SDB symptoms regardless of underlying ND condition, (2) a high proportion of CWND in a community sample reporting a SDB symptom burden comparable to those in a tertiary sleep clinic, and (3) parent preference for home based diagnostic sleep testing options. This preference may reflect the increased worry experienced by CWND during in-laboratory PSG and parental concern that sleep measured in this setting is not representative of their child's typical sleep. Conclusion: This study confirms that SDB is an important comorbidity that requires proactive screening in CWND and provides rationale for exploring alternative approaches to diagnostic testing that better meet the needs of CWND and their families.

Maternal Prenatal Depression and Child Sleep: A Systematic Review

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Introduction: Previous research suggests a potential association between maternal prenatal depression and child sleep outcomes; however, findings have been inconsistent. The present review aims to systematically synthesize and critically evaluate the existing literature on the associations between maternal prenatal depression and sleep in children aged 0-17 years.

Materials and methods: Following PRISMA guidelines, a systematic literature search was conducted in PsycINFO, Medline, and SCOPUS electronic databases to identify studies examining associations between maternal prenatal depressive symptoms, or diagnoses of depression, and child sleep dimensions. In total, 1088 titles and abstracts and 68 full-text articles were screened, yielding 27 studies that met inclusion criteria.

Results: Most studies (74.0%) reported significant associations between maternal prenatal depression and at least one child sleep dimension. The most frequently assessed sleep dimension was sleep problems, with 76.9% of studies reporting an association between greater maternal prenatal depression and greater child sleep problems. Although studies were scarce, some studies found associations between greater maternal depression and shorter total sleep duration, shorter daytime sleep duration, and a higher number of nocturnal awakenings. However, no consistent associations were found between maternal prenatal depression and child nocturnal sleep duration, wake after sleep onset, or sleep efficiency.

Conclusions: Findings suggest that maternal prenatal depression may be linked to certain adverse child sleep outcomes, particularly greater sleep problems. However, most findings are based on maternal reports of child sleep, which may be influenced by maternal mood. As such, reported sleep problems may partly reflect maternal perceptions rather than objective difficulties in the child. Future research should aim to replicate these findings using validated parent-report questionnaires, incorporate objective sleep assessments, and examine potential mediating and moderating factors underlying these associations.

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Obstructive sleep apnea and sleep disorders in children with attention deficit hyperactivity disorder

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Introduction: Sleep disorders are common yet often underdiagnosed in children with attention-deficit/hyperactivity disorder (ADHD). These disturbances can exacerbate ADHD symptoms and negatively affect cognitive, emotional, and behavioral functioning. This study aimed to describe the prevalence of obstructive sleep apnea (OSA) and other sleep disorders in children with ADHD using standardized diagnostic criteria, and to identify associated clinical and behavioral factors

Materials and methods: A cross-sectional study was conducted on 629 children aged 6 to 12 years (mean age: 7.8 ± 1.5 years) who were diagnosed with ADHD. Sleep disturbances were assessed using the Children's Sleep Habits Questionnaire (CSHQ), the Pediatric Sleep Questionnaire (PSQ), and Respiratory polygraphy. Sleep disorders were classified based on the International Classification of Sleep Disorders, Third Edition (ICSD-3). Multivariate logistic regression was used to identify associated risk factors.

Results: Sleep disorders were diagnosed in 70.0% of children with ADHD. The most common disorders were insomnia (40.2%), OSA (23.4%), parasomnias (27.8%), restless legs syndrome (10.5%), and delayed sleep-wake phase disorder (4.8%). The inattentive ADHD subtype, psychiatric comorbidities, tonsil and adenoid hypertrophy, iron-deficiency anemia, and sleep-related behaviors in children with ADHD were significantly associated with sleep disturbances.

Conclusions: Sleep disorders are highly prevalent and diverse in children with ADHD. Early identification and targeted management of sleep disturbances, particularly OSA and insomnia, are essential to improving sleep quality and optimizing ADHD outcomes. Routine sleep screening should be integrated into clinical ADHD evaluations.

"PEDOSA-7: Development, Validation, and Clinical Utility of a Simplified Screening Tool for Pediatric Obstructive Sleep Apnea- A Pilot Study

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Introduction: Pediatric obstructive sleep apnea (OSA) is a prevalent yet underdiagnosed disorder linked to significant morbidity. Current screening tools, such as the Pediatric Sleep Questionnaire (PSQ), face limitations in clinical utility due to complexity and time constraints. This pilot study aimed to develop and validate the PEDOSA-7, a simplified 7-item screening tool with binary (Yes/No) responses and weighted scoring, designed to enhance accessibility and efficiency in OSA risk stratification.

Materials and methods: A cross-sectional observational study enrolled 83 children (aged 3–16 years) with sleep-related complaints. Participants underwent polysomnography (PSG; AHI ≥ 5 for OSA diagnosis) and completed the PEDOSA-7 and PSQ. Demographics, BMI, and symptom profiles were analyzed. Validation metrics included internal consistency (Cronbach's alpha), sensitivity, specificity, negative predictive value (NPV), and AUC-ROC. Comparative analysis with PSQ assessed practicality and diagnostic accuracy.

Results: Of the cohort, 31.3% (26/83) had OSA (AHI ≥ 5). The OSA group exhibited higher mean BMI (22.3 vs. 18.0; $p < 0.05$) and a strong BMI-AHI correlation ($r = 0.73$). PEDOSA-7 demonstrated sensitivity of 84.6%, specificity of 54.4%, NPV of 88.6%, and AUC of 0.728 at a cutoff score ≥ 3 . Key items (snoring, breathing pauses) showed high sensitivity (92%). Internal consistency was suboptimal (Cronbach's alpha = 0.49), reflecting item redundancy. Compared to PSQ, PEDOSA-7 achieved comparable sensitivity (PSQ: 61.5–90%) with superior practicality due to its binary scoring. Lowering the AHI threshold to >1 improved specificity (83.3%) but reduced sensitivity (37.1%), highlighting trade-offs in screening accuracy.

The PEDOSA-7 offers a clinician-friendly tool for rapid OSA screening, particularly in resource-limited settings. Its high NPV supports efficient triage, reducing unnecessary referrals. However, moderate specificity necessitates integration with clinical judgment. Limitations include a small, gender-imbalanced sample (non-OSA group: all male) and lack of cultural/age diversity. Future studies should validate PEDOSA-7 in larger, multicenter cohorts and refine psychometric properties.

Conclusions: In conclusion, the PEDOSA-7 represents a pragmatic advancement in pediatric OSA screening, balancing diagnostic accuracy with usability. While not replacing PSG, it serves as a valuable first-line tool to improve early detection and resource allocation. Further validation across diverse populations and settings is warranted to optimize its clinical impact.

Keywords: Pediatric obstructive sleep apnea, screening tool, PEDOSA-7, validation, polysomnography, sensitivity.

Acknowledgments: NA

Perceived Parental Sleep Quality Improvement Following a Brief Child Sleep Intervention: Preliminary Evidence

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Introduction: Sleep difficulties are common in preschool-aged children and often disrupt parental sleep, contributing to heightened stress, depressive symptoms, and family dysfunction. Interventions targeting child sleep have shown promise in improving parental outcomes, but the mechanisms driving these changes remain unclear. This preliminary study evaluated the effects of a brief, group-based child sleep intervention on parental sleep quality over time and examined whether changes in child sleep quality and parental mental health following the intervention predict these improvements.

Materials and methods: Seventy-eight families with 3- to 5-year-old children participated in the project. Parents were offered a two-hour group session focusing on sleep hygiene, bedtime routines, and nightmares, while in parallel, children engaged in sleep-related educational activities. Two weeks later, parents participated in a follow-up group session where they shared their successes and obstacles and received additional support from the clinician. Data were collected at baseline (T1), two weeks post-intervention (T2), and about eight weeks post-intervention (T3). The Children's Sleep Habits Questionnaire (CSHQ) and the Pittsburgh Sleep Quality Index (PSQI) were administered at T1, T2 and T3, while the Beck Depression Inventory (BDI-II) and the Parenting Stress Index (PSI) were administered at T1 and T3. Repeated measures ANOVAs assessed changes in PSQI and CSHQ scores, and paired t-tests evaluated changes in BDI-II and PSI scores over time. Hierarchical linear regression was used to determine whether changes in child sleep quality and parental mental health predicted parental sleep quality at T3, controlling for parental income.

Results: Repeated measures ANOVAs revealed significant improvements in parental sleep quality (PSQI total scores) between T1 and T3 [$F(2,114) = 8.72; p < .001$], while children's sleep quality (CSHQ total scores) improved from T1 to T2 and remained enhanced at T3. Paired-sample t-tests showed reductions in depressive symptoms [BDI-II total scores: $t(67) = 4.47; p < .001$] and parenting stress [PSI total scores: $t(67) = 6.13; p < .001$] at T3. The hierarchical regression showed that the first model (parental income and baseline predictors) explained 25.4% of the variance in parental sleep quality [$F(5, 72) = 4.90, p < .001$]. Adding changes in CSHQ, BDI-II, and PSI scores significantly improved the model fit [$\Delta R^2 = .08, p = .04$], with the final model explaining 33.8% of the variance [$F(8, 69) = 4.40, p < .001$]. Changes in parental depressive symptoms (BDI-II scores; $\beta = .27, p = .047$) and baseline parental sleep quality (PSQI scores; $\beta = .37, p = .001$) were significant predictors of parental sleep quality at T3, while changes in children's sleep quality (CSHQ scores; $p = .33$) and parenting stress (PSI scores; $p = .91$) were not.

Conclusions: These findings suggest that a brief child sleep intervention can improve perceived parental sleep outcomes, driven by reductions in depressive symptoms. However, the lack of association with changes in children's sleep quality and parenting stress indicates that unexplored factors may influence these results. Future studies should aim to better identify and understand these factors to optimize intervention design and improve family outcomes.

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Perioperative Sleep Quality in Pediatric Cardiac Surgery: A Scoping Review

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Introduction: To conduct a scoping review of research on perioperative sleep quality in children undergoing cardiac surgery. The aim is to provide guidance for the early diagnosis, treatment, and intervention of perioperative sleep disturbances in this population in China.

Materials and methods: Following the methodology of a scoping review, literature related to perioperative sleep quality in children undergoing cardiac surgery was systematically searched in the following databases: PubMed, MEDLINE, Web of Science, Embase, CINAHL, PsycINFO, Cochrane Library, Ovid, Scopus, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, Sinomed, CNKI, Wanfang Data, and VIP Information Services Platform. The search covered all records from database inception to August 10, 2024. Two researchers independently screened the literature and extracted key characteristics, including title, authors, publication year, data collection period, country of sample collection, study objective, sample size, study population, age group, study type, and measurement tools.

Results: A total of 1,306 articles were retrieved, and 18 studies were ultimately included, all of which were published in English. Among them, 6 were retrospective studies, 5 were prospective studies, 4 were observational studies, 2 were interventional studies, and 2 were cross-sectional studies. The analysis indicated that sleep disorders are relatively common among children undergoing cardiac surgery and are associated with significant adverse outcomes. Four objective assessment tools or methods were used: electroencephalogram (EEG), continuous electroencephalogram (cEEG), amplitude-integrated electroencephalography (aEEG), and actigraphy (Micro Motion Logger, Ambulatory Monitoring, Inc.). Seven subjective assessment tools or methods were identified: the Brief Infant Sleep Questionnaire (BISQ), Children's Sleep Habits Questionnaire (CSHQ), Pittsburgh Sleep Quality Index (PSQI), Échelle de dépistage des troubles de sommeil pédiatriques (HIBOU; Pediatric Sleep Disorders Screening Scale), online questionnaire items related to sleep, child self-reported sleep problems, and parent-reported sleep problems. The influencing factors of perioperative sleep quality in children undergoing cardiac surgery were analyzed across four time points: preoperative period, admission to the CICU postoperatively, transfer to the general ward, and post-discharge follow-up. Intervention measures included the SNOO® Smart Sleeper (responsive bassinet) and eye masks. However, current research on prevention and intervention remains limited.

Conclusions: Children undergoing cardiac surgery have a high prevalence of sleep disorders, which are associated with significant adverse outcomes. Existing research reflects limited awareness and insufficient understanding of sleep disturbances in this population. The range of available assessment tools is narrow and lacks specificity. Influencing factors are complex and vary across different perioperative stages. Research on prevention and intervention remains limited.

Persistent Sleep Disturbances in Pediatric COVID-19 Survivors: A Longitudinal Follow-Up and Association with Neuropsychiatric Symptoms

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Introduction: Sleep disturbances are common in pediatric COVID-19 survivors, especially those with **neuropsychiatric (NP)** symptoms. This study investigated the persistence and nature of sleep disorders in children post-COVID-19 using validated sleep questionnaires.

Materials and methods: The observational study enrolled pediatric patients (6-18 years) with confirmed COVID-19 within the preceding six months and included an age- and sex-matched healthy control group (C, n=62). Neuropsychiatric (NP) symptoms were assessed using the Weighted Neuropsychiatric Severity Scale (WNPSS). Patients scoring ≥ 3 were classified as Group Y (significant NP symptoms), while those scoring < 3 formed Group N (mild/no NP symptoms). Questionnaires (Epworth Sleepiness Scale for Children and Adolescents - ESS-CHAD; Sleep Disturbance Scale for Children - SDSC) and actigraphy evaluated sleep at **two time points**: initially, 6-12 months post-infection (Time 0), and at follow-up, 1.5-2.5 years later (Time 1). Statistical comparisons between groups (C, N0, N1, Y0, Y1) were performed using appropriate tests, including Kruskal-Wallis and ANOVA, with post-hoc analyses. The study involved 31 COVID-19 survivors (N0: n=25, N1: n=25; Y0: n=6, Y1: n=6) and 62 controls (C).

Results: The mean ages were 9.61 ± 1.86 years in controls (C), 9.90 ± 2.63 years in the N0 group, 11.08 ± 2.58 years in the N1 group, 10.05 ± 2.53 years in the Y0 group, and 11.22 ± 2.47 years in the Y1 group, with no significant differences between groups ($p=0.1188$). A Kruskal-Wallis test revealed statistically significant differences in both the Sleep Disturbance Scale for Children (SDSC) total scores ($p=0.0437$) and Disorders of Excessive Somnolence (DOES) subscale ($p=0.0163$) among the groups. For DOES, patients with NP symptoms exhibited markedly elevated median scores at both time points (Y0 and Y1: 10.50) compared to controls and non-NP groups (C, N0, and N1: all 7.00). Similarly, total SDSC scores were higher in NP groups (Y0: 50.00, Y1: 47.50) compared to controls (C: 41.50) and non-NP groups (N0: 43.00, N1: 41.00).

However, no significant differences were observed between groups in other sleep domains: disorders of initiating and maintaining sleep (DIMS, $p=0.0888$), disorders of arousal (DA, $p=0.0980$), sleep breathing disorders (SBD, $p=0.6871$), sleep-wake transition disorders (SWTD, $p=0.5113$), or sleep hyperhidrosis (SHY, $p=0.2705$). Additionally, the Epworth Sleepiness Scale showed no significant group differences ($p=0.3426$).

Conclusions: Pediatric COVID-19 patients with neuropsychiatric symptoms showed significantly higher sleep disturbance **compared to controls and those without neuropsychiatric symptoms**, specifically in excessive somnolence (DOES) but not in other sleep domains.

Predictors of Napping Frequency Across Early Childhood: Investigating the Effects of Social Factors on Developmental Trajectories

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Introduction: Napping frequency declines dramatically over the first few years of life, and the rate of this decline is thought to reflect an interaction between social and neurophysiological development. However, whether social or contextual factors also effect napping frequency and cessation timing is not well understood. This is problematic, as children's napping behaviours have been associated with a variety of health and developmental outcomes. Previous studies of napping development and its environmental correlates have relied heavily on cross-sectional data and aggregate measures (i.e., asking parents to report 'typical' napping behaviours). These methodological limitations mean that it has been difficult to analyse how sensitive napping frequency is to environmental influence, and have marred our ability to accurately capture variability in developmental trajectories of napping frequency. One social factor in particular, the effect of attending childcare, may have a particularly marked effect on napping frequency due to many childcare centres enforcing a mandatory single nap schedule on children irrespective of their developmental stage. However, the effect of this and other social factors on napping patterns remain largely unknown.

Materials and methods: Data was collected as part of the Sleep Transitions and Regularity Study (STARS), a 4-year longitudinal study tracking the sleep behaviours of ~200 Australian children between the ages of 1 to 5 years. Once per month parents were asked to complete a 1-week recording of their child's napping patterns, childcare attendance, and life events (e.g. illness, family stress, change in living situation, etc.). We performed a hybrid multilevel logistic regression model, controlling for within subjects repeated measures to investigate whether childcare attendance significantly predicted napping frequency over and above the developmental effect associated with age.

Results: Results of a hybrid multilevel logistic regression model indicate that the within-subject effect of attending childcare is associated with a significant reduction in napping frequency until about the age of 3.5 years, at which point the effect diminishes. In other words, very young children who attend childcare nap significantly less than they would otherwise. The effects of other social factors, such as moving home or significant family stress are still to be determined.

Conclusions: This study demonstrates with unprecedented specificity that social factors, alongside ageing, can significantly influence developmental napping frequency behaviours. Our findings have implications for understanding of the relative influence of social and developmental factors on napping frequency, as well as implications for childcare policy and practice around sleep and naps.

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Prescribing with sleep in mind: Polypharmaceutical considerations in children with neurodevelopmental disorders

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Introduction: Sleep disturbances affect up to 80% of children with neurodevelopmental disorders (ND), reflecting complex interactions between physiological, behavioural, pharmacological, and environmental factors. This study explores medication use in a large cohort of Australian children with

ND, aiming to characterise pharmaceutical burden and its potential influence on sleep quality. Further, this study aimed to explore the interactions of sleep and non-sleep medications in the context of known sleep difficulties within this population.

Materials and methods: This cross-sectional survey involved carers of children aged 2–18 with clinician-diagnosed NDs across three major Australian hospitals and community settings. Data were collected via a study-specific online questionnaire capturing demographics, diagnoses, sleep-related parameters, and medications. Sleep problems were characterised using the 58-item Modified Simonds and Parraga Questionnaire (MSPSQ), where a raw score greater than 56 or composite score greater than 4 is indicative of a clinically significant sleep problem. Medications were standardised, categorised, and analysed using descriptive statistics and appropriate statistical testing.

Results: Data from a total of 300 eligible participants were available for analysis (59% male, 50% 5–12 years old). The majority of children had clinically significant sleep problems, as characterized by the MSPSQ (raw score 69.2 ± 15.8 , composite score 5 ± 2.9). Melatonin was the most frequently used sleep medication, with 59% of children having used it at some point over their lifetime, two thirds having found melatonin useful, and more than one in four children currently taking melatonin. α -2 agonists, benzodiazepines, and sedating antihistamines were also being prescribed for sleep in this cohort. A wide range of non-sleep-related medications were reported, with 29% of children taking medications with known negative impacts on sleep. Most children were on at least one prescription medication (69.3%), with polypharmacy (2 or more regular medications) being identified in 42% of children (median 1, range 0–9). When also considering over-the counter medications, 50% of children met criteria for polypharmacy (median 2, range 0–13). Non-sleep medications which influenced sleep were common, with stimulants being most prevalent.

Conclusions: Sleep problems in children with ND are common and likely complicated by their significant pharmacotherapeutic burden. Half of children in this study met criteria for polypharmacy, with one in three children being prescribed medications known to have negative impacts on sleep. Given the prevalence and complexity of sleep problems in children with ND, emphasis should be placed on the review and rationalisation of medications when these patients present with sleep problems. Additionally, the development of targeted guidelines to support clinicians in managing sleep disturbances in this population needs to be prioritised.

Prevalence of high-risk obstructive sleep apnea in overweight and obese children and its impact on quality of life

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Introduction: Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by intermittent partial or complete upper airway obstruction, leading to disrupted sleep and oxygen desaturation. Obesity significantly increases the risk of OSA. However, few studies in Thailand have examined the prevalence of high-risk OSA in obese children and its impact on quality of life.

Materials and methods: We conducted a cross-sectional study to determine the prevalence of high-risk OSA in overweight and obese children and to evaluate its impact on their quality of life. Children aged 2–12 years diagnosed as overweight or obese based on WHO BMI-for-age z-scores were recruited. The risk for OSA was assessed using the Thai version of the Pediatric Obstructive Sleep Apnea Screening Tool (POSA), and quality of life was evaluated using the OSA-18 questionnaire. Physical examinations, including tonsillar assessment, were conducted.

Results: Sixty-eight overweight and obese children were recruited. The prevalence of high-risk OSA, as defined by POSA, was 41.2%. Tonsillar hypertrophy was significantly associated with high-risk OSA (adjusted OR: 10.92; 95% CI: 3.04–39.15; $P < 0.001$). Additionally, 20.8% of children experienced a moderate to severe impact on their quality of life. High-risk OSA (adjusted OR: 14.59; 95% CI: 1.94–109.86; $P = 0.009$) and attention-deficit hyperactivity disorder (adjusted OR: 11.84; 95% CI: 1.52–92.14; $P = 0.02$) were significantly associated with reduced quality of life.

Conclusions: High-risk OSA is common among overweight and obese children and is significantly associated with impaired quality of life. These findings highlight the need to screen for OSA in this at-risk population and to address related quality of life issues in clinical practice.

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Prevalence of Sleep Disorder Diagnosis in the Pediatric Population at a Children's Hospital in Northeastern México

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Introduction: Sleep disorders in the pediatría population have been the subject of numerous studies due to their impact on children's physical, cognitive, and emotional development. Despite their high prevalence, these disorders often go unnoticed and are underdiagnosed, which can lead to long-term consequences on children's quality of life. There is a need for adequate knowledge and practical, simple, and easy-to-use tools for use in primary care. General screening questionnaires are available and can be useful during pediatric consultations in primary care settings.

Materials and methods: A prospective observational descriptive study. Surveys were conducted in the emergency department over 30-day period. Age-specific screening tools were used: The BISQ questionnaire was applied for infants, focusing on sleep routines and problems. The BEARS questionnaire and the Sleep Disturbance Scale for Children (SDSC) by Bruni were used for screening and identifying sleep disorders in newly admitted patients who agreed to participate.

Results: A total of 60 surveys were completed: 40 males (66%) and 20 females (33%). The age distribution was as follows: 23 infants (38.3%), 12 preschoolers (20%), 10 school age children (16.6%), and 8 adolescents (13.3%). Among them, 7 patients had epilepsy, 4 had neurodevelopment delay, 4 had pneumonia, and 4 had asthma and allergic rhinitis. Based on survey results: 23 patients (38.3%) had no sleep disorder, 11 (17.8%) had wakefulness and sleep disorders (8 were assessed with BISQ, 6 had mild insomnia, and 2 had moderate to severe insomnia), 10 (16.2%) had disorders related to sleep onset and maintenance, 6 (9.7%) had sleep-related breathing disorders, of whom only 33% had respiratory conditions like asthma or allergic rhinitis. 5 (8.1%) had excessive daytime sleepiness, 3 (4.8%) had parasomnias, 2 (3.2%) met criteria for restless leg syndrome according to the SDSC. Among the surveyed population: 65% of infants had no sleep disorders, 66% of preschoolers had a sleep disorder, 60% of adolescents had a sleep disorder.

Conclusions: The prevalence of sleep disorders in our study was high 61%. This study aims to provide a general overview and emphasize the importance of these often-overlooked disorders, which are frequently underreported by families and overlooked by first-contact physicians. Sleep disorders in our setting are underdiagnosed. Our findings demonstrate that high-cost or complex diagnostic tests are not required to identify these disorders. It is concerning that more than half of the surveyed children would benefit from timely referral to a sleep specialist. In conclusion, pediatricians should raise awareness and routinely include sleep disorders screening as part of the clinical interview.

Prospective Associations Between Adolescent Sleep Characteristics and Depression, Anxiety, and Their Co-Occurrence in Early Adulthood: A 9-Year Cohort Study

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Introduction: Depression and anxiety frequently co-occur during the transition to adulthood, leading to heightened symptom severity and severe adverse health outcomes. Although sleep disturbances are common in adolescence, their prospective relationships with comorbid depression and anxiety remain unclear. This study aimed to examine the longitudinal associations between adolescent sleep patterns

and sleep quality at age 15, predicting depressive and anxiety symptoms in early adulthood, with a specific focus on their comorbidity.

Materials and methods: We analyzed data from a subsample of the Avon Longitudinal Study of Parents and Children (ALSPAC), a UK population-based birth cohort. Sleep patterns and sleep quality were assessed at age 15 during a clinical visit. Depressive symptoms were measured at ages 17, 21, and 24, and anxiety symptoms at age 21. We estimated associations using binary logistic regression for depression and anxiety separately, and multinomial logistic regression to distinguish depression-only, anxiety-only, and comorbid cases.

Results: Depressive symptoms were prevalent at ages 17 (34.7%), 21 (28.0%), and 24 (36.3%), while 19.2% reported anxiety symptoms at age 21. Females consistently reported higher symptoms than males (p -value < 0.05). At age 21, 14% had depression only, 5% reported anxiety only, and 14% experienced comorbid symptoms. After covariate adjustment, each sleep disturbance at age 15 was associated with increased odds of depression at all follow-up ages (p < 0.05). In multinomial models, poor sleep quality (aOR = 2.79), perception of insufficient sleep (aOR = 1.84), daytime sleepiness (aOR = 2.15), frequent night awakenings (aOR = 2.07), short or long sleep duration (aOR = 1.63), and prolonged sleep onset latency (aOR = 1.80) each conferred higher risk of comorbid depression and anxiety (all p -value < 0.001) than of either disorder alone.

Conclusions: Adolescent sleep disturbances were linked to increased depressive and anxiety symptoms up to nine years later, with the strongest associations observed for comorbid presentations. Early identification and intervention for sleep problems in mid-adolescence may be critical for preventing later psychological health.

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Pulmonary Rehabilitation in Pediatric Scoliosis: A Prospective Pilot of a Risk-Stratified Perioperative Respiratory Pathway involving polysomnography and transcutaneous carbon dioxide measurements

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Introduction: Children with scoliosis are predisposed to perioperative respiratory complications due to restrictive lung mechanics, impaired muscle strength, and ventilation-perfusion mismatch. These risks are further amplified in neuromuscular and syndromic subtypes. Preoperative pulmonary compromise often remains subclinical but becomes evident under the stress of anesthesia and postoperative recovery. This study aimed to evaluate a structured, risk-based pathway that integrates pulmonary assessment and individualized respiratory support to optimize surgical outcomes in children undergoing scoliosis correction.

Materials and methods: This was a prospective observational study involving 19 children referred to pediatric pulmonology 2–4 weeks prior to scoliosis surgery. Each patient underwent a comprehensive preoperative evaluation, including clinical assessment, spirometry (pre- and post-bronchodilator), extended pulmonary function testing (PFTs) in children over 8 years, polysomnography (PSG), transcutaneous CO₂ (TcCO₂) monitoring, and arterial blood gas analysis when indicated.

Patients were stratified into high-risk (presence of neuromuscular disease, Cobb angle >90°, FVC <60%, or sleep hypoventilation) or low-risk groups. High-risk patients were initiated on non-invasive ventilation (NIV) for at least 2–4 weeks preoperatively. Mechanical insufflation-exsufflation (MI-E) was added based on clinical judgment. Postoperatively, all patients received NIV support for at least one month. Respiratory outcomes were monitored through chest radiographs and clinical evaluation.

Results: Nineteen patients (mean age 10.7 years; 10 females) were enrolled, of whom 15 underwent surgery. The etiologies of scoliosis included syndromic (40%), neuromuscular (26%), congenital (20%), and idiopathic (13%). Six children were classified as high-risk (five with neuromuscular disease, one with FVC <40%). These patients were initiated on BIPAP with a median preoperative duration of six months. In contrast, low-risk patients used BIPAP for a median of one week preoperatively.

Five neuromuscular patients underwent PSG, with 75% demonstrating moderate-to-severe sleep-disordered breathing and hypoventilation. Postoperatively, NIV was continued in all patients, with long-term continuation in neuromuscular cases. MI-E was used in seven patients, including both with FVC <40%. Two complications were reported—one dural tear with cerebrospinal fluid pleural leak and one case of hypotension. The average hospital stay was 5.4 days, with a mean PICU stay of 2 days.

Statistical analysis showed a significant difference in preoperative FVC values between high- and low-risk groups ($p = 0.031$). However, no statistically significant differences were observed in hospital stay ($p = 0.529$) or MI-E use ($p = 1.0$), likely due to small sample size and variability in disease severity.

Conclusions: This risk-stratified perioperative respiratory pathway effectively identified high-risk children and facilitated the implementation of tailored respiratory interventions. The integration of preoperative NIV and postoperative continuation, along with MI-E where indicated, was feasible and likely contributed to favorable clinical outcomes. While statistical significance in outcome differences was limited, the pathway demonstrated clinical value and safety. Future studies with larger cohorts and control groups are warranted to validate and refine this model of personalized perioperative respiratory care.

Robin Sequence: from dilemmas to developing an adaptable standardized stepwise approach to treat upper airway obstruction

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Introduction: Pierre Robin sequence, more recently known as the Robin sequence (RS), is characterized by the clinical triad of micrognathia, glossoptosis and upper airway obstruction (UAO). The lack of a standardized approach to treat upper airway obstruction (UAO) in infants with Robin Sequence (RS) leads to delay in resolution of OSA, poor sleep, hypoxia or hypercarbia, poor feeding, suboptimal growth, and neurodevelopmental impairment, prolonged hospital stays and increases the burden on families and the healthcare service.

Materials and methods: We aimed to review the literature to identify key issues causing variation in clinical practice, assess the knowledge gap, and develop a standardized pathway for managing upper airway obstruction in infants with Robin Sequence. The tripartite framework of Evidence-Based Practice was used. This framework included a systematic review of the literature, extensive consultation with a multidisciplinary team of experts, and feedback from the patients. The consensus was reached over 12 months period by the working group consisting of the hospital's neonatologists, respiratory and sleep specialists, ENT specialists, plastic and craniomaxillofacial surgeons, dentists, geneticists, speech pathologists and patient feedback.

Results: Of the 2672 articles from the initial search, 66 were studied in detail. We identified five pivotal issues prevalent while managing upper airway obstruction in the Robin Sequence which are: 1) how to gain consensus; 2) how to assess the severity of UAO/OSA; 3) which treatment to choose; 4) how to assess treatment effectiveness; and 5) when to follow up or stop treatment. These issues were addressed systematically to develop an adaptable stepwise standardized approach (ASSA) for the assessment and management of UAO/OSA in infants with RS. ASSA has two phases: phase one is the conservative arm and phase two is the escalation arm to more invasive treatment. The main pillars of the pathway are a) early objective assessment of the severity of upper airway obstruction using polysomnography, b) graded treatment approach based on centre-specific preferences, c) early and regular multidisciplinary team discussions, and d) clearly defined criteria for treatment escalation or cessation, discharge, and follow-up.

Conclusions: This unique pathway is based on evidence, consensus of experts and patients feedback. Early objective assessment of UAO/OSA using daytime polysomnography and a graded approach to treatment supports improved outcomes. The pathway provides a stepwise guide to the clinician for the management of upper airway obstruction in infants with Robin Sequence, adaptability for centre-specific treatment preferences and a framework for future comparisons of different treatments.

Acknowledgments: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors for the development of the pathway.

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Screening for Paediatric Obstructive Sleep Apnoea (OSA) on a Specialist Outpatient Waitlist: Insights from the First Year of a Sleep Nurse-led Triage Clinic (SNTC)

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Introduction: Development of a Sleep Nurse-led triage clinical pathway for tertiary paediatric sleep referrals aimed to screen for Obstructive sleep apnoea (OSA) and reduce wait-times for tertiary sleep outpatient appointments. OSA is a common condition in children that, if left untreated, can lead to developmental and cognitive challenges. While polysomnography (PSG) remains the gold standard for diagnosis, overnight home oximetry has emerged as a more efficient and affordable preliminary test. Overnight oximetry utilisation for paediatric patients on a sleep clinic waitlist expedites screening for OSA as referral numbers exceed clinical capacity, often leading to long wait-times for specialist assessment.

Materials and methods: Sleep Nurse-led Triage Clinic (SNTC)

Paediatric patients aged 2-18 years, referred for suspected OSA at the Queensland Children's Hospital, were triaged from the Category 2 sleep clinic waitlist to the Sleep Nurse-led Triage Clinic from May 2024 - May 2025 (Category 2 recommended OPD appointment <90 days). A clinical workflow was developed and a nurse phone or in-person appointment was conducted. Demographics, medical/surgical history, neurodevelopmental diagnoses, Paediatric Sleep Questionnaire (PSQ) and home oximetry data was collected. Home oximetry data was analysed by McGill oximetry score (MOS). PSQ>0.75 or McGill 2-4 oximetry score patients were expedited to early sleep physician review and early PSG.

Results:

- 256 SNTC patients were seen from May 2024-May 2025.
- SNTC attendance rate 79%.
- SNTC Appointment summary: Failed to Attend appointment (FTA) (n=55), Sleep behaviour information/support i.e. night terrors, night-time waking (n=5), Refused oximetry (n=3), Follow-up SNTC phone call arranged 3 months post ENT surgery (n=15), Booked Sleep specialist appointment (n=25) i.e. SNTC CN identified clinical concern or complex patient/complex medications, nil evidence of OSA by reported history and PSQ or parental concern. Regional QLD location (n=2), NSW location (n=1) (unable to courier oximeter >200km or across QLD/NSW boarder).
- 147 home oximetry tests were conducted and 135 patients had sufficient data for sleep specialist scoring of MOS1-4. Completed PSQ score was matched for all 135 patient oximetry's.
- **MOS1 (n=122) (n=19 flagged as high risk using automated analysis methods)**
- PSQ 0.14-0.95, Diagnostic PSG (n=7), CPAP Titration (n=1), AHI 0.6-20.1/OAHI 0.0-16.6, Age 2-16yrs
- 9.6% of children were MOS2-4, 23% of children were flagged as high risk using automated analysis methods.
- **MOS2-4 (n=13) (n=12 of 13 flagged as high risk using automated analysis methods)**
- Diagnostic PSG (n=9), Referred ENT (n=2), CPAP Titration (n=3)

MOS2 (n=7); PSQ 0.32-0.90, PSG AHI 6.4-24/OAHI 2.6-22.8, Age 4-14 years

MOS3 (n=4); PSQ 0.71-0.76, PSG AHI 0.6-6.6/OAHI 0-4.4, Age 5-11 years

MOS4 (n=2); PSQ 0.45-0.86, PSG AHI 26.4-78/OAHI 26.2-78, Age 3-15 years

Conclusions: The SNTC model improved access and prioritisation for children with suspected Obstructive sleep apnoea (OSA).

Paediatric patients who were asymptomatic or no longer required specialist sleep appointments were discharged, improving clinic capacity. Category 2 appointments exceeding 90 days were reduced. Clinician-evaluated McGill scored oximetry (MOS1-4) and high-risk oximetry by automated analysis methods, were used to identify children for priority review by sleep specialist.

Children with suspected OSA received expedited access to specialist care, reducing delays in management and treatment.

Acknowledgments: Queensland Children's Hospital Sleep Medicine Department

Sleep and emotion regulation in elementary school children

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Introduction: Various aspects of sleep, like sleep disorders, especially insomnia symptoms, nightmares or restricted sleep, are closely associated with daytime impairments like behavior problems. In children and adolescents sleep problems and sleep deprivation are also associated with a decrease in functional emotion-regulating behavior and impaired emotion generation, whereas prolonged sleep enhances better mood and affect. In this study, we investigated various facets of sleep and emotion regulation in elementary school children. We hypothesized that sleep problems, like insomnia symptoms or impaired sleep, are associated with emotional problems and emotion-regulation problems.

Materials and methods: Participants were 62 elementary school children (6-11 years) and their parents. The mean age of the children was 8.71 (± 1.4), with 50.8% being girls. Parents filled in the Children's Sleep Habit Questionnaire (CSHQ-DE) and the Strengths and Difficulties Questionnaire (SDQ-DE), whereas the children completed the Sleep Self Report (SSR-DE). CSHQ-DE and SSR-DE focused on sleep anxiety, bedtime resistance, night-waking, sleep duration, sleep-onset delay, daytime sleepiness, sleep disordered breathing, and parasomnias, whereas the SDQ-DE contained questions regarding conduct problems, hyperactivity inattention, emotional symptoms, peer problems, and pro-social behavior. The emotion-regulation profile was calculated based on recommendations published.

Results: We found that children exceeding the SSR-DE cut-off had significantly more dysregulation symptoms and overall emotional problems. Comparisons of children with healthy scores and children with clinically relevant scores resulted in significant differences regarding the SDQ-DE Total Problem Score, the Subscale Conduct Problems, the Subscale Hyperactivity Inattention and SDQ-DE Dysregulation Profile based on parental ratings. Concerning children's assessments, sleep problems were associated with emotional dysregulation problems, emotional problems, and peer problems. Results regarding nightmares show similar effects.

Conclusions: Results show that parents, clinicians, and teachers should assess sleep problems in children to prevent emotional and peer problems in children. Early or secondary prevention, like school programs or sleep-related therapeutic stories, might help those children cope with sleep difficulties.

Sleep Characteristics, Patterns, and Problem in Children at Respiriology Clinic in Jakarta

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Introduction: Sleep is essential in child's growth and development. Optimal sleep habit and routines are important to support healthy growing and developing children. Sleep is a multifactorial phenomenon, and sleep problems in children maybe due to interplay of biological, psychological, and social influences from environment. We aim to describe characteristics, patterns, and problems of sleep in children who came to pediatric respirology clinic in a tertiary hospital, Jakarta.

Materials and methods: A cross sectional study was conducted in pediatric respirology clinic at Cipto Mangunkusumo Hospital in June 2025, by asking parents or caretakers of their children's, who came the clinic, sleeping habit and problem.

Results: Data were collected from 100 subjects, 52% were boys, mean age was 7 years old (the youngest was 2 months and oldest was 17 years). Majority was in the clinic for tuberculosis treatment (42%), followed with asthma (14%). Most subjects (29%) had 8 hours of sleep, followed by 9 hours (28%) and 10 hours (23%). Majority (84%) reported of nap times. Thirty-five percent of subjects had bedtime at 9 pm, with rise-time at 6 am. Fifty-two percent of subjects was using gadgets before sleeping, and 73% slept with dim-light or no-light. Seventy-eight percent of subjects was co-sleeping with parents/care-takers in one bed. Most subjects (62%) had become respiratory patients for 1 year or less, and only 37% reported sleeping problems appeared after the diagnosis. Occasional snoring was

reported in 33% subjects, 10% had habitual snoring, and 11% of parents/care-takers witnessed cessation of breathing. Majority (56%) reported of nighttime waking, with 54% of them reported twice or more. Reason for waking was mostly thirsty and asking for drink (27%) and coughing (24%).

Conclusion Most respirology clinic patients have sufficient nighttime sleep

Conclusions: Most respirology clinic patients have sufficient nighttime sleep and co-sleep with parents/care-takers. Signs of sleep disordered breathing are found in 10% patients with habitual snoring and 11% with cessation of breathing. Only 37% reported sleep problems appearing after respiratory diagnosis.

Sleep Health Among Children in Foster Care: Understanding Impacts, Interventions, and Research Gaps

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Introduction: Children in foster care face numerous developmental challenges due to early exposure to trauma, maltreatment, and environmental instability. These adverse childhood experiences (ACEs) significantly impact physical and mental health, with growing evidence indicating sleep health as a particularly vulnerable domain. Despite sleep being critical for healthy development, research on sleep disturbances in foster youth remains limited. Disruptions to the hypothalamic-pituitary-adrenal (HPA) axis, psychological stress, and perceptions of environmental insecurity all contribute to poor sleep outcomes. This abstract reviews the literature on sleep health among children in foster care, evaluates interventions, and identifies areas requiring further investigation.

Materials and methods: This review synthesizes peer-reviewed articles, surveys, and intervention studies exploring sleep disturbances in children and adolescents in foster care. Sources were selected for their relevance to foster care populations, inclusion of sleep-related outcomes (e.g., duration, latency, parasomnias), and exploration of psychological and environmental factors affecting sleep. Interventional studies including behavioral, digital, and pharmacological approaches were included to assess the breadth of strategies currently employed. Research findings were categorized into themes: sleep quality, sleep disorders, trauma impact, and intervention effectiveness.

Results: Sleep Quality and Disorders: Children in foster care exhibit higher rates of poor sleep quality across all five domains of sleep health: duration, efficiency, timing, sleepiness, and quality. Studies show prolonged sleep latency, frequent awakenings, and increased parasomnias such as nightmares and sleep terrors. Foster children often report shorter total sleep duration and increased symptoms of insomnia, with prevalence rates of parasomnias markedly higher than in the general population. For instance, nightmares are reported in over 50% of foster children in some studies.

Impact of Trauma: Exposure to ACEs and instability in caregiver relationships elevate stress responses, often resulting in HPA axis dysregulation and hypervigilance. These biological and psychological changes contribute to difficulty initiating and maintaining sleep. Placement transitions and environmental insecurity further exacerbate sleep disruptions. Trauma-related sleep disturbances are often left unaddressed due to limited caregiver training and systemic oversight.

Interventions: Intervention efforts have focused on behavioral strategies, caregiver education, and digital platforms. Programs like SAFE-T—a trauma-informed telehealth sleep intervention—have demonstrated promising results in reducing night awakenings and internalizing symptoms. Caregiver involvement in consistent bedtime routines was associated with fewer sleep disturbances, even in children with multiple placement histories. While melatonin is commonly used, it has shown mixed results and may correlate with worsened daytime behaviors in foster youth.

Conclusions: Foster care youth are disproportionately affected by sleep disturbances stemming from trauma and instability. These sleep issues contribute to broader mental and physical health disparities. Promising interventions include trauma-informed digital therapies and structured caregiver routines, yet gaps remain in long-term data, objective sleep measurement, and systemic integration of sleep health in foster care practices. Future research should prioritize personalized, trauma-sensitive approaches and policy reforms that recognize sleep health as a vital component of foster care support.

Strengthening caregiver training and standardizing sleep assessments can significantly improve outcomes for this vulnerable population.

Sleep Phenotypes in Infancy and Their Continuity into Toddlerhood

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Introduction: Sleep patterns undergo significant developmental changes during infancy and early childhood, with increasing consolidation and regulation over time. Research has shown that individual differences in sleep duration, night wakings, and sleep-onset behaviors emerge early and persist into toddlerhood, influencing cognitive, emotional, and behavioral outcomes. Prior research in a sample of infants aged 9-13 months utilized cluster analysis (hierarchical Ward's method and k-means clustering) and identified three stable sleep phenotypes—Long Sleepers (LS), Interrupted Sleepers (IS), and Short Sleepers (SS)—based on differences in total sleep time, night wakings, parental nighttime visits, sleep efficiency, bedtime, and wake-up time measured with autovideosomnography. Given the developmental changes in sleep over time, the present study aimed to examine whether similar differences in sleep duration, bedtime, night wakings, sleep efficiency between the sleep phenotypes were observed in the same sample at a one year followup.

Materials and methods: A total of 623 infants aged 9-13 months were recruited from the Nanit customer database in 2023, and three distinct sleep phenotypes were identified. To examine whether these clusters remained consistent over time, a follow-up survey was conducted with the same participants. In total, 110 parents of children aged 22-30 months (27.50±1.0, 52.6% males) participated in the follow-up study. Objective sleep data from Nanit autovideosomnography were collected for 2 weeks (average 11.56 nights per child) measuring total sleep time at night (TST), bedtime (BT), night wakings (NW), nighttime sleep efficiency, and parental nighttime visits. Differences between clusters were analyzed using ANOVA and post-hoc pairwise comparisons.

Results: Auto-videosomnography data showed significant differences in TST ($p=0.001$), with LS sleeping 33.72 minutes (95% CI: 10.08, 56.64) more than SS ($p=0.002$) and IS sleeping 39.48 minutes (95% CI: 10.56, 66.4) more than SS ($p=0.004$). BT differences were also significant ($p=0.007$), with SS having later bedtime by 30 minutes than IS ($p = 0.009$; 95% CI: 5.58, 48.36) and by 27 minutes than LS ($p=0.023$; 95% CI: 3.24, 57.24). However, we did not find significant differences in NW ($p = 0.86$), parental nighttime visits ($p = 0.508$), or nighttime sleep efficiency ($p=0.74$) across clusters.

Conclusions: TST and BT remained significantly different across sleep clusters which aligns to the previous research, with LS having the longest sleep duration and SS the shortest and later bedtimes at follow up. No significant differences in NW, parental nighttime visits, or nighttime sleep efficiency were found across clusters. This suggests that infants with more night wakings at 9-12 months of age do not display the same behavior at 22-24 months, possibly reflecting the increasing consolidation of sleep patterns in toddlerhood. This longitudinal analysis of sleep phenotypes highlights the importance of sleep in infancy and its relationship with sleep health in early childhood.

Sleep problems in infants and children with prenatal alcohol exposure: a systematic review and meta-analysis

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Introduction: Sleep disturbances are common in children with fetal alcohol spectrum disorders (FASD) and prenatal alcohol exposure (PAE), worsening behavioural and cognitive deficits. Despite this, no review has systematically assessed the timing or severity of these sleep issues. The aim of this review was to identify sleep problems in children with FASD or PAE.

Materials and methods: A systematic search across seven databases followed PRISMA guidelines. Studies included children aged 3-10 with FASD or PAE and provided quantitative sleep data. Two reviewers independently screened articles. A meta-analysis of subjective sleep outcomes used a random-effects model, with heterogeneity assessed via I^2 .

Results: Fourteen studies met inclusion criteria. Children with FASD or PAE had consistently worse sleep than typically developing peers, including longer sleep onset, shorter duration, more awakenings, lower sleep efficiency, and greater sleep variability. Higher PAE levels were linked to earlier onset and persistence of sleep problems, with more severe issues in early pregnancy exposure. Meta-analysis of seven studies showed high heterogeneity ($I^2=0.91$) with medium to large effect sizes, particularly for night awakenings ($d=1.04$) and sleep duration ($d=0.89$).

Conclusions: Children with FASD/PAE face persistent sleep issues, worsening with heavier or earlier exposure, highlighting the need for early screening and interventions.

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Slower maturation of the circadian rest-activity rhythm is associated with weight gain across infancy

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Introduction: Circadian-driven sleep-wake regulation rapidly matures across infancy. Evidence suggests that poor regulation and blunted circadian rhythms are associated with weight gain in childhood. Rapid weight gain (RWG; $> .67$ increase in weight-for-age Z-score) during infancy is a potent early risk factor for childhood obesity, yet the relationship between circadian sleep-wake rhythmicity and weight gain in infancy has rarely been studied. This study examined whether actigraphy-assessed circadian rest-activity rhythmicity (CRA) development is associated with RWG across the first year of life. We hypothesized that blunted CRA maturation would be associated with RWG.

Materials and methods: In an ongoing longitudinal, observational cohort (Snuggle Bug |Acurrucadito study), full-term (≥ 37 wk), singleton infants, born of normal weight (parent-reported: 2.5-4kg) were recruited along with their mothers from the Phoenix, Arizona, USA metropolitan area to participate in six home visits across their first year of life at 3 and 8 weeks, and 3, 6, 9, and 12 months. At each visit, infants were weighed with a Seca scale and wore a Micro Motionlogger (Ambulatory Monitoring, Inc.) around their left ankle for five 24-hr periods post-visit. CRA metrics were derived from actigraphy data in one-minute epochs including mesor, amplitude, goodness-of-fit R^2 , interdaily stability, intradaily variability, and relative amplitude. Demographic information, including whether mother-infant dyads were enrolled in the U.S. Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), a program for qualified caregivers of low-income, was collected. Visit-to-visit changes in CRA metrics and their relationship to the occurrence of RWG status since birth were examined with logistic time-varying effect models adjusting for time-varying birth weight and time-invariant WIC status using the *tvem* package in R. Model A examined each CRA metric by its global sample mean as the exposure. Model B examined the between-person and within-person effects of each CRA metric as exposures in the same model.

Results: Preliminary results from the first 117 participants of a possible 205 are presented. Across infancy, regardless of timepoint, there were consistent, mostly trending, negative associations between lower sample-level mean goodness-of-fit R^2 (Model A coefficient range across time points ≈ -0.58 – -0.29 , Lower CI range: -1.56 – -0.59 , Higher CI range: -0.007 – 0.41), and lower person-centered mean goodness-of-fit R^2 (Model B coefficient range ≈ -0.50 – -0.32 , Lower CI range: -1.93 – -0.64 , Higher CI range: -0.002 – 0.93) and lower visit-to-visit within-person variability in goodness-of-fit R^2 (Model B coefficient range ≈ -0.36 , 95%CI: -0.74 , 0.03) with having experienced RWG. In Model A, statistical significance was reached at three months of age. In Model B, the between-person effect reached significance at eight weeks, three months, and six months of age, but the within-person effect did not reach significance. Similar results were found for amplitude and interdaily stability. No other CRA metrics were trending or significantly associated with RWG status.

Conclusions: Slower maturation of the circadian rest-activity rhythm across infancy is associated with a trend toward increased risk of RWG, suggesting that early differences in circadian rhythm development may play a role in the emergence of obesity risk during infancy.

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Socioeconomic Risk, Parenting, and Sleep: Impacts on Kindergarten Academic and Socioemotional Outcomes

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Introduction: The transition to schooling is a pivotal point for children, and adjustment to first-time schooling is predictive of subsequent academic performance (Fitzpatrick et al., 2020). A large literature has identified socioeconomic context, parenting, and children's sleep prior to starting kindergarten as important determinants of school adjustment in socioemotional and academic domains (Barger et al., 2019; Larson et al., 2015; Teti et al., 2022; Raby et al., 2015; Zaslow et al., 2006). However, it is unclear how these determinants work in concert with one another to confer risk or resilience in adverse environments. The current study utilized a multi-informant and multi-method longitudinal design to examine socioeconomic risk, parenting quality, and actigraphic sleep prior to kindergarten as unique and interactive predictors of children's adjustment to kindergarten.

Materials and methods: Data for this investigation came from 225 families who participated in assessments across the kindergarten year in mid-to-late August (pre-K), late September, early-mid November, and April. Observations of parenting at pre-K were scored from video recordings of children's bedtimes, using reliable coders trained on the Emotional Availability Scales (EA) (Biringen et al., 1998). Mothers and fathers EA scores were related ($r = .59, p < .001$) and averaged to create a composite EA score for each parent. Socioeconomic risk (SER) was a composite of family income-to-needs ratio, parental education, and subjective reports on monetary resources.

Children wore AW-64 actiwatchs (Philips Respironics, Inc) for 7 consecutive nights at pre-K, which were used to derive multiple sleep parameters including average sleep minutes (minutes scored asleep from sleep onset to morning wake time). Teachers reported on academic and socioemotional outcomes across the year. Academic achievement was assessed via the Academic Competence Evaluation Scale (DiPerna & Elliot, 2000), Academic Performance Rating Scale (DuPaul et al, 1991), and School Readiness Questionnaire (Bierman et al., 2008). Socioemotional and learning outcomes were reported on the Learning Behavior Scale (McDermott et al., 2002), Student-Teacher Relationship Scale (Pianta, 2001), and the Teacher Observation of Classroom Adaptation- Revised (Werthamer-Larsson et al., 1991).

Results: Multilevel models were fit to examine how SER, parent EA, and child sleep individually and interactively predicted outcomes. Main effects of individual predictors, controlling for the other two, revealed that SER was a robust predictor of poor socioemotional and academic outcomes. Parent EA was predictive of greater prosocial and learning behaviors and better academic outcomes. Greater nighttime sleep minutes predicted better academic competence, performance, and school readiness. Also obtained was a significant interaction between EA and sleep predicting academic performance. Children who had good sleep and emotionally available parents showed the highest levels of performance. By contrast, children with poor sleep and emotionally unavailable parents had the lowest levels of performance. Importantly, simple slopes testing revealed that children with at least one protective factor at pre-K (i.e., greater EA or longer sleep minutes) showed improvements in academic performance across kindergarten.

Conclusions: The present findings suggest that parenting quality as well as child sleep prior to the kindergarten year are important points of entry for interventions aiming to promote children's adjustment to first-time schooling.

Spectral Analysis of EEG Activity in Different Sleep Stages Across the Puberty Period by Fast Fourier Transform

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Introduction: EEG total power reduction has been observed in post-pubertal adolescents, and brain maturation during sleep is reflected in EEG changes, which can be analyzed using Fast Fourier Transform (FFT). During adolescence, FFT may reveal increased power in the theta and beta bands, particularly during the pubertal period. This study aimed to analyze sleep EEG spectral changes via FFT in peripubertal and post-pubertal children, focusing on all sleep stages to evaluate potential puberty-related changes.

Materials and methods: Twenty healthy children were divided into two groups based on Tanner stage: early puberty (n=10; 5 girls, mean age: 9.8 ± 1.2 , range 8-12) and late puberty (n=10, 5 girls, mean age: 14.3 ± 0.8 , range 13-17). Participants underwent two consecutive nights of polysomnography, with the first night serving as an adaptation period and a minimum of 7.5 hours of recordings. The EEG was recorded using a 32-channel sleep system with a sampling rate of 256 Hz, including 20 EEG leads, two EOG channels, two EMG channels, and an ECG channel. FFT was applied to the C3-A2 derivation throughout the night in 4-second windows, and using Hanning window function before applying independent component analysis. Spectral power for delta1 (0.5-2.0 Hz), delta2 (2.0-4.0 Hz), theta (4.0-8.0 Hz), alpha (8.0-12.0 Hz), sigma (12.0-16.0 Hz), and beta (16.0-20.0 Hz) was calculated for each sleep stage. The Mann-Whitney U-test was used to compare sleep parameters, with significance set at $p < 0.05$. Spearman's correlation coefficient (r_s) was used to explore correlations between sleep parameters and FFT values, with a significance level of 0.05.

Results: The EEG Power spectral analyses in all sleep stages were significantly lower in Tanner 4/5 than in Tanner 2/3 children, compared to the absolute mean EEG power spectral between the two groups. No differences in EEG power spectral analyses were obtained between boys and girls. Differences in spectral sleep EEG were observed between the two groups (U-test, $p < 0.05$) across all sleep stages. Delta 2 ($p = 0.02$) and theta power ($p = 0.04$) were higher in the early puberty group. Delta power correlated negatively with N1 duration ($r_s = -0.46$, $p < 0.05$) and wake time after sleep onset ($r_s = -0.48$, $p < 0.05$), but positively with sleep efficiency ($r_s = 0.45$, $p < 0.05$) in the early puberty group. Theta power during REM sleep positively correlated with N3 duration ($r_s = 0.45$, $p < 0.05$) in the early puberty group.

Conclusions: Our results suggest that sleep EEG undergoes significant changes during puberty, reflecting brain maturation. We observed a decrease in theta and delta activity during REM sleep in the post-pubertal group, indicating a shift in brain function with puberty. These differences may be influenced by hormonal and environmental factors associated with puberty. REM sleep may serve as a useful biomarker of brain function for future therapeutic strategies.

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Study of Sleep Habits and Nutritional Status in Children in a Tertiary Care Hospital: Cross-Sectional Study

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Introduction: Sleep and nutrition are essential components of children's health and development. Sleep is vital for physiological functions like repair, growth, and memory consolidation, while proper nutrition supports physical and cognitive development. Malnourished children—both undernourished and obese—often experience disruptions in their sleep patterns, which can negatively affect their overall health. This study aimed to explore the relationship between sleep habits and nutritional status in malnourished children, providing valuable insights into how nutritional imbalances impact sleep quality.

Materials and methods: This cross-sectional study was conducted at the Regional Advanced Pediatric Care Centre (RAPCC), Mangalore, India, from March to May 2024. A total of 400 children aged 6 months to 10 years were enrolled through convenience sampling. Inclusion criteria were children visiting the outpatient department (OPD) of RAPCC, while those with acute or known chronic diseases or on medication that could affect sleep were excluded. Sleep habits were assessed using the Children's Sleep Habits Questionnaire (CSHQ), completed by parents with translations available when necessary. Nutritional status was categorized based on BMI into undernourished, normal, and obese groups. Data were analyzed using SPSS version 29, employing descriptive statistics, chi-square tests, and ANOVA.

Results:

The mean age of the cohort was 5.42 years (SD = 2.91), with 50.5% male and 49.5% female participants. Among the 400 children, 58.5% were under 5 years old, and 41.5% were aged 5-10 years. Nutritional assessments revealed that 30% of the children were undernourished, 57% had normal nutritional status, and 13% were obese. Sleep quality, measured by the total CSHQ scores (mean $\pm$ SD), was poorest among obese children (48.29 ± 9.55), followed by undernourished children (45.32 ± 8.81), and was significantly better in children with normal BMI (37.12 ± 7.24) (ANOVA $F = 112.43$, $p < 0.001$). Obese children exhibited significantly higher scores for bedtime resistance (mean = 6.78, $p < 0.001$) and sleep-disordered breathing (mean = 7.45, $p < 0.001$), while undernourished children showed higher sleep anxiety scores (mean = 5.92, $p = 0.002$). Parasomnias were more common in obese (56.7%) and undernourished children (38.3%) compared to their normal-weight peers (23.6%) (chi-square = 345.64, $p < 0.001$). Sleep-disordered breathing was observed in 62.5% of obese children and 33.3% of undernourished children, significantly higher than in normal-weight children (18.4%) (chi-square = 285.42, $p < 0.001$). A negative correlation between BMI and total CSHQ scores ($r = -0.27$, $p < 0.001$) indicated that higher BMI was associated with poorer sleep quality, as reflected by higher CSHQ scores.

Conclusions: Malnourished children, including those who are undernourished and obese, exhibit significantly worse sleep quality compared to their normal-weight counterparts. Common sleep issues in these groups include bedtime resistance, sleep anxiety, and sleep-disordered breathing. These findings emphasize the need for targeted interventions to address sleep disturbances in malnourished children, which could improve their overall health and development. This is particularly important in developing countries like India, where malnutrition remains a significant public health challenge.

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Sustained Myofunctional Therapy in Pediatric Sleep-Disordered Breathing: Correlates of Adherence and Clinical Outcomes

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Introduction: Pediatric sleep-disordered breathing (SDB) poses significant health risks, yet effective non-invasive therapies remain underexplored. This study evaluates the efficacy of myofunctional therapy (OMT) in children with SDB, focusing on clinical outcomes, adherence predictors, and the role of therapy duration.

Materials and methods: Data from 39 pediatric patients (mean age: 8.8 years; 82.1% male) undergoing OMT were analyzed. Variables included demographics (age, sex, BMI), clinical metrics (AHI, DI, SpO₂), therapy details (duration, daily minutes), and outcomes (PSQ scores, sleep quality, medication reduction). Statistical analyses identified correlations, adherence predictors (dropout flag = "N"), and effect sizes (Cohen's d).

Results: Clinical Outcomes:

- PSQ Scores: Mean improvement of -4.36 points ($p < 0.0001$), with progressive gains in longer therapy quartiles (Q4: -7.12 vs. Q1: -2.42).
- Sleep Quality: 94.9% reported improvement, achieving 83% success even in short-term therapy (7–30 days).
- Medication Reduction: 66.7% reduced medication use, strongly correlated with therapy duration ($r = 0.56$, $p < 0.001$).

Adherence and Dropouts:

- Adherent patients (n = 28) received significantly longer therapy (173 vs. 43 days, $p = 0.0022$) and longer daily sessions (18.75 vs. 10.45 minutes, $p < 0.001$).
- Dropouts (n = 11, 28%) were unrelated to demographics (age, sex, BMI) or clinical severity (AHI, DI, SpO₂).

Key Correlations:

- Therapy Duration: Strong negative correlation with PSQ ($r = -0.61$) and positive with medication reduction ($r = 0.56$).
- BMI and AHI: Higher BMI predicted worse apnea severity ($r = 0.64$).
- Sleep Quality: Rapid improvement (83% in Q1) but weak duration dependence ($r = 0.22$, $p = 0.17$).

Intervention Characteristics:

- Optimal outcomes occurred with sustained therapy (>180 days), particularly for ESS improvement (Cohen's $d = -1.78$) and medication reduction.
- Patients exceeding 360 days (Q4) achieved near-maximal benefits.

Conclusions: This study underscores the efficacy of OMT in pediatric SDB, demonstrating significant improvements in sleep quality, daytime sleepiness, and medication reliance. Adherence—driven by therapy duration and daily session consistency—emerged as the critical modulator of success, independent of demographics or baseline severity. Clinically, these findings advocate for:

1. Prolonged Therapy: Recommend durations >180 days, with >360 days for maximal PSQ and medication benefits.
2. Adherence Strategies: Universal support for daily sessions (≥ 19 minutes) and early intervention to mitigate dropouts.
3. BMI Monitoring: Address obesity as a modifiable risk factor for apnea severity.

As the first analysis linking OMT adherence to pediatric SDB outcomes, this work provides actionable insights for optimizing non-invasive therapies. By prioritizing sustained engagement, clinicians can amplify therapeutic benefits, reducing long-term health burdens in pediatric sleep disorders.

Keywords: Pediatric sleep-disordered breathing, myofunctional therapy, adherence, therapy duration, clinical outcomes.

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The Association between Sleep and Behavioral Problems in Primary School Children in Shanghai

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Introduction: This study examined the associations between sleep disturbance (SD) and behavioral problems (BP) in primary school children in Shanghai.

Materials and methods: We enrolled 18 316 children in Xuhui district, Shanghai. Baseline assessments and follow-up used the Children's Sleep Habits Questionnaire (CSHQ) to classify SD, and the Conners' Parent Rating Scale (CPRS) to evaluate BP. Cross-sectional associations were analyzed via logistic regression; changes in SD status and their impact on BP remission or new onset were assessed with multilevel regression.

Results: With cross-sectional data, SD was linked to higher odds of any BP, including study problems, conduct problems, impulsivity-hyperactivity, hyperactivity index, psychosomatic complaints, anxiety. Daytime sleepiness correlated most strongly with BP symptoms. During follow-up, compared to children without SD, those with persistent or newly developed SD showed reduced BP remission and increased BP onset. Children whose SD remitted experienced no significant change in BP remission or onset.

Conclusions: In urban primary school children, SD closely related to BP. Early detection and targeted management of SD may help prevent or mitigate childhood behavioral difficulties.

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The Clinical Utility of Repeat Pediatric Polysomnographies

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Introduction: Pediatric sleep-disordered breathing is common and requires a Polysomnography (PSG) for objective diagnosis. In certain cases, such as trisomy 21, post-Adenotonsillectomy (AT), or part of the routine care of children with neuromuscular disorders (NMD), repeat PSGs are needed for diagnosis or follow-up. However, the real-life utilization and yield of repeat studies are unclear. In this study, we aimed to investigate the use of repeat PSGs and their yield in the general pediatric population and in children with background morbidities.

Materials and methods: A retrospective observational, descriptive, cross-sectional study. Data was collected on all children, 0-18 years old who completed two or more PSGs at the Hadassah Medical Center between 2019 and 2023. Demographic, clinical and PSG data was collected, the indications for the repeated PSG, changes in severity, and time elapsed between tests.

Results: A total of 158 (58 female) children were included, of whom 128 completed 2 PSGs, and 69 children 3 or more, at a mean age of 4.4 ± 4.1 years. Patient characteristics included: 76 children after AT, 34 with central sleep apnea (CSA). Common background diseases included trisomy 21 (n=30), prematurity (n=38) and chronic lung disease (n=17). The indication for repeated PSGs included assessment of OSA after an AT (33%), follow-up studies as requested by the treating physician or the parents (25%), and assessment of the need for oxygen or non-invasive ventilation (NIV, 17%). OSA improved in 74% after an AT, but resolved in only 12% of those that had not had an AT ($p < 0.001$). Severity of diagnosis differed following the repeat study in 63% of children with a history of prematurity, 54% with Trisomy 21, and 38% with NMD ($p < 0.001$). CSA diagnosis remained unchanged after repeat studies in 44%, after a mean of 8 months. A major change, defined as a change from moderate-severe to no or mild OSA and vice versa, was found in 39% of the entire cohort and 53% of children after an AT. Children who underwent their first PSG before the age of 1 showed a major change at 1.88 years (SD 1), whereas children who underwent their first PSG between ages 1-18 showed a major at 5.1 years (SD 4.13).

Conclusions: In this study, repeated PSGs revealed changes in sleep apnea diagnosis in a majority of children after AT, but to a far lesser extent in those with underlying morbidities. The study shows a high yield if the initial study was performed in an infant but suggests delaying repeat studies, for indications other than post AT, in older children. We hope our results will assist clinicians when considering the need and timing of a repeat PSG.

The connection between sleep, substance use, and mental well-being in rural Canadian Youth – Preliminary observations from a community-based youth collaboration

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Introduction: Sleep is essential for healthy development, particularly during adolescence – a period when risk factors for mental health challenges and substance use often emerge. Previous Canadian estimates suggested that 30% of adolescents do not meet national sleep recommendations, and over 60% of illicit substance users are between 15 to 24 years old. Insufficient sleep during adolescence has been linked to low self-esteem, difficulties with emotion regulation, and substance use. Many Canadian adults are using alcohol and cannabis as sleep aids. However, the potential connections between sleep, substance use, and mental well-being remain unclear in adolescents and are especially understudied in rural communities. There is also a need to identify modifiable factors associated with better sleep.

Materials and methods: Planet Youth is an ongoing project implementing the Icelandic prevention model in different communities across the world for upstream community action. As part of the Canadian portion of this project, 705 adolescents ($M_{age}:16.1\pm0.26$); 49.7% boy/man, 43.0% girl/woman, 1.8% non-binary, 0.6% gender fluid/non-conforming, 0.4% trans) completed a survey designed to assess risk and protective factors in key community domains (family, school, peer groups, and leisure/out-of-school time activities) and substance use. ACHIEVE, a local youth advisory committee ensuring youth voices are at the forefront of Planet Youth's initiatives, actively contributed to shaping the scope of secondary data analyses of this survey. A series of mediation analyses were conducted to examine the direct relationship between habitual sleep quantity, self-esteem, and anger, as well as the potential moderating role of cannabis and alcohol use in the past 30 days. Logistic regression was used to identify protective factors linked to sleep quantity at or above recommended values based on Canadian guidelines.

Results: In this rural sample of adolescents, 68% reported sleeping less than 8 hours. Insufficient sleep had direct effects increasing anger ($b=-0.77$, $t=-7.23$, $p<.001$) and decreasing self-esteem ($b=-1.67$, $t=-9.74$, $p<.001$). Additionally, insufficient sleep had significant indirect effects on anger that were mediated by higher alcohol (bootLLCI : $-.08$; $-.01$) and cannabis (bootLLCI : $-.11$; $-.01$) use. Insufficient sleep also had an indirect effect on self-esteem through cannabis (bootLLCI : $-.111$; $-.002$), but not alcohol use. Feeling safer at school and having a daily life filled with things that interest youth were the strongest independent protective factors associated with sufficient sleep duration ($|B|>.20$, $p<.003$).

Conclusions: Insufficient sleep was twice as frequent in this rural adolescent sample compared to national estimates. Insufficient sleep had a double effect where, it directly predicted more anger and poorer self-esteem, and had additional indirect effects whereby it increased alcohol and cannabis use, which in turn further worsened anger and self-esteem. Creating safe, stimulating environments for adolescents – both in and outside of school – may contribute to improving sleep, with positive impacts on substance use and mental well-being.

Acknowledgments: *Joint first authorship: the first two authors have contributed equally to this work.

The effectiveness of transcranial magnetic stimulation on sleep structure and quality of life in children with autism

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Introduction: Sleep disorders are common in children with autism spectrum disorder (ASD). Transcranial magnetic stimulation (TMS) could be effect the excitability of neuronal cells that leading to improvements of sleep and quality of life in autistic children. Now a day, studies on clinical mechanisms of TMS in sleep disorders associated with ASD are limited. Therefore, our study aimed to explore the effects of TMS on sleep structure and quality of life in children with ASD.

Materials and methods: The recruitment was directly informed through parents of autistic children in special education school in Nakhon Pathom Province, Thailand. Twenty children with ASD who met the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, were selected in our protocol. The low-frequency TMS 2Hz, 5Hz and 5Hz respectively and intensity of 3mT, 15mT and 30mT respectively were targeted on the prefrontal and dorsolateral cortex on both sides in children with ASD 2 times per week. The frequency and intensity were adjusted every 2 weeks up to maximum frequency and intensity at 6 weeks of treatment. The Sleep Disturbance Scale for Children (SDSC) was performed before treatment and at 12 weeks of intervention. Independent sample *t*-tests and difference *t*-tests were used for statistical analysis of the data.

Results: Before treatment the total SDSC score in difficulty falling asleep, sleep maintenance, awakening disorders, sleep-wake transition disorders, excessive daytime sleepiness, and nocturnal hyperhidrosis scores were high in all ASD children. After TMS were performed in all ASD children, after 8, 16 and 24 session of TMS Treatment with protocol of intensity and frequency adjustment every 4 weeks, the total SDSC score in difficulty falling asleep, sleep maintenance, sleep-wake transition disorders, and excessive daytime sleepiness scores were significantly decreased at 24 sessions of treatment ($P<0.01$). The difference *t*-test analysis showed that after 24 treatment sessions, the reduction rates of the total SDSC score, difficulty falling asleep, sleep maintenance, awakening disorders, sleep-wake transition disorders, excessive daytime sleepiness, and nocturnal hyperhidrosis dimensions were significantly decreased. ($P<0.01$).

Conclusions: Low-frequency TMS targeting the prefrontal and dorsolateral cortex in children with ASD can effectively improve their sleep status, and significant improvement can be achieved after 12 weeks (24sessions) of treatment. Moreover all of children had improved in quality of life in field of ability to learn and communication. Further study in multicenter and large scale population should be performed to achieve more significant statistic data and could be advocated to apply as a non invasive choice of treatment in clinical practice worldwide to improve quality of sleep and quality of life in autistic children.

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The Mechanism of Ferroptosis in Chronic Intermittent Hypoxia Induced Liver Injury and the Regulation Role of Nrf2

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Introduction: Obstructive sleep apnea (OSA) is characterized by chronic intermittent hypoxia (CIH), which can induce or exacerbate liver injury. Ferroptosis, marked by iron overload and lipid peroxidation, is closely linked to liver injury, but its mechanistic role in CIH-related liver damage remains unclear. Evidence suggests that the antioxidant regulator Nrf2 may protect against ferroptosis-driven injury, though the mechanisms require further exploration. This study established a CIH-induced liver injury mouse model to investigate the role of ferroptosis in CIH-induced liver injury and the protective effect and molecular mechanism of Nrf2 in ferroptosis mediated CIH-induced liver injury.

Materials and methods: In this study, utilizing a CIH model in 4-week-old male mice, we investigated ferroptosis and the potential involvement of Nrf2 in CIH-related liver injury. Post-modeling, serum ALT/AST activity, hepatic iron, MDA, SOD, GSH, histopathology (HE, Masson, Prussian blue staining), mitochondrial ultrastructure (TEM), and ferroptosis-related molecules (GPX4, SLC7A11, TFR1, ACSL4) mRNA/protein levels were analyzed.

Results: Chronic intermittent hypoxia (CIH) exposure in mice induced liver ferroptosis, evidenced by elevated ALT/AST levels, disrupted hepatic architecture, fibrosis, iron overload, mitochondrial damage (outer membrane rupture, cristae loss), oxidative stress (increased MDA, decreased SOD/GSH), and dysregulated ferroptosis markers (downregulated GPX4/SLC7A11, upregulated TFR1/ACSL4). Interventions with DFO (iron chelator) and Lip-1 (ferroptosis inhibitor) reversed these effects, restoring liver function, reducing iron deposition, mitigating mitochondrial injury, and normalizing oxidative/ferroptosis-related biomarkers. Nrf2 activation via sulforaphane (SFN) further alleviated CIH-induced damage, lowering body/liver weight, reducing fibrosis, and modulating ferroptosis markers (upregulating GPX4/SLC7A11/FSP1, downregulating TFR1/ACSL4), whereas Nrf2 inhibition (brusatol, BRU) exacerbated injury.

Conclusions: Chronic intermittent hypoxia exposure can induce lipid peroxidation and iron ion overload, triggering ferroptosis and leading to liver injury in mice. Activation of the Nrf2 signaling pathway can effectively alleviate chronic intermittent hypoxia-related liver injury by reducing iron ion accumulation and upregulating FSP1 expression to inhibit lipid peroxidation, thereby suppressing the ferroptosis process.

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The presence or absence of sleep apnea in a healthy newborn aged 2 days

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Introduction:

A study was conducted on 171 healthy newborns aged 2 days using a quartz optical fiber-type sleep apnea sensor for approximately 2 hours and 5 minutes in an unrestrained manner, measuring the possibility of the presence of sleep apnea.

Materials and methods: So far, measurements of overnight sleep (ranging from 5 to 8 hours) have been conducted on individuals aged from 0 years and 2 months to 81 years using a plastic optical fiber type sleep apnea sensor, suggesting a possibility of sleep apnea at around 10%. This time, since the measurement is of a lighter weight newborn just 2 days old, a quartz optical fiber type sleep apnea sensor was used to increase sensitivity. Measurements were taken in an unconstrained manner for approximately 2 hours and 5 minutes on 171 healthy newborns aged 2 days, assessing the possibility of sleep apnea.

Results: In this study involving 177 healthy newborns (2 days old), fortunately, there were no instances of rolling over or standing up, allowing for very smooth measurements. Analysis was possible for 171 cases, while 6 cases were deemed unmeasurable due to too low signal levels. For the 171 measurable cases, an apnea was determined if there was a period of apnea of more than 2 breaths (which varies by individual but measured approximately from 2.1 seconds to 4.1 seconds). As a result, among the 171 newborns, 116 had an RDI (Respiratory Disturbance Index) of <5 , indicating normal, 45 cases were mild at $5 \leq$ and <15 , and 9 were moderate at $15 \leq$ and <30 . This showed that 67.8% were normal, 26.3% were mild, and 5.3% were moderate, indicating that even 2-day-old newborns display a distribution similar to that of infants and adults. Further analysis with more cases is needed to substantiate this conclusion.

Conclusions: Using a quartz optical fiber type sleep apnea sensor, measurements were taken regarding the possibility of sleep apnea in a healthy newborn at two days old, yielding results that indicate a distribution of sleep apnea likelihood consistent with infants and adults aged 2 months to 81 years. Going forward, it will be important to continue monitoring how this result may change or remain constant as these newborns grow into toddlers.

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Thermal Properties of Infant Bedding: An Evaluation of Heat Dissipation Efficiency

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Introduction: Melatonin secretion increases rapidly during the first year of life, contributing to the development of a circadian sleep-wake rhythm. Therefore, establishing an appropriate sleep environment during infancy is essential. In particular, optimizing the thermal environment is believed to reduce nighttime awakenings and shorten sleep onset latency. In Japan, traditional infant bedding typically consists of firm polyester fiber mattresses and comforters. However, bedding systems incorporating 3D fiber structure mattresses and wearable blankets (sleepers), designed to improve thermal regulation, have recently gained popularity.

This study aimed to evaluate the thermal characteristics of infant bedding systems with high heat dissipation performance.

Materials and methods: Fifteen healthy infants aged 1 to 4 months residing in Japan participated. Three bedding types were tested: Bedding P (a newly developed 3D fiber structure mattress with enhanced surface heat dissipation and a sleeper), Bedding Q (a commercially available 3D fiber

mattress with a waterproof sheet and comforter), and Bedding R (a traditional firm polyester fiber mattress with a waterproof sheet and comforter). Each bedding system was used during approximately one hour of daytime napping in a climate-controlled chamber (25°C, 50% RH).

Measurements included sweat rate, mattress surface and underside temperature and humidity, and skin surface temperature at the groin and ankle.

Results: Results showed that Bedding P had the lowest sweat rate (0.108 mg/cm²/min), significantly lower than Bedding Q (0.264 mg/cm²/min, $p = 0.020$). Mattress surface temperature at the back was significantly higher in Bedding R (36.1°C) compared to P and Q (both 34.8°C, $p < 0.001$), indicating heat accumulation. Underside mattress temperature was higher in P and Q (27.4°C) than R (26.6°C, $p = 0.012$), suggesting better heat dissipation. Absolute humidity beneath the mattress was lower in P and Q (15.3 and 14.2 g/m³) than R (16.2 g/m³, $p < 0.001$). The distal-proximal skin temperature gradient showed no significant differences among groups.

Conclusions: Overall, Bedding P demonstrated superior thermal performance, with lower sweat rate and reduced heat accumulation, indicating a more favorable sleep environment. Bedding Q, despite using the same 3D fiber mattress as P, retained more heat due to the waterproof sheet and comforter. Bedding R, with its high-density polyester fiber, showed the greatest heat retention. For infants who cannot adjust posture or wipe sweat, Bedding P's ability to facilitate heat dissipation may help reduce thermal stress and improve sleep quality.

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The Role of Simple Hematological Indicators in the Assessment of Obstructive Sleep Apnea Syndrome in School-Age Children

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Introduction: To explore the correlation between simple hematological indicators, including blood routine, biochemical and their combination indicators, and the severity of obstructive sleep apnea hypopnea syndrome (OSAS) in children, providing a certain basis for screen and follow-up after treatment in outpatient or primary hospitals.

Materials and methods: School-age children who visited the respiratory department of Children's hospital of Soochow University from January 2017 to June 2022 for snoring and/or mouth breathing were enrolled. Polysomnography (PSG) were performed and peripheral venous blood was collected for routine blood tests and biochemical tests, and the values of combined indicators were calculated, including Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Monocyte-to-Lymphocyte Ratio (MLR), Systemic Immune Inflammation Index (SII), Systemic Immune Response Index (SIRI), Aggregated Inflammation Score Index (AISII), White Blood Cell-to-Mean Platelet Volume Ratio (WMR), and High-Sensitivity C-Reactive Protein-to-Albumin Ratio (HCAR). SPSS 26.0 statistical software was used for analysis to examine the correlation between various hematological indicators and severity of OSAS.

Results: 1. A total of 343 school-age children were included, with 104 cases (30.3%) diagnosed with simple snoring, 155 cases (45.2%) with mild OSAS, and 84 cases (24.5%) with moderate to severe OSAS. There were no statistically significant differences in gender ($\chi^2=0.886$, $P=0.642$), age ($H=3.871$, $P=0.144$), or BMI ($H=4.456$, $P=0.108$) among the three groups.

2. The WBC and NE of the moderate to severe OSAS group were $7.94 (6.73, 8.85) \times 10^9/L$ and $3.17 (2.56, 3.94) \times 10^9/L$, respectively, which were significantly higher than those of the mild OSAS group $7.25 (6.23, 8.28) \times 10^9/L$ and $2.99 (2.41, 3.76) \times 10^9/L$. The MPV, PDW, and hs-CRP of the moderate to severe group were 10.3 (9.6, 10.9) fL, 11.8 (10.5, 13.1)%, and 0.44 (0.17, 1.25) mg/L, respectively, which were significantly higher than those of the simple snoring group 9.9 (9.4, 10.4) fL, 10.8 (9.7, 11.7)%, and 0.22 (0.08, 0.7) mg/L, and the mild OSAS group 10.2 (9.6, 10.9) fL, 11.6 (10.4, 12.9)%, and 0.3 (0.11, 1.05) mg/L. The WMR of the mild OSAS group was 703 (607, 859), lower than that of the simple snoring group 782 (658, 898) and the moderate to severe OSAS group 792 (658, 919). The HCAR of the moderate to severe group was 0.009 (0.003, 0.026), significantly higher than that of the simple snoring group 0.005 (0.002, 0.013), with statistically significant differences ($P < 0.05$).

No statistically significant differences were found among the other groups.

3. WBC, NE, PDW, hs-CRP, WMR, and HCAR were positively correlated with OAH1 ($r=0.189, 0.199, 0.165, 0.247, 0.185, 0.184, P<0.05$). WBC, NE, PDW, hs-CRP, WMR, and HCAR were positively correlated with ODI ($r=0.237, 0.215, 0.162, 0.241, 0.202, 0.203, P<0.05$). WBC, NE, PDW, hs-CRP, WMR, and HCAR were negatively correlated with LSpO2 ($r=-0.209, -0.193, -0.162, -0.181, -0.179, -0.151, P<0.05$).

Conclusions: WBC, NE, PDW, hs-CRP, WMR, and HCAR can be used as auxiliary indicators for assessing the severity of OSAS in school-age children.

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The temporal associations between sleep and circadian preference, and mental health among Norwegian adolescents

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Introduction: Eveningness, short sleep, sleep problems and mental health problems are all common amongst adolescents. While research has indicated a bidirectional relationship between sleep and mental health, fewer studies have explored the relationship between circadian preference and mental health. The aim of the present study was to explore the temporal associations between sleep, circadian preference, and mental health in adolescents.

Materials and methods: In 2019, all 1st year high school students in two Norwegian counties were invited to complete a web-based survey assessing sleep, circadian preference, and anxiety and depression (response rate 42.0%). Responders were invited to complete a follow-up survey in 2021 (response rate 42.4%). The analyzed sample comprised 1,456 students born in 2002 who completed both surveys (61.4% girls, mean age 16.4 years at baseline). Instruments included the Munich ChronoType Questionnaire, the Bergen Insomnia Scale, the reduced Morningness-Eveningness Questionnaire, the Generalized Anxiety-Disorder-7 (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9). Two sets of logistic regression analyses were conducted: i) Sleep and circadian preference at baseline (continuous parameters) as independent variables, and anxiety (GAD-7 ≥ 8) and depression (PHQ-9 ≥ 10) at follow-up (dichotomous parameters) as dependent variables, controlling for sex, maternal education and anxiety/depression at baseline, and ii) Anxiety and depression at baseline (dichotomous parameters) as independent variables, and sleep and circadian preference at follow-up (dichotomous parameters) as dependent variables, controlling for sex, maternal education and sleep/circadian preference at baseline.

Results: Baseline school night sleep duration was negatively, and insomnia symptom severity positively, associated with anxiety [OR 0.87 (0.78-0.96) and OR 1.07 (1.04-1.09), respectively] and depression [OR 0.81 (0.73-0.89) and OR 1.07 (1.05-1.09), respectively] at follow-up. Higher morningness scores at baseline predicted lower risk for both anxiety and depression at follow-up [OR 0.96 (0.91-0.99) and OR 0.94 (0.91-0.98), respectively]. Social jetlag and free night sleep duration at baseline were not associated with anxiety and depression at follow-up. The reverse analyses showed that both anxiety and depression at baseline were associated with higher risk for chronic insomnia [OR 1.84 (1.37-2.48) and 1.74 (1.27-2.38) respectively] and lower risk for social jetlag ≥ 2 hours [OR 0.74 (0.55-0.99) and 0.66 (0.48-0.90) respectively] at follow-up. Depression but not anxiety predicted evening preference at follow-up [OR 1.40 (1.01-1.96)]. Neither anxiety nor depression at baseline was associated with sleep duration ≥ 8 hours on school nights or free nights at follow-up.

Conclusions: Overall, these results attest to temporal associations, not only between sleep and mental health but also between circadian preference and mental health, in adolescents. Interestingly, whereas short school night sleep duration at baseline predicted anxiety and depression at follow-up, results did not support the reverse association in that anxiety and depression at baseline did not predict short school night sleep duration at follow-up. When promoting adolescent health, it seems important to target both sleep, circadian preference and mental health in order to reduce the risk of later sleep- and mental health problems.

Toddler Sleep Patterns: Exploring Associations Between Bedtime Consistency and Routines, Parental Involvement and Sleep Outcomes

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Introduction: Optimal sleep is essential for physical growth, cognitive and emotional development. Sleep patterns in toddlers are influenced by biological maturation, environmental factors, and parental practices. Regarding the latter, previous research has shown that falling asleep independently and a regular and early bedtime are associated with longer total sleep duration, later wake-up times, and fewer nighttime parental visits. Nonetheless, these behaviors have often been investigated independently. To overcome this limitation, we sought to identify distinct patterns of parent-mediated bedtime practices and explore the relationship between these patterns and explore their implications for toddler sleep health.

Materials and methods: A total of 518 parents of toddlers aged 18-48 months ($M = 26.77 \pm 6.8$ months, 52.31% males) from the user base of the Nanit baby monitor in the United States participated in this study. They completed the Brief Infant Sleep Questionnaire-Revised (BISQ-R). Objective sleep metrics from the Nanit autovideosomnography system were available for 241 participants for two weeks (average 10.78 nights per child). K-modes clustering analysis was used to classify patterns of parental practices based on parental report of bedtime routines, bedtime, bedtime consistency, and methods of having their child fall asleep. Differences in objective sleep metrics of Total Sleep Time (TST), Bedtime Variability (BTV), Wakeup Time (WK), Parental Visits (PV), and Night Awakenings (NW) were examined across the identified profiles.

Results: Three distinct profiles were identified: Early Consistent Sleepers (ES, 45.75%, 25.27 ± 6.04 months), Inconsistent Sleepers (IS, 12.16%, 29.4 ± 7.30 months) and Late Consistent Sleepers (LS, 42.08%, 27.65 ± 7.22 months). ES had the earliest bedtime on average (19.59 ± 0.73). ES and LS had the highest proportion of children with a consistent bedtime (97.46%, 93.50%) and the same bedtime routine for 5 or more nights/week (91.56%, 96.3%) respectively, compared to IS with 20.63% of children with consistent bedtime and 9.5% with 5 or more nights/week of same bedtime routine. Additionally, 82.27% of ES fell asleep independently, compared to 50.79% in IS and 70.18% in LS.

Significant differences in sleep outcomes were observed across the profiles. ES slept on average 39.96 minutes (95% CI: 17.28, 62.7) longer than IS and 35.64 minutes (95% CI: 21.18, 50.4) longer than LS. IS had significantly higher BTV than ES by 9.88 minutes (95% CI: 1.8, 17.94) and ES woke up on average 35.28 minutes (95% CI: 16.92, 53.7) earlier than IS and 23.93 minutes (95% CI: 12.24, 35.64) earlier than LS. There were no significant differences observed in NW and PV across the profiles.

Conclusions: One of the strengths of this study is relying on objective sleep data to measure variability in toddler bedtime. These findings provide valuable insights into parental bedtime practices, including timing, consistency, and routines related to toddler sleep. Results suggest that consistent and earlier bedtimes may support longer sleep duration. Understanding these patterns can help tailor targeted sleep interventions to support healthy sleep habits in young children.

Two Cases of Delayed Hemorrhage Following Coblation Adenoidectomy

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Introduction: Coblation adenoidectomy is widely adopted for pediatric obstructive sleep apnea (OSA) due to its precision and minimal invasiveness. Delayed hemorrhage (>24 hours post-surgery), though rare, poses life-threatening risks.

Materials and methods: Through analysis the clinical data of two pediatric cases of delayed hemorrhage following coblation adenoidectomy and discusses the etiology, treatment, and preventive strategies based on a literature review.

Results: Case 1: A 3-year-4-month-old girl with severe adenoid hypertrophy (IV degree) and OSA (OAHI 1.9/h) underwent coblation adenoidectomy. On postoperative day (POD) 14, she presented with recurrent bleeding unresponsive to nasal packing. Emergency exploration under general anesthesia revealed mucosal erosion with active bleeding at the nasopharynx-posterior choanae junction, managed via plasma coagulation (Smith&Nephew Coblator II; cut:7, coagulation:3). Severe anemia (HGB 53g/L postoperatively) required transfusion. Recovery was uneventful, with no recurrence at 1-month follow-up.

Case 2: A 5-year-10-month-old boy with adenotonsillar hypertrophy (IV degree) and OSA (OAHI 5.4/h) underwent concurrent coblation adenoidectomy and tonsillectomy. On POD 16, he developed pulsatile bleeding at the left posterior choanae margin, resistant to nasal packing. Intraoperative endoscopy identified a bleeding site with pseudomembrane detachment, successfully controlled via plasma coagulation. No recurrence occurred during follow-up.

Conclusions: Delayed hemorrhage after coblation adenoidectomy, though rare, requires heightened vigilance. Early recognition, endoscopic exploration, and targeted hemostasis are vital to prevent complications. Further studies are needed to optimize surgical protocols and risk stratification.

Understanding the impact of growth hormone on ventilatory control stability in children with Prader-Willi syndrome

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Introduction: A hallmark feature in children with Prader-Willi syndrome (PWS) is dysfunction in the hypothalamic-pituitary axis, which results in markedly reduced growth hormone (GH) secretion in some children. As such, children with PWS often receive GH replacement therapy early in life. However, administration of GH therapy has been implicated in the development of sleep disorders such as obstructive sleep apnoea (OSA). The mechanisms underlying this development are poorly understood but may be related to the impact that the therapy has on the mechanisms known to cause OSA in children, including unstable ventilatory control. Therefore, our study investigated the impact of GH treatment on ventilatory control stability (i.e. loop gain [LG]) during sleep in children with PWS.

Materials and methods: Polysomnographic data pre- and post-GH commencement in 25 children (aged 2 months to 18 years) were collected, with an average time between studies of 6.4 months. To investigate the stability of the negative feedback loop governing ventilation, we utilised a published method that estimates LG from the ventilation changes following spontaneous sighs during sleep. Data were analysed in RStudio using linear mixed-effects modelling. Covariates that could impact LG including: age, obstructive and central sleep apnoea severity (measured as the obstructive-apnoea hypopnoea index (OAHI) and central apnoea-hypopnoea index (CAHI) respectively) were added using a stepwise, manual forward approach and only those with significant associations were retained in the final model.

Results: Loop gain was not altered by GH administration (0.003, 95% CI: [-0.049, 0.042], p=0.878). Adding age, OAHI and CAHI into the main model did not alter the impact of GH on LG. Older children tended to have a slightly higher LG, with each month of age associated with an estimated increase of 6.5×10^{-4} (95% CI: [1.0×10^{-4} , 1.2×10^{-3}], p=0.032) independent of GH treatment. OAHI and CAHI had positive, but very small associations with LG, where higher OAHI and CAHI were associated with higher LG.

Conclusions: Initiation of GH therapy did not impact LG which suggests GH does not alter ventilatory control. The development of OSA post-GH requires further investigation as it is likely related to other mechanisms, such as hypertrophy of the adenoids and tonsils. The contribution of ventilatory control to sleep-disordered breathing in PWS outside of any impact of GH also warrants further investigation.

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Validation of a national actigraph in children and adolescents

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Introduction: Sleep is a neurophysiological process essential to child and adolescent development, playing a central role in cognitive, behavioral, and emotional functions. Early identification of sleep disorders is key to prevent health impairments, which highlights the need for reliable evaluation methods. While polysomnography (PSG) offers detailed analysis of sleep architecture, actigraphy has emerged as a less invasive, more accessible alternative capable of prolonged sleep monitoring. However, validation of actigraphy in children and adolescents is still lacking.

Objectives: This study aimed to validate the ActTrust2 actigraph and to compare the performance of three algorithms (Actiware, Cole-Kripke, and Sadeh) in estimating sleep parameters in children and adolescents, using PSG as the reference.

Materials and methods: Methods: Thirty-three participants, aged 2 to 16 years, underwent simultaneous PSG and actigraphy recording. Evaluated parameters included total sleep time, sleep latency, wake after sleep onset (WASO) and sleep efficiency. The three algorithms were compared using performance metrics such as accuracy, sensitivity, specificity, positive predictive value and negative predictive value. Data normality was assessed using the Shapiro-Wilk test, normality was assessed using the Shapiro-Wilk test, followed by nonparametric analyses including Friedman, Wilcoxon, and Spearman correlation tests with Bonferroni correction.

Results: Results: The Actiware algorithm showed the best overall performance, with higher accuracy (82.4%), sensitivity (86.6%), lower bias, and strong correlations with PSG for total sleep time, WASO, and sleep efficiency. However, its correlation for sleep latency was weak non-significant. The Cole-Kripke algorithm demonstrated intermediate performance, with balanced sensitivity (76.0%) and specificity (78.6%), and moderate bias. Despite higher bias, lower accuracy (69.5%), and sensitivity (65.6%), the Sadeh algorithm was the only one that did not show a significant difference in sleep latency compared to PSG suggesting better agreement.

Conclusions: Conclusions: The results demonstrate that the ActTrust2 actigraph, when combined with appropriate algorithms, is a valid and reliable tool for assessing sleep in children and adolescents.

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Validity and Reliability of a Filipino and Cebuano Version of the BEARS Pediatric Sleep Questionnaire

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Introduction: Sleep is central to the overall health and development of children, yet sleep-related problems are prevalent affecting a significant portion of the pediatric population. The BEARS questionnaire-offers a comprehensive approach to screening for sleep problems. However, the lack of versions in local and familiar languages like Filipino and Cebuano limits its widespread use. The objective of this study is to translate, cross-culturally adapt, and validate the BEARS pediatric sleep questionnaire into Filipino and Cebuano languages This will enable healthcare professionals to effectively screen for sleep-related issues in Filipino children, allowing for early detection and intervention.

Materials and methods: The study was conducted from November 2023 to February 2024. The translation process involved forward-backward translation techniques carried out by a team of linguistic experts, clinicians, and non-clinicians. Cross-cultural adaptation involved testing the translated questionnaires in a sample of 467 pediatric patients 2 to 18 years old and their parents, legal guardians, or primary caregivers. Face validity was assessed qualitatively, while content validity was measured using the Content Validity Index (CVI). Test-retest reliability was evaluated using Cohen's Kappa (κ).

Results: The content validity assessment by subject matter experts (SME) found the questionnaire items highly relevant with strong consensus on item importance (BEARS-Filipino CVI =1, BEARS-Cebuano CVI 0.78-1). While most questions were deemed clear and comprehensive, some suggestions were made to refine language and structure for better understanding among target respondents. Following SME feedback, pre-final versions of the questionnaires were developed and tested on a sample of participants with face validity assessment revealing minimal difficulties and generally positive feedback. Test-retest reliability showed a range from minimal to perfect level of consistency and agreement (BEARS-Filipino 2-5 years κ = 0.2785 to 1, 6-12 years κ = -0.1 to 0.6796, 13-18 years κ = -0.2 to 0.6429; BEARS-Cebuano 2-5 years κ = 0 to 0.7272, 6-12 years κ = 0 to 1, 13-18 years κ = 0 to 1).

Conclusions: The comprehensive analysis underscores the complex nature of pediatric sleep problems and the challenges in capturing these through standardized questionnaires. The findings of this study suggest that the translated tools can be used in the assessment of pediatric sleep problems in the Philippines, most especially in children age 2 to 12 years old, enhancing our ability to address sleep-related concerns effectively

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WatchPAT tolerance and validity as a sleep assessment tool in children and adolescents

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Introduction: The WatchPAT (WP, Itamar Medical) is a home sleep assessment device validated in adults, however few studies have assessed its accuracy in the paediatric population, and none have reported patient tolerance or data quality. Tolerability is a key determinant of success in paediatric sleep investigations. The WP measures peripheral arterial tonometry using a one-size finger probe with an inflatable cushion, designed for use in $\geq 12y$. As accurate calculation of total sleep time (TST) is critical for calculation of obstructive sleep apnoea (OSA) severity, we aimed to firstly assess the validity of sleep/wake recording using the WP in children aged 8- $<12y$ and adolescents aged $\geq 12y$ compared to simultaneous polysomnography (PSG), and secondly report tolerability in this population.

Materials and methods: Prospective study of children aged 8-18 years undergoing diagnostic in-laboratory PSG for suspected OSA, with simultaneous WP-300. TST (minutes), wake after sleep onset (WASO; minutes), rapid eye movement sleep (REM; %), light sleep (N1 and N2; %) and deep sleep (N3; %) from the WP automated study report were compared to PSG sleep scored using standard clinical paediatric criteria. As the WP does not quantify signal loss, good quality data was defined as participants having: PSG-TST $>4h$, WP technically valid sleep time $>4h$, and <40 minutes discrepancy between WP and PSG recording time.

Results: Data were collected in 100 patients. All participants tolerated PSG; WP was aborted in 6 participants (6% of $<12y$, 6% of $\geq 12y$; $p>0.05$) prior to sleep onset, mainly due to discomfort from the finger probe. Good quality WP recording was achieved in 79 participants (79%), which was similar in both age groups (82% $<12y$, 76% $\geq 12y$; $p>0.05$), with median (IQR) age 11.9y (9.9, 13.6), BMI z-score 1.1 (0.1-2.1) and 44% were female. Median PSG-TST was 423.5 (387.5, 456.6) minutes compared to WP-TST 444 (402, 474). Median difference from PSG for WP was +14min for TST, +7.4% for %REM, -6.8% for %light sleep (all $p<0.001$), and +1.4% for %deep sleep ($p>0.05$). Moderate correlation was seen between PSG and WP-calculated TST ($Rho=0.66$, $p<0.001$), with weak correlation for %REM ($Rho=0.13$, $p<0.001$) and %light sleep ($Rho=0.19$, $p<0.001$); %deep sleep and WASO were weakly correlated not statistically significant. A similar pattern was seen in both $<12y$ ($n=40$) and $\geq 12y$ ($n=39$) with the exception of in children $<12y$, WP-TST and PSG-TST were not significantly different ($p>0.05$), however WP overestimated WASO ($p=0.002$).

Conclusions: Approximately 4 out of every 5 children tolerate the WP, with similar tolerance and data quality in those above and below 12 years. Compared to PSG, WP significantly overestimates TST in adolescents, and overestimates WASO in children below 12 years. In both children and adolescents, compared to PSG, WP overestimates REM sleep and underestimates N1+N2 sleep. In both children and adolescents, median percentage of WP N3 sleep does not differ from PSG overall, however the large spread of both over- and under-estimation by WP may be clinically significant. How the overestimation of TST affects WP accuracy in assessment of OSA severity in this population is yet to be determined.

“You cannot sleep good sleep if you are in Nigeria”: Perspectives on adolescent sleep in Nigeria

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Introduction: The social determinants of sleep health in developed countries have been explored. However, there is limited data on the risk and protective factors for adolescent sleep health in Nigeria, and the perspectives of stakeholders need to be understood. Hence, an exploration of the perspectives of stakeholders like parents, teachers and adolescents is relevant. We aimed to understand the perspectives of adolescents, parents and teachers on the barriers and enablers of adolescents' sleep health in Nigeria.

Materials and methods: We utilised pre-tested topic guides to ask participants about the barriers and enablers of adolescents' sleep in Nigeria. We conducted focus group discussions (FGDs) and in-depth interviews (IDIs). There were 12 FGDs for adolescents and 6 for teachers, while IDIs were held for 18 adolescent-parent pairs. Data was transcribed verbatim and coded inductively. Qualitative data were subject to thematic analysis using NVivo-12 software.

Results: Using the socioecological model for sleep health, we identified themes on the barriers and enablers of adolescent sleep health at multiple levels. The sleep enablers identified at the individual level include a correct understanding of sleep needs by adolescents and their parents and good sleep hygiene practices. At the family level, parental control of bedtime was reported as a sleep enabler while living in a safe and quiet neighbourhood was protective at the neighbourhood level and the school level, early school closing time and lecture-free periods were sleep enablers.

Conversely, the barriers to adolescent sleep health at the individual level include bedtime screen use, stress and mental illness. Parental risk factors include parental work-schedule, poor understanding of sleep needs and poor parent-adolescent relationships. Family-level risk factors include bed-sharing, gender roles and sleeping environment. Neighbourhood risk factors include urban residence and noise at night, while school-level factors include early start time, late closing time, afterschool lessons, homework burden, and academic pressures.

These findings are supported by the following quotes:

“Some of us, when we were younger, our parents always tell us go and sleep... but recently, ... for the past three or four years, there's a specific time we must wake up and if you like don't sleep overnight, it's your problem just wake up the time they want you to wake up” - Adolescent FGD participant.
Sleep is disturbed by the “presence of churches and mosques and clubs, loud music, when there's like a party overnight, and distractions... when your house is built near the road like the streets where cars are passing” - an Adolescent IDI participant.

“Some of them stay in school till 6, 7, even past 7 pm.” -Teacher, FGD participant

Another Adolescent IDI participant said “Sometimes when I have plenty of work at school without free periods, it affects my sleep at night”

Conclusions: Many Nigerian adolescents struggle to achieve good sleep due to various factors that impact their sleep health. Comprehensive interventions are necessary to enhance the sleep health of Nigerian adolescents.

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Pharmacology

Association of Hypnotics with Dementia and Cognitive Function in Insomnia Patients: An Observational and Two-sample Mendelian Randomization study

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Introduction: Dementia is a global public health problem that imposes a tremendous economic burden on both individuals and society. Existing evidence has shown significant comorbidity between insomnia and dementia in clinically. Hypnotic agents, such as benzodiazepines (BZDs) and Z-drugs, are usually prescribed to improve sleep quality in patients with insomnia or dementia. Previous observational studies have suggested associations between hypnotics use and dementia as well as cognitive function, but the conclusions from these studies have been contradictory. Observational studies are vulnerable to residual confounders and reverse causality, and whether there is a causal association between hypnotics use and dementia risk as well as cognitive function in participants with insomnia is still unclear. Therefore, we aimed to explore the causal association between hypnotics use and dementia as well as cognitive function in participants with insomnia by an observational and Mendelian Randomization (MR) study.

Materials and methods: In the UK Biobank (UKB), a propensity score-matched cohort was constructed for individuals with insomnia. The Cox proportional hazards model was used to estimate the association between hypnotics use and dementia outcomes. In the sensitivity analyses, inverse probability of treatment weighting and shared frailty models were further applied. Linear regression models were further used to evaluate the impact of hypnotics on cognitive function. A two-sample MR analysis was used to investigate the potential causal associations between target genes of hypnotics with dementia and cognitive functions. Co-localization, summary-data-based MR, external cohort validation and protein-protein interaction (PPI) were used for sensitivity analysis to enhance the credibility of the results.

Results: During a median follow-up of 15.5 years, a total of 195 dementia cases were identified in all participants of the matched cohort. Observational analysis provides strong evidence supporting that the hypnotics use (Hazard ratios [HR]: 1.61, 95% Confidence Interval [CI]: 1.19-2.17, $P = 1.79 \times 10^{-3}$), specifically for benzodiazepines (HR: 1.82, 95%CI: 1.23-2.64, $P = 1.52 \times 10^{-3}$) but not for Z-drugs (HR: 1.35, 95%CI: 0.90-2.04, $P = 1.50 \times 10^{-1}$), is associated with an increased risk of dementia and impaired cognitive function, as well as reasoning, reaction time, visual memory, and numeric memory. Drug-target MR analysis suggested a potential causal association between the benzodiazepine target genes and dementia, as well as impaired cognitive function. These associations were largely replicated in the summary-data-based MR and external cohort validation. Protein-protein interaction network revealed that benzodiazepine drug targets, such as GABRG3 and BRD3 interacted with the risk genes of cognitive function. Co-localization analysis provides further evidence supporting the true causal association between GABRG3 in the brain and impaired reasoning ability.

Conclusions: Our results suggest that benzodiazepine use may be causally linked to increased risk of dementia and impaired cognitive function. Both observational and genetic evidence highlight safety concerns related to the adverse effects of benzodiazepines on dementia risk and cognitive function among individuals with insomnia.

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Becoming sleep-drunk during alcohol withdrawal treatment: narcolepsy-like condition displaying sleep attacks and cataplexy, related to baclofen

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Introduction: Baclofen, a GABA-B receptor agonist, is commonly used for hypertonic muscular spasticity and off-label for alcohol use disorder (AUD). Narcolepsy is a hypersomnia disorder, mainly defined by excessive daytime sleepiness (EDS), symptoms related to REM sleep impairments and cataplexy (in type 1 narcolepsy). We report a case of a supposedly drug-induced narcoleptiform condition, involving cataplectic events and sleep attacks, appearing related to baclofen.

Materials and methods: A 40-year-old man, treated for AUD, increased the dosage of baclofen intake to 200 mg per day. Subsequently he developed severe EDS (Epworth Sleepiness Scale - ESS scoring at 17 /24) and experienced transient episodes of muscle atonia and uncontrollable sleep attacks (with reported average durations ranging from 60 seconds up to approximately 5 minutes), appearing to be triggered by intense and/or sudden emotions. These symptoms were distinct from any latent sedation. HLA phenotyping has been carried out alongside extensive blood sample tests. Polysomnography and multiple sleep latency tests (MSLT) have been performed accordingly, after the condition's acute phase.

Results: Clinical symptoms of EDS and signs of cataplexy progressively displayed complete remission upon gradual reduction of baclofen to alternating dosages of respectively 87.5 and 100 mg per day (ESS scoring at 3 /24). HLA class assessment did not reveal any alleles commonly associated with a genetic risk for narcolepsy. Moreover, both polysomnography and MSLTs ruled out narcolepsy and other significant primary sleep disorders. The striking temporal occurrence relations, between high-dose baclofen administration, the sudden symptom onset and its subsequent total remission upon dosage decrease, suggest a possibly causal tie. Causal relation is further suggested by the herewith documented absence of a formerly undiagnosed narcolepsy-cataplexy. The present observations thereupon contrast with prior studies suggesting a potentially beneficial effect of baclofen on cataplexy. The observed clinical signs, could possibly be explained by an inhibition of neuronal orexinergic activity via baclofen-induced enhanced GABA-B receptor stimulation.

Conclusions: Our case report suggests that high-dose baclofen may generate a reversible condition that partially mimics narcolepsy-like signs, such as sleep attacks and cataplexy. Clinicians should be aware of this potential side effect, particularly when using baclofen at higher dosages and especially in an off-label context of an AUD treatment.

Acknowledgments: na

Chronic cannabis use and sleep architecture: A cross-sectional study using polysomnography in a clinical sample

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Introduction: The utilisation of cannabis as a self-administered remedy for sleep disturbances is increasingly common. The existing body of research on the subject encounters many challenges in delineating effects accurately, due to the multifaceted nature of influencing factors such as individuals' prior history of cannabis consumption, concurrent substance and medication use, and the presence of other medical conditions that are often not adequately controlled for. In addition, polysomnographic evidence remains limited.

Materials and methods: We conducted a retrospective cohort study of 1,449 patients referred to a Canadian sleep clinic between 2022 and 2024 for overnight polysomnography. Chronic cannabis use ($\geq$ once daily for $\geq$ 1 year) was reported by 151 patients (10.4%). Eleven polysomnography outcomes—total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency, REM latency, and N1, N2, N3, and REM sleep (both presence and duration were measured for the latter two, resulting in eleven

measured outcomes)—were modelled with outcome-appropriate regressions adjusted for 28 demographic, lifestyle, comorbidity, medication, and sleep-related covariates. HC3 standard errors and false-discovery-rate correction were applied. Robustness was evaluated via winsorised and trimmed datasets, two minimal-covariate specifications, exclusion of medication and morbidity blocks, and a 1:1 propensity score matched model.

Results: After multiple-correction testing, chronic cannabis use was associated with higher wake after sleep onset ($\beta = 21\%$; 95% CI +6.7% to +37.2%), lower sleep efficiency ($\beta = -3.8\%$; 95% CI -6.6% to -1.0%), and elevated N1 stage sleep ($\beta = +2.8$ percentage points (pp); 95% CI 0.3pp to 5.6pp). Nominally, total sleeping time was lower among individuals using cannabis ($\beta = -3.3\%$; 95% CI -6.3% to 0.3%). Effect directions and magnitudes persisted across sensitivity analyses. Compared to cannabis-naïve patients, individuals using cannabis were more likely to be male (SMD = 0.251), younger (SMD = -0.595), and showed higher rates of nicotine (SMD = 0.866), sedative (SMD = 0.244), antidepressant (SMD = 0.219), antipsychotic (SMD = 0.355), and opioid use (SMD = 0.207), as well as a higher rate of psychiatric disorders (SMD = 0.418).

Conclusions: Among sleep-clinic patients, long-term daily cannabis use was associated with greater nocturnal wakefulness and a slightly larger proportion of light sleep. The demographic and clinical profile of cannabis users in this study align with existing data, supporting ecological validity and generalisability of the findings. Our results highlight the need for better-controlled longitudinal studies examining dose, frequency, and formulation.

Acknowledgments: This study was performed through the Tranq Sleep Care network of clinics.

Dual-Edged Dosing: Dexamphetamine and Lisdexamfetamine Suppress Binge-like Eating but Disrupt Sleep in Female Rats

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Introduction: Binge eating disorder (BED), defined by recurring episodes of fast-paced, excessive food consumption over which individuals perceive a loss of control, is also frequently comorbid with sleep disturbances, particularly insomnia. Lisdexamfetamine, the only FDA-approved medication for BED, reduces the frequency of binge episodes and broadly suppresses appetite. However, its stimulant properties—mediated via the metabolic conversion to dexamphetamine—have raised concerns about sleep disruption, especially when lisdexamfetamine is taken in the evening to target when episodes of binge eating typically occur. Despite clinical subjective reports of iatrogenic sleep disturbances, little to no clinical or preclinical studies have objectively/quantitatively examined the impact of these medications on sleep physiology at efficacious binge-suppressant doses.

Materials and methods: To investigate the sleep-related consequences of lisdexamfetamine and dexamphetamine used to treat BED, adult female Long Evans rats were implanted with wireless telemetry devices capable of continuous polysomnographic (PSG) monitoring of EEG (fronto-parietal), EMG, activity, and temperature. Sleep stages (wake, NREMS, REMS) were scored over 19-hour periods (ZT23–ZT18) following intraperitoneal administration of dexamphetamine hemisulfate (0.1875–1.5 mg/kg) and equivalent doses of lisdexamfetamine mesylate (0.463–3.71 mg/kg) at ZT23. Binge-like eating was assessed separately using an intermittent access model, where animals with ad libitum access to standard chow received twice weekly 30-minute periods of exposure to a highly palatable fat-sugar mixture (8.6 kcal/g; 90% fat, 10% sugar) on non-consecutive days. Dosing for binge-like eating assessment occurred 30 minutes prior to binge access (ZT20–22) to model evening consumption patterns.

Results: Both lisdexamfetamine and dexamphetamine dose-dependently suppressed binge-like eating, but at the lowest effective doses, significant sleep disruptions were also evident. Specifically, both medications dose-dependently delayed sleep and REM sleep onset, increased the proportion of time spent awake, and reduced both NREM and REM sleep during the early light phase (i.e., first 3-6 hours post-administration). Notably, these effects occurred without overt compensatory rebound sleep during the remaining period of the light or dark phases.

Conclusions: These findings provide objective preclinical evidence that these stimulant-based treatments for BED induce substantial sleep impairments even at the lowest effective doses for effects on eating behaviour. This aligns with clinical concerns of subjective iatrogenic sleep disturbances

associated with lisdexamfetamine and its active metabolite, dexamphetamine. Given the bidirectional relationship between sleep loss and dysregulated appetite—including increased craving for calorie-dense foods following sleep loss—these results highlight a critical need for the development of BED treatments that do not interfere with sleep processes, especially in individuals vulnerable to comorbid binge eating and insomnia.

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Impact of Benzodiazepine Dose Reduction on Subjective Sleep and Anxiety in Insomnia Patients

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Introduction: Long-term prescription of benzodiazepine receptor agonists (BZRAs) for insomnia is common in clinical practice, despite the associated risks, such as cognitive impairment, dependence, and withdrawal symptoms. Although reducing or discontinuing BZRA use is recommended, few studies have examined its impact on subjective sleep and anxiety symptoms using validated rating scales after long-term hypnotic use. This study retrospectively investigated the effects of BZRA dose reduction or discontinuation on insomnia severity, subjective sleep quality, anxiety symptoms, and adverse events in patients with long-term hypnotic use.

Materials and methods: We reviewed the medical records of 13 patients with ≥ 12 months of BZRA use who underwent dose reduction or discontinuation between April 2018 and May 2019 at Kyoto University Hospital. Insomnia severity was evaluated using the Japanese version of the Insomnia Severity Index (ISI-J). Secondary outcomes included sleep quality (Pittsburgh Sleep Quality Index Japanese version, PSQI-J) and anxiety symptoms (Generalized Anxiety Disorder-7, GAD-7). BZRA doses were converted to diazepam-equivalents. Concomitant medications (antipsychotics and antidepressants) were converted to chlorpromazine- and imipramine-equivalents, respectively. Assessments were conducted at baseline and 2–4 weeks post-intervention. Adverse events and persistence of dose changes were monitored. This study conformed to the Declaration of Helsinki and was approved by the Ethics Committee of Graduate School of Medicine of Kyoto University (R0545-2).

Results: Diazepam-equivalent doses significantly decreased in both the discontinuation group (mean change: -4.6 ± 0.9 mg, $p < 0.05$) and the reduction group (-6.7 ± 4.9 mg, $p < 0.05$). Mean ISI-J scores showed no significant change: 12.0 ± 3.5 to 10.0 ± 4.0 ($p = 0.07$) in the discontinuation group and 8.2 ± 5.6 to 8.3 ± 6.1 ($p = 0.91$) in the reduction group. PSQI-J and GAD-7 scores also did not change significantly. Most patients in both groups had well-controlled insomnia ($\text{ISI-J} < 14$) at baseline. The incidence of adverse events, including somnolence, fatigue, abnormal dreams, and irritation, did not increase significantly. The maintenance rate of dose reduction/discontinuation was 100% in the discontinuation group and 83.3% in the reduction group over three months.

Conclusions: Dose reduction or discontinuation of BZRA after long-term use did not significantly worsen sleep or anxiety symptoms. Our findings suggest that, with appropriate monitoring and individualized support, particularly in patients with mild baseline insomnia, deprescribing BZRAs can be safe and feasible in clinical practice.

Optimizing timing and dose of melatonin administration: a randomized, double-blind controlled trial in healthy adults

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Introduction: Exogenous melatonin is widely used as a sleep aid, yet its overall effectiveness remains under debate because of inconsistent findings that possibly arise from heterogeneous experimental designs. In our recent meta-analysis, we demonstrated that administering exogenous melatonin mimicking its endogenous circadian rhythm—i.e., 3 hours before the desired bedtime—optimizes its sleep-inducing effects, while increasing the dose to 4 mg appeared to enhance sleep maintenance. This study aimed to replicate those findings in a clinical trial.

Materials and methods: Fourteen healthy adults (aged 22–40 years; 50% female) with no history of sleep disorders participated in this double-blind, randomized controlled trial. They underwent five experimental conditions:

Condition 1: 2 mg melatonin administered 30 minutes before bedtime, placebo 3 hours before bedtime.

Condition 2: Placebo 30 minutes before bedtime, 2 mg melatonin 3 hours before bedtime.

Condition 3: 4 mg melatonin 30 minutes before bedtime, placebo 3 hours before bedtime.

Condition 4: Placebo 30 minutes before bedtime, 4 mg melatonin 3 hours before bedtime.

Condition 5: Placebo 30 minutes and 3 hours before bedtime.

After the recruitment, participants also completed a habituation night without receiving any active substance or placebo. Polysomnography was used to assess sleep parameters. Sleep onset latency (SOL) was selected as the outcome measure for sleep promotion, while wake after sleep onset (WASO) served as the outcome measure for sleep maintenance. The impact of administration timing and dosage was analyzed using random-effects linear regression models.

Results: All melatonin conditions resulted in an approximate 10-minute reduction in SOL compared to placebo. Among the active treatment conditions, earlier time of administration was associated with a further SOL reduction ($\beta = -0.041$, $p = 0.034$). WASO was significantly reduced in Condition 4 ($\beta = -15.77$, $p = 0.049$) and showed a trend in Condition 3 ($\beta = 14.22$, $p = 0.084$). When conditions were grouped by dose, the 4 mg dose produced a significant reduction in WASO compared both to placebo and to the 2 mg dose ($\beta = -15.03$, $p = 0.028$). Adjusting for the time interval between administration and bedtime did not substantially change these results, and timing itself did not significantly predict WASO ($\beta = -0.006$, $p = 0.867$). Notably, compared to placebo, Condition 4 only was associated with a significant increase in N3 stage duration ($\beta = 30.07$, $p = 0.036$) and REM latency ($\beta = 28.47$, $p = 0.047$).

Conclusions: Our findings confirm that administering melatonin to mimic its endogenous, circadian pattern enhances its sleep-promoting efficacy. Specifically, melatonin administration 3 hours before bedtime significantly reduced SOL. Consistent with our meta-analysis, a dose of 4 mg improved sleep maintenance independently of the timing of administration. Moreover, for the first time, we provide evidence that the combination of an earlier administration time and a higher dose induces changes in sleep macroarchitecture suggestive of deeper sleep. Further research is needed to clarify the clinical relevance of these findings for insomnia treatment and to explore whether optimized melatonin administration parameters might lead to sustained changes in sleep microarchitecture.

Psychotropic Drug Induced Sleep Bruxism

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Introduction: Bruxism, a stereotyped oromandibular movement disorder, is a repetitive jaw muscle activity characterized by clenching or grinding of teeth and / or thrusting of the mandible. Two distinct circadian manifestations of Bruxism are (i) Sleep Bruxism which occurs during sleep and classified under the subgroup of Sleep related Movement Disorders (ii) Awake Bruxism, which occurs during wakefulness. Sleep Bruxism primarily occurs in younger population, more common amongst children as compared to adults. Sleep Bruxism can be comorbid with other sleep disorders like Obstructive Sleep Apnea (OSA), Parasomnias, Restless Leg Syndrome (RLS), Mandibular myoclonus and Rapid Eye Movement disorders. Bruxism can lead to several complications including jaw muscle hypertrophy, tooth wear, fracture or failure of teeth restorations and implants, sensitivity and pain in teeth, muscle or joints, Temporomandibular joint disc displacements, myofascial pain, headaches, insomnias and other sleep disturbances.

Materials and methods: The etiology of Sleep Bruxism is multifactorial which includes biological, physiological, psychosocial, environmental, genetic factors or can be secondary to medication usage. The most recent hypothesis on the etiology of Sleep Bruxism supports the roles of Central and

Autonomic Nervous Systems in the genesis of oromandibular activity during sleep. Moreover, Sleep bruxism may be seen as a centrally mediated condition which may be modulated by medications acting on the neurotransmitters of the Central Nervous System (CNS).

Results: An imbalance between Serotonergic and Dopaminergic pathways may play an important role in the genesis of rhythmic masticatory muscle activity and sleep bruxism. Iatrogenic Sleep Bruxism has been reported following treatment with several Psychotropic medications such as Selective Serotonin Reuptake Inhibitors (SSRIs), Antidepressants, Antipsychotics. A Psychotropic (or psychoactive) drug is a chemical substance that crosses the blood-brain barrier and acts primarily on the CNS where it affects brain function, resulting in alterations in perception, mood, consciousness, cognition and behavior.

Conclusions: One of the side effects of psychotropic drugs is Sleep bruxism. It is postulated that the mesocortical disinhibition provided by SSRIs may lead to dopamine depletion that manifests itself as Sleep Bruxism. Buspirone, an anxiolytic, corrects Bruxism by reducing Serotonergic activity and increasing Dopaminergic Activity. A detailed history, including past and current medications is a must for every patient reporting with a complaint of sleep bruxism.

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Rationale and Study Design for the Evaluation of Samelisant (SUVN-G3031) in a Phase-2 Study for the Treatment of Cataplexy in Patients with Narcolepsy

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Introduction: Samelisant (SUVN-G3031) is a potent and selective histamine 3 receptor inverse agonist, which works by modulating the histamine system, a key part of the brain's sleep-wake regulation. In animal models, Samelisant has shown wake-promoting effects and also modulated neurotransmitters with role in wake promotion and anticataplectic effects.

Materials and methods: Samelisant was evaluated in animal models of narcolepsy like orexin knockout mice and orexin-B SAP lesioned rats. Effects on cataplectic like episodes were measured using Electroencephalography (EEG). Rat brain microdialysis was performed to evaluate the modulation of cortical norepinephrine levels.

Results: Samelisant produced significant reduction in cataplectic like episodes in orexin knockout mice, similarly significant decrease in DREM (direct wake to REM sleep) episodes was observed in orexin-B SAP lesioned rats. Samelisant produced significant increase in cortical norepinephrine levels in rats. Based on the evidence from animal studies, Samelisant will be evaluated in a Phase-2 proof-of-concept study in the USA and Canada to treat cataplexy in patients with narcolepsy. The study will recruit about 129 narcolepsy type 1 (NT1) patients with an established diagnosis of NT1 according to the ICSD-3 TR or DSM-5 TR.

The proposed Phase-2 study is a placebo-controlled, double blind randomized, parallel-group study. After a prescreening period of 4-weeks, eligible patients will enter a 2-week baseline period to assess number of cataplexy attacks. Patients confirmed with continued presence of cataplexy as defined by at least 14 cataplexy attacks in a typical 2-week baseline period will be eligible for the double-blind treatment period. Patients will be treated for eight weeks with the investigational product.

The primary objective of the study will be to evaluate changes in weekly cataplexy rates in NT1 patients. Secondary objectives will be to evaluate the effectiveness of Samelisant on the Clinical Global Impression–Severity score and total Epworth Sleepiness Scale score. Other exploratory measures will be Clinical Global Impression of Change and Patient Global Impression of Change score, with regard to cataplexy, Health-related quality of life 5-dimension, 5-level questionnaire and Narcolepsy Severity Scale score.

Conclusions: Outcomes from animal models of narcolepsy suggest that Samelisant may have anticataplectic effects. The Phase-2 study results will inform the therapeutic utility of Samelisant for the treatment of cataplexy in NT1 patients.

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Self-reported sleep changes among medical cannabis users: Associations with symptom targets and use patterns

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Introduction: Cannabis is commonly used to manage sleep disturbances, with many users reporting improved sleep quality. However, it remains unclear which types of users experience sleep benefits and the specific aspects of sleep most affected. This study explored self-reported sleep changes among individuals who use cannabis for medical purposes and examined how changes related to use patterns and symptom targets.

Materials and methods: A cross-sectional online survey was conducted in British Columbia, Canada and completed by 614 participants recruited via social media ads; 490 reporting cannabis use for medical reasons were analysed. Most were long-time users (97.6% ≥ 1 year), used cannabis at least daily (88.2%), used within one hour of bedtime (77.1%), preferred smoked or vaporised methods (80.4%), and most commonly reported using cannabis to help sleep (78.8%), reduce/control anxiety (67.7%), or reduce pain (64.7%). Participants were predominantly female (58.5%) and White (87.5%), mean age 44.7 ± 14.7 years, with 80.4% having education below the bachelor's level. Measures included an adapted version of the Pittsburgh Sleep Quality Index to assess perceived changes in sleep since initiating cannabis use, a checklist of 31 symptom targets (covering mental health, pain, and neurological issues), and cannabis usage patterns. Univariable regressions (n=468) examined associations between sleep changes and demographics, symptom motivations, and usage patterns.

Results: Most participants reported improved sleep quality (78.6%), reduced sleep onset latency (75.5%), longer sleep duration (67.6%), and fewer awakenings (55.3%). Among prior sleep aid users (n=249), 65.5% reported reducing their usage since initiating cannabis use. Targeting anxiety (p = 0.002), targeting trauma (p = 0.002), and younger age (p < 0.001) predicted perceptions of reduced sleep onset. Female gender predicted greater perceived improvement in nighttime anxiety (p = 0.002) and sleep quality (p = 0.017), though the latter did not survive multiple-comparison correction. Longer cannabis use duration predicted less perceived improvement in waking during the night (p < 0.001) and ability to fall asleep within 30 minutes (p = 0.008). No clear associations emerged between THC:CBD ratios and sleep outcomes, nor between targeting pain and improved sleep.

Conclusions: Regular cannabis users frequently perceive improvements in their sleep, particularly those targeting anxiety and trauma symptoms. However, some benefits may diminish with longer use. Findings are based on retrospective, cross-sectional self-report; further research integrating diagnostic and subjective assessments is needed to better understand cannabis' impact on sleep across different populations.

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Psychiatric Disorders Affecting Sleep/Wake

Accurately predicting mood episodes in mood disorder patients using wearable sleep and circadian rhythm features

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Introduction: Wearable devices enable passive collection of sleep, heart rate, and step-count data, offering potential for mood episode prediction in mood disorder patients. However, current models often require various data types, limiting real-world application.

Materials and methods: Here, we develop models that predict future episodes using only sleep-wake data, easily gathered through smartphones and wearables when trained on an individual's sleep-wake history and past mood episodes. Using mathematical modeling to longitudinal data from 168 patients

(587 days average clinical follow-up, 267 days wearable data), we derived 36 sleep and circadian rhythm features.

Results: These features enabled accurate next-day predictions for depressive, manic, and hypomanic episodes (AUCs: 0.80, 0.98, 0.95). Notably, daily circadian phase shifts were the most significant predictors: delays linked to depressive episodes, advances to manic episodes.

Conclusions: This prospective observational cohort study shows sleep-wake data, combined with prior mood episode history, can effectively predict mood episodes, enhancing mood disorder management

A comparative study of sleep and suicidality in Major Depressive Disorder and bipolar depression

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Introduction: Both Major Depressive Disorder (MDD) and bipolar disorder (BD) are associated with sleep problems. Presence of sleep disturbances is manifested as more severe physical, mental, and psychological impairment in both the disorders. In BD it is associated with rapid cycling, anxiety, substance use comorbidities and suicide. The aim of the present study was to compare sleep disturbances and suicidality in patients with MDD and BD.

Materials and methods: Adult population of either sex having diagnosis of MDD or BD (irrespective of number of episodes and treatment status) as per DSM-5 were included in the study. Participants of BD having current manic episode, suffering from any other psychiatric disorder or use of any substance in dependent pattern except nicotine were excluded. The participants were evaluated on socio-demographic profile, depression severity, suicidal ideation and sleep problems with the help of Hamilton Depression Rating Scale (HAM-D), Becks scale for suicidal ideation, insomnia severity index (ISI), Epworth sleepiness scale (ESS) and Pittsburgh sleep quality index (PSQI) respectively.

Results: A total of 44 patients (32 males & 12 females) participated in the study (n=22 each, 15 males and seven females in MDD group and 17 males and five females in BD group). The mean age of the unipolar group and bipolar group was 23.7 (7.7) years and 38.1 (12.7) years respectively. Most of the participants in MDD group were unmarried (n=20,90.9%). BD group had more married participants (n=17,77.3%). The mean subjective sleep latency and total sleep time in the MDD and BD group were 102.3 minutes, 343.6 minutes and 98.9 minutes, 337.5 minutes respectively suggesting an average sleep of less than six hours with high sleep latency in both the groups. The mean HAM-D score of MDD and BD group were 18.7 and 17.3 respectively suggesting moderate depression in both groups. The mean score on Beck's suicidal ideation scale were 9.5 and 8.5 in MDD and BD group respectively. The total scores on ISI and PSQI were high in both the groups suggesting significant sleep problems and clinical insomnia of moderate severity as per ISI scores (MDD group: ISI-19(3.4),PSQI-12.6 (3.3); BD group: ISI-15.2 (6.6),PSQI-12.1 (3.9). No significant difference was observed between depressive scores, suicidal intent and total PSQI scores between the two groups. However, significant difference was observed between total ISI scores and subscores between both the groups. No significant correlation was observed between depression and sleep problems and suicidality and sleep problems in the MDD group. However, a significant positive correlation was observed between HAM-D scores and total ISI scores, sleep latency, total PSQI scores in the BD group. A significant positive correlation was also observed between suicidal ideation and total ISI scores, sleep latency, total PSQI scores in the BD group. A significant negative correlation was observed between HAM-D scores and total sleep time and between suicidality and total sleep time in the BD group.

Conclusions: Both the MDD and BD group showed significant sleep problems. However, depressive symptoms and suicidal ideation correlated with sleep problems in BD group only.

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A Long-Lasting Low-Threshold Spiking in Laterodorsal Tegmental Glutamatergic Neurons Regulates Anxiety Hyperarousal

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Introduction: Anxiety-associated hyperarousal represents one of the most prevalent emotional sleep disturbances globally. In the context of an increasingly fast-paced and high-stress society, this condition significantly compromises quality of life and poses a substantial public health burden. Although conventional anxiolytic agents can alleviate symptoms to some extent, their clinical utility is often limited by issues of drug tolerance and adverse side effects. The lack of effective, targeted interventions is largely attributable to an incomplete understanding of the underlying neural circuitry. The laterodorsal tegmentum (LDT), a brainstem nucleus implicated in arousal regulation, receives dense projections from multiple anxiety-related regions, suggesting a potential integrative role in mediating anxiety-related hyperarousal states. Utilizing a chronic stress-induced anxiety model, we identified the LDT as a candidate node in this regulatory network. The present study aims to elucidate the functional involvement of the LDT in anxiety-related hyperarousal and to dissect the underlying neurobiological mechanisms.

Materials and methods: This study established a chronic unpredictable mild stress (CUMS) model to induce anxiety in mice, verified through open field and elevated plus maze tests, while monitoring sleep-wake alterations and identifying anxiety-related brain regions. In vitro electrophysiology was used to examine neuronal changes in the laterodorsal tegmentum (LDT), focusing on ion dynamics underlying the long-lasting low-threshold spike (LLTS) in glutamatergic neurons. Optogenetics combined with behavioral assays enabled precise induction of LLTS to assess its effects on anxiety and sleep. Neural circuitry was mapped using retrograde tracing and the Cre-loxP system to trace inputs regulating anxiety hyperarousal. Neuropharmacological approaches evaluated the impact of Cav 3.1 channel inhibitors and anxiolytics on behavior and arousal, while RNA interference of Cav 3.1 further validated its role through behavioral and sleep assessments.

Results: After CUMS, mice showed anxiety-like hyperarousal and a 132% increase in wakefulness, with elevated c-fos in LDT. LDT glutamatergic neurons shifted toward a higher proportion (76%) of long-lasting low-threshold spike (LLTS), while GABAergic and cholinergic neurons remained unchanged. Optogenetic activation of LLTS neurons induced anxiety and wakefulness; general activation of LDT glutamatergic neurons increased only wakefulness. LDT glutamatergic neurons receive diverse upstream inputs, with 16% from the LH. The LH^{GABA}-LDT^{Vglut2} circuit was key in anxiety hyperarousal. LLTS was mediated by T-type calcium channels; pharmacological inhibition of T-type calcium channels and genetic knockdown of Cav3.1 expression in LDT neurons reduced LLTS firing and normalized anxiety hyperarousal.

Conclusions: These findings suggest that Cav3.1 channels are crucial mediators of LDT glutamatergic plasticity in anxiety hyperarousal, offering a potential therapeutic target for treating anxiety hyperarousal and related sleep disorders. Our work offers insights into the neural mechanisms underlying anxiety-related sleep disorders.

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An AI-Driven Model for Depression Detection Using Sleep Heartbeat and Breathing Signals

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Introduction:

Autonomic dysfunction, marked by changes in heart rate and breathing patterns, is a core symptom of depression. However, the role of autonomic dysfunction during sleep as a marker for depression is not well understood. This study evaluates the utility of polysomnography (PSG)-derived cardiorespiratory signals for depression detection.

Materials and methods:

We examined clinical polysomnography (PSG) data and electronic health records collected between 2021 and 2025 from Sir Run Run Shaw Hospital (RRS). Depression cases were identified based on the International Classification of Diseases, 10th Revision (ICD-10) diagnosis codes, Hamilton Depression Rating Scale (HAMD) scores of 8 or higher, and/or chief complaints suggestive of depression. Age- and sex-matched controls were selected based on ICD-10 diagnoses or HAMD scores. A foundational model approach was employed: abdominal (ABD) signals and RR intervals (RRI) derived from electrocardiogram signals were first used to pre-train a model to predict other PSG channels. Subsequently, the model was fine-tuned using logistic regression for depression classification. Data from RRS was used for model training and internal validation (randomly split into 90% training and 10% internal testing sets). Model performance was assessed using the area under the receiver operating characteristic curve (AUROC), sensitivity, and specificity.

Results:

The study included 1303 depression cases and 1978 controls. The mean age was 48.9 ± 17.4 years for cases and 48.9 ± 17.3 years for controls, with 66.2% and 66.1% female, respectively. The model achieved an AUROC of 0.761, with an accuracy of 0.706, sensitivity of 0.735, and specificity of 0.674 in the internal validation set.

Conclusions:

Our findings demonstrate that AI-driven analysis of sleep-derived heartbeat and breathing signals can effectively detect depression, with moderate sensitivity and specificity. By leveraging cardiorespiratory signals, this model offers a sleep-based solution for in-home depression screening. This approach paves the way for precision mental health tools that support early identification and intervention for depression in community settings.

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An AI Prediction Model for Depression and Anxiety Using Polysomnographic Electroencephalography Signals

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Introduction:

Depression and anxiety are two of the most prevalent mental disorders globally, yet a significant portion of symptomatic cases remain undiagnosed. Sleep disturbances often emerge early in the course of depression and anxiety and are among their most prevalent symptoms, with electroencephalography (EEG) features detectable via polysomnography (PSG). This study aims to determine whether PSG-EEG signals can predict depression and anxiety using an AI model.

Materials and methods:

We analyzed PSG-EEG and clinical records from Shanghai Mental Health Center from 2023 to 2024. Participants were classified as depressed (HAMD ≥ 17) or non-depressed (HAMD < 17) based on the Hamilton Depression Rating Scale, and as anxious (HAMA > 21) or non-anxious (HAMA ≤ 14) based on the Hamilton Anxiety Rating Scale. We designed a token-based machine learning framework, which transforms PSG-EEG signals into symbolic representations. A tokenizer is pretrained via self-supervised learning on miscellaneous EEG data. The tokenizer discretizes continuous brain signals into a sequence of symbolic tokens using a codebook of 512 entries. For each sample, we identified the most informative tokens by computing class-wise frequency differences between groups. Tokens showing statistically significant group differences ($p < 0.05$) were further ranked by Cramér's V to assess their effect size, and the top 20 tokens were selected as features. We then extracted term frequency-inverse document frequency (TF-IDF) representations over these tokens for each subject and trained a support vector machine (SVM) for binary classification. Models were trained and evaluated using an 80/20 train-test split. Model performance was assessed using accuracy, unweighted average recall, macro F1, and weighted F1 for binary classification.

Results:

We analyzed 93 cases (mean age 40.5 years, 66.1% female) and 128 controls (mean age 39.2 years, 72.0% female) for depression, and 69 cases (age 38.7 years, 75.4% female) and 83 controls (mean age

42.9 years, 63.9% female) for anxiety. In the binary classification task predicting depression from controls, our model achieved an accuracy of 0.73, unweighted average recall of 0.72, macro F1 of 0.72, and weighted F1 of 0.73. In the binary classification task predicting anxiety from controls, our model achieved an accuracy of 0.74, unweighted average recall of 0.76, macro F1 of 0.74, and weighted F1 of 0.74. We observed distinct patterns in the frequency distribution of tokens across sleep stages. For instance, one token appeared more frequently during light sleep (N1/N2) but not in deep sleep (N3) or REM. These findings indicate that the model has learned internal representations that correspond meaningfully to different stages of sleep. The frequency distribution of these components may serve as interpretable, stage-sensitive markers reflecting underlying neural or physiological dynamics.

Conclusions:

This study demonstrates that PSG-EEG features can predict depression and anxiety with an interpretable AI model. These findings highlight the utility of sleep physiology in enabling sleep-based depression screening, offering precision mental health risk assessment and intervention in Asian mental health settings.

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A PVT^{D2R}-CeA circuit underlies sleep disturbance and negative effects induced by morphine withdrawal

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Introduction: Opioid use disorder (OUD) is a chronic, relapsing condition that contributes to a substantial global health burden. Individuals suffering from OUD often experience intense and prolonged withdrawal symptoms, including sleep disturbance and negative emotional states, which significantly increase the risk of relapse. The paraventricular nucleus of thalamus (PVT) plays a crucial role in opioid withdrawal, yet its specific role in the sleep disturbance and negative effects induced by opioid withdrawal remains unclear.

Materials and methods: Firstly, following six days of chronic morphine administration, we monitored sleep architecture and negative affective states of mice during withdrawal, and further assessed the impact of chronic sleep deprivation on these affective states. Secondly, we utilized immunofluorescence staining, in situ hybridization and fiber photometry recording to determine the involvement of PVT and dopamine D2 receptor-expressing neurons in the PVT (PVT^{D2R} neurons) in morphine withdrawal. Finally, using whole-cell patch clamp recordings and chemogenetic approaches, we investigated the role of PVT^{D2R} neurons and their projections to the central amygdala (CeA) in sleep disturbance and negative effects induced by morphine withdrawal.

Results: During the first week of withdrawal, mice exhibited increased wakefulness, which was accompanied by anxiety-like and depression-like behaviors. Notably, chronic sleep deprivation during this withdrawal further aggravated these negative affective states. To investigate the underlying neural mechanisms, the immunofluorescence staining and in situ hybridization study revealed the activation of PVT^{D2R} neurons in the PVT. Consistently, real-time fiber photometry recordings further confirmed the activation of these neurons during withdrawal. Moreover, electrophysiological recordings demonstrated that PVT^{D2R} neurons projecting to the CeA showed a significant reduction in both frequency and amplitude of spontaneous inhibitory post synaptic currents one week after withdrawal. Subsequently, chemogenetic inhibition of either PVT^{D2R} neurons or PVT^{D2R}-CeA projection during withdrawal alleviated sleep disturbance and negative emotional symptoms, while chemogenetic activation of same neurons or projection exacerbated these symptoms.

Conclusions: In conclusion, this study highlights the critical role of PVT^{D2R} neurons and PVT^{D2R}-CeA circuit in mediating sleep disturbance and negative emotional states induced by morphine withdrawal, offering new insights to the mechanisms of OUD and providing potential strategies to prevent relapse.

Association between EEG Power during Sleep and Attention Levels in Patients with Major Depressive Disorder

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Introduction: Major depressive disorder (MDD) is associated with cognitive impairment through unclear mechanisms. We examined the relationship between sleep electroencephalogram (EEG) power and attention level in MDD.

Materials and methods: Forty-seven untreated patients with MDD and forty-seven age- and sex-matched controls were included. We examined relative EEG power during non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep by fast Fourier transform. The Attention Network Test (ANT) was performed to evaluate attention levels.

Results: Compared to controls, patients with MDD had lower theta power during NREM ($P = 0.018$) and REM ($P = 0.002$) sleep, while higher beta power ($P = 0.050$) during NREM sleep and delta power ($P = 0.018$) during REM sleep. Regarding attention level, patients with MDD had lower levels of accuracy ($P = 0.021$), longer mean reaction time ($P < 0.001$), poorer manifestations of the alerting effect ($P = 0.038$) and worse executive control ($P = 0.048$). Moreover, decreased theta power during NREM sleep was correlated with worsened accuracy ($\beta = 0.329$, $P = 0.040$), decreased theta power during REM sleep was correlated with worsened alerting effect ($\beta = 0.355$, $P = 0.020$), and increased delta power during REM sleep was correlated with longer mean reaction time ($\beta = 0.325$, $P = 0.022$) in patients with MDD. No association between ANT performance and other frequency bands was observed in patients with MDD.

Conclusions: Our findings suggest that patients with MDD manifest impaired selective attention function that is associated with decreased theta power during NREM/REM sleep and increased delta power during REM sleep.

Associations Between REM Sleep and Depressive Symptoms in Pediatric Narcolepsy Type 1

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Introduction: Children and adolescents with Narcolepsy Type 1 (NT1) have higher rates of depression and more disrupted nighttime sleep than healthy controls (HC) (Abenza-Abidula et al., 2023; American Academy of Sleep Medicine, 2014). In the otherwise healthy adolescents, sleep disruptions, particularly in REM sleep, have been associated with depressive symptoms (Riemann, 2020; Pesonen et al., 2019, Thorpy et al., 2024). However, the relationship between REM disturbances and depressive symptoms in pediatric NT1 is understudied. We hypothesized that shorter REM onset latency, increased total REM duration, and more REM fragmentation would be associated with depressive symptoms in NT1 and HC groups, with stronger associations in the NT1 group.

Materials and methods: 24 NT1 and 25 HC participants, aged 9-20 years old, completed the Children's Depression Inventory (CDI) and underwent an in-lab polysomnogram. We used linear regression controlling for age, gender, and SSRI/SNRI use to determine associations between depressive symptoms and REM sleep onset latency, total REM duration, and median REM bout duration as well as other sleep fragmentation variables such as N3 median bout duration and global transitions index.

Results: NT1 participants had higher CDI T-scores than HC participants indicating higher depressive symptoms ($p < 0.001$). Across groups, shorter REM median bout duration, shorter N3 median bout duration, and increased global transitions index were associated with higher CDI total score (p 's < 0.05). Within groups, increased global transitions index was associated with higher CDI total scores in HC ($p = 0.003$), but we found no significant associations with sleep variables and CDI scores within the NT1 group.

Conclusions: Sleep fragmentation, across sleep and notably affecting REM and N3 sleep, may reflect or contribute to increased depressive symptoms in children and adolescents. Future studies should recruit larger cohorts of children and adolescents with NT1 with varying degrees of mood symptoms to clarify these relationships and guide targeted interventions for depression in this population.

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Associations of Atypical Depressive Features with Sleep disturbances: Evidence from the Cluster Analysis

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Introduction: Depression remains a leading cause of global disease burden, with atypical Depression (ADep) as a clinically distinct subtype characterized by mood reactivity, hypersomnia, increased appetite, and fatigue. Despite its unique symptomatology, the relationship between ADep and sleep disturbances in Asian populations is underexplored. This study examines associations among atypical depressive features, insomnia, and sleep quality among individuals in Hong Kong.

Materials and methods: We recruited 115 participants (mean age: 53.4 ± 11.0 ; female: $n = 76$, 66.1%) with non-remitted major depressive disorder (MDD) from the local public psychiatric outpatient clinics. They were assessed by the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Supplement (SIGH-ADS). Sleep quality and disturbances were measured with Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Epworth Sleepiness Scale (ESS). Unsupervised clustering algorithms, including k-means clustering, hierarchical clustering, and Gaussian mixture model, were applied to define symptom-based clusters. K-means clustering with two clusters was selected based on validity indices.

Results: Two clusters were identified after adjustment for age, sex and education, with cluster 1 ($n = 45$, 39.1%, female: $n = 33$) having significantly higher score on 17-item Hamilton Rating Scale for Depression (HDRS-17) and 8-item atypical neurovegetative symptoms (ANS) (HDRS, Cluster 1 mean score = 19.34 ± 2.73 vs Cluster 2 mean = 11.75 ± 2.72 , $p < 0.01$; ANS, Cluster 1 mean score = 8.24 ± 1.74 vs Cluster 2 mean = 4.50 ± 1.73 , $p < 0.01$, respectively). Cluster 1 showed a higher proportion of clinically significant insomnia ($ISI \geq 15$) and excessive daytime sleepiness ($ESS \geq 14$) (Insomnia, 66.7% vs. 37.1%, OR: 3.57, 95% CI: 1.44, 8.85, $p = 0.01$; EDS, 31.1% vs. 18.6%, OR: 2.93; 95% CI: 1.06, 8.10, $p = 0.04$, respectively) than Cluster 2. Ostensibly, cluster 1 exhibited significantly higher scores on PSQI (Cluster 1 mean score = 14.61 ± 3.15 vs Cluster 2 mean = 12.36 ± 3.15 , $p = 0.01$) and ISI (Cluster 1 mean score = 12.75 ± 3.15 vs Cluster 2 mean = 9.04 ± 4.48 , $p < 0.01$), indicating poorer sleep quality and greater insomnia severity. For the single item from SIGH-ADS, there was no significant difference on the item "hypersomnia" across two clusters, but "difficulty awakening" (Cluster 1 mean = 1.68 ± 0.72 vs Cluster 2 = 0.28 ± 0.72 , $p < 0.01$) was more pronounced in Cluster 1.

Conclusions: This study reveals that there was a cluster having more atypical depressive symptoms (39.1%) among individuals with non-remitted MDD in the psychiatric clinic, with significant associations between atypical depressive features and a series of sleep disturbances characterised by more severe and prevalent insomnia, poor sleep quality, difficulty awakening and excessive daytime sleepiness. Future research should incorporate objective sleep measures, larger and broader samples to validate these results for better subtyping and potential personalised intervention.

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Can Wake after nightmare duration (WAN) serve as a Clinical marker of Trauma-related nightmares' impact during sleep?

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Introduction: Trauma-related nightmares (TRNs) are vivid and specific sleep phenomena with strong ties to traumatic events, provoking intense distress and abrupt awakenings. Beyond being a PTSD symptom, TRNs can persist independently and vary in replicativity: replicative (REP) closely mirror the trauma, partially replicative (PREP) mix trauma elements with symbolic content, and non-replicative (NREP) retain only thematic traces. Despite their impact, objective markers of TRNs' severity remain scarce. Wake After Nightmare (WAN) duration—the time a patient remains awake after a TRN—may index TRN intensity. This study evaluates WAN as a potential clinical marker of TRN burden during sleep.

Materials and methods: We conducted a prospective, multicentric observational study (SOMMEPT) involving 74 French former military personnel with PTSD (PCL-5 > 44) from a cohort of 131. Sleep was recorded at home over seven nights using the Dreem V2 EEG headband and Empatica E4 wristband. Across the last five nights, 412 TRN-related awakenings were identified. Median WAN duration per patient was calculated, and participants were divided into tertiles (Low, Mid, High WAN). Assessments included standardized clinical questionnaires (PTSD, depression, insomnia, sleep quality), EEG-derived sleep metrics, and TRN replicativity/phenomenological features from the TRNS-FR. Group comparisons used Kruskal-Wallis, Mann-Whitney U, and Fisher's exact tests.

Results: Weekly TRN frequency was 4.40/week across participants. WAN groups showed: Low (n = 24) = 0.97 min (3.03 TRNs/week), Mid (n = 25) = 2.06 min (3.53 TRNs/week), High (n = 25) = 13.40 min (2.63 TRNs/week). Although TRN frequency did not differ significantly, the High WAN group displayed higher BDI scores (p = 0.0499) and a trend toward elevated PTSD re-experiencing symptoms (p = 0.0355). They also had shorter total sleep time (p = 0.0147) and reduced NREM duration (p = 0.0262) compared to the Low WAN group. High WAN patients reported more NREP TRNs (p = 0.0488), vivid sensations (p = 0.0488), realistic imagery (p = 0.0223), tremors (p = 0.0378), and fear of dying (p = 0.0209).

Conclusions: Longer WAN durations may indicate stronger nocturnal TRN burden, with heightened emotional aftereffects, disrupted sleep, and more trauma-specific content. While frequency remained stable, the association between WAN and nightmare replicativity supports its clinical relevance as a simple, objective marker of TRN severity. Further studies should assess its potential for real-time monitoring and personalized follow-up in trauma-exposed populations.

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Circadian Motor Asymmetry and Homeostatic Dysregulation in Adults with ADHD: An Actigraphic Study

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Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental condition characterized by persistent inattention, motor hyperactivity, and impulsivity, often persisting into adulthood.

Concerning wakefulness, a motor hyperactivity is commonly reported, while reduced sleep efficiency and prolonged sleep onset latency are reported during sleep. Taken together, these dimensions might reflect altered circadian rhythmicity.

As hyperactivity represents one of the core features of ADHD, objective measurement of motor activity could enhance diagnostic precision, and inform follow-up strategies.

Actigraphy—an accelerometer-based wrist-worn device—offers an ecological method to monitor motor activity across 24-hour periods in both wake and sleep states.

Prior studies have suggested a small but reliable phase difference in circadian motor activity between the dominant and non-dominant wrist, interpreted as a potential reflection of asymmetric hemispheric regulation of sleep-wake processes. The left hemisphere, being more sensitive to homeostatic sleep pressure (Process S), may deactivate earlier in the evening, while the right hemisphere may remain

active longer, influenced more by the circadian drive (Process C). This functional asymmetry has been documented in a healthy population. Investigating such asymmetry in adults with ADHD may shed light on altered regulation of circadian and homeostatic mechanisms and potentially serve as an objective biomarker of the disorder.

We investigated:

1. Between-group differences in left wrist motor activity to detect the presence or absence of the post-lunch dip, previously reported as blunted in ADHD;
2. Within-group differences in acrophase (right vs. left wrist) as an index of hemispheric asymmetry;
3. Presence of a circadian phase shift between wrists, particularly in healthy controls.

Materials and methods: We enrolled 21 adults with ADHD (11 females; mean age 39.7 ± 8.9) and 13 healthy controls (7 females; mean age 22.7 ± 1.06). Participants wore Actiwatch AW64 devices on both wrists for seven consecutive days, pressing the event marker to signal bedtime and wake-up. Data were analyzed with the Actiwatch Activity & Sleep Analysis software.

Results: 1. Post-lunch dip: Functional linear modeling (FLM) of left wrist activity showed a reduced post-lunch dip in the ADHD group compared to controls, especially between 14:00 and 16:00. Although the F-statistic did not exceed the maximum critical threshold, pointwise values indicated a subtle but consistent difference

2. Acrophase: ADHD: no significant difference between left (14.85 ± 1.37) and right (14.96 ± 1.25) wrist acrophase ($p = 0.200$). Controls: significant difference between left (15.47 ± 1.26) and right (15.24 ± 1.21) wrist acrophase ($p = 0.043$).

An ANOVA revealed a significant Group $\times$ Side interaction ($F(1,54) = 5.35, p = 0.025$),

3. Circadian pattern: Controls showed a statistically significant difference between wrists, absent in ADHD.

Conclusions: Our findings reveal altered circadian motor patterns in ADHD: absent post-lunch dip, absence of differences in acrophase and absence of differences between wrists in the circadian pattern, potentially caused by a homeostatic dysregulation. Motor asymmetry may serve as a non-invasive biomarker in ADHD. However, small sample size and age differences limit generalizability. Larger, age-matched studies are needed to confirm these results.

Clinical Association Between Current Depressive Symptoms and Odds Ratio Product in US Sleep Centers

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Introduction: The Odds Ratio Product (ORP) is a well-established metric for assessing sleep depth and the sleep-wake continuum. Compared to traditional sleep measurements, ORP has demonstrated superior sensitivity in evaluating sleep quality. While several studies have examined ORP variations across sleep stages and their correlations with both objective and subjective sleep parameters in healthy individuals and those with sleep-wake disorders, evidence remains limited regarding its role in psychiatric conditions. Nevertheless, it is plausible to hypothesize that ORP may serve as a novel and sensitive biomarker for identifying sleep characteristics associated with depressive symptoms.

Materials and methods: Methods

We conducted a retrospective analysis of 829 adults whose overnight polysomnography (PSG) recordings and clinical data were collected in two naturalistic, multicentre studies: the Sleep Analysis of Depressive Burden (SADB) study (ClinicalTrials.gov Identifier: NCT04232267) and the Sleep Signal Analysis for Current Major Depressive Episode (SAMDE) study (ClinicalTrials.gov Identifier: NCT05708222). Before PSG, all participants completed a demographic/medical questionnaire and the Patient Health Questionnaire-9 (PHQ-9). PSG recordings were sleep-staged automatically with the

STAGER software, and the ORP was calculated from central EEG derivations via Cerebra Medical's algorithm. Mean and standard-deviation ORP values were extracted for the whole night and for Wake, N1 + N2, N3 and REM periods. Associations between ORP metrics and depressive burden were tested with linear regression for PHQ-9 total score, and with logistic regression for PHQ-9 ≥ 10 , incorporating linear and quadratic ORP terms, and adjusting for age and sex. Fixed- and mixed-effects model structures (random intercepts $\pm$ slopes by clinical centre group) were compared with Akaike Information Criterion (AIC); the best-fitting model for each analysis was refitted with restricted maximum likelihood.

Results:

Fixed-effects models consistently outperformed mixed-effects alternatives (lowest AIC), indicating that centre-to-centre variability did not significantly influence the findings. Mean ORP across the entire night and in light-sleep (N1 + N2) showed a significant quadratic (U-shaped) association with both the PHQ-9 Total Score and PHQ-9 ≥ 10 . Thus, individuals with either elevated (indicative of shallower sleep) or reduced (indicative of deeper sleep) mean ORP values across the night and in deep sleep exhibited higher depression scores compared to those with average ORP values. Instead, the mean ORP in deep sleep (N3) showed a significant and positive linear association with them. The standard deviation of ORP across the entire night showed a linear negative association the PHQ-9 Total Score and PHQ-9 ≥ 10 , while the standard deviation of ORP in deep sleep (N3) showed a significant and positive linear association with only the PHQ-9 Total Score.

Conclusions:

A complex relationship between mean ORP and PHQ-9 scores was found in our study, highlighting a direct correlation in deep sleep and a U-shaped pattern in lighter sleep stages and overall sleep architecture. Our findings demonstrate the potential utility of ORP analysis in clinical sleep settings as a non-invasive marker of depression severity. Since ORP can be readily derived from PSG data, its integration into routine sleep evaluations may improve the detection of clinically relevant depressive symptoms.

Discordance in Physiological and Subjective Stress Measurements: Hair Cortisol, Self-reported Stress Scales and Heart Rate Variability in Healthcare Night-shift Workers

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Introduction: Chronic stress increases risks of multiple diseases. Stress is usually evaluated by subjective psychological scales. Hair cortisol concentration (HCC) and Heart rate variability (HRV) have also been used as stress indicators. However, there is no gold standard to measure stress.

Materials and methods: In-total 74 healthcare workers with regular night-shifts were recruited. HCC was measured by liquid chromatograph/mass spectrometer. Subjective psychological scales were performed, including Perceived Stress Scale-14 (PSS), Depression Anxiety Stress Scales-21, Epworth Sleepiness Scale, Fatigue Assessment Scale and Subjective Happiness Scale. HRV indices (SDNN, RMSSD, HF and LF) were measured from 24h-Holter. All these data were collected both before and after 3-month stress management.

Results: HCC showed positive correlation with PSS ($r = 0.228$, $P = 0.050$) but not with other scales and HRV indices in cross-sectional analysis based on baseline data. Longitudinally, subjective scales showed a significant remission in stress and adverse mood after 3-month intervention. However, HCC was significantly elevated after stress management, and HRV indices, including 24h SDNN, nighttime SDNN, RMSSD, HF and LF/HF, were decreased (all $P < 0.05$). Upon the 3-month intervention, the changes of HCC did not correlate with the changes of scale scores, but correlated with the changes of HRV indices (negatively with 24h and daytime LF/HF and LFnu, and positively with daytime HF).

Conclusions: This study aims to explore the correlation between physiological stress indicators and subjective psychological scales. Subjective and objective measures of stress could exhibit differential

changes upon the same interventions. The combined measurements would be recommended as routines for the clinical practice.

Effect of transcranial direct current stimulation on the sleep electroencephalogram in major depressive disorder: findings of intrinsic multiscale entropy from a randomized controlled study

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Introduction: Transcranial direct current stimulation (tDCS) is a non-invasive method of brain stimulation used to treat individuals with major depressive disorder (MDD). In this study we determined the differences in sleep electroencephalogram (EEG) complexity between patients with and without MDD.

Materials and methods: Twenty-two healthy controls (HCs) and 37 MDD patients were recruited. The patients were assigned randomly to receive either active tDCS stimulation (n = 19) or sham stimulation (n = 18). To assess sleep structure and EEG complexity, polysomnography was applied to all MDD patients and HCs. Intrinsic multi-scale entropy (iMSE) was utilized to quantify the complexity of EEG signals.

Results: By comparison with PSG data from HCs, the characteristic EEG complexity during rapid eye movement (REM) sleep was validated in MDD patients. More importantly, there was a notable increase in the iMSE of non-REM sleep stage 1(N1) following active tDCS stimulation compared to pre-stimulation, and there was no longer a significant distinction between patients and HCs. There was a marked contrast in complexity between the sham group and HCs both before and after tDCS sham stimulation.

Conclusions: tDCS was shown to nearly restore the sleep N1 EEG complexity in MDD patients to that of HCs. The intervention effect of tDCS stimulation in MDD patients is characterized by iMSE of EEG signals.

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Effects of a Dual Orexin-receptor Antagonist on Sleep Architecture and Opioid Withdrawal Severity during a Buprenorphine Taper

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Introduction: Sleep disturbance is a key component of opioid withdrawal that drives negative opioid use disorder (OUD) treatment outcomes, but the relationship between sleep architecture and opioid withdrawal severity during treatment initiation remains poorly understood. This study builds on prior research by examining associations between sleep architecture and opioid withdrawal during administration of suvorexant, a dual-orexin receptor antagonist, versus placebo during an opioid withdrawal paradigm.

Materials and methods: These analyses were conducted on N = 26 participants who completed the 11-day (10 night) parent study. In brief, participants with OUD who were seeking supervised withdrawal treatment were first inducted and maintained on 8/2mg to 16/4mg buprenorphine/naloxone (hereafter buprenorphine) for 3 days, then randomized to 0mg, 20mg, or 40mg suvorexant for the duration of the study. Participants were then tapered off buprenorphine over a 4-day period followed by a 4-day post-taper observation. Each night, participants wore a 3-lead electroencephalography device (Sleep Profiler) to objectively measure sleep architecture. Participants also completed the 16-item Subjective Opiate Withdrawal Scale (SOWS) at 4 timepoints each day.

Linear regression models were used to model the correlation of total rapid eye movement (REM) sleep, REM percent, REM onset latency, total sleep time (TST), and total NREM3 sleep with subjective opioid withdrawal outcomes (assessed via the SOWS). For the linear regression models, each continuous variable was averaged per participant within each phase (stabilization, taper, post-taper), to account for

repeated measures. The effect of suvorexant versus placebo on sleep architecture and subsequent opioid withdrawal symptomatology was modeled with a 2-group comparison, without differentiation of suvorexant dose. Suvorexant moderation was only examined during the taper and post-taper phases, as suvorexant had not yet been administered in the stabilization phase. All analyses were conducted using R version 4.2.3 with statistical significance set at $\alpha = 0.05$.

Results: During the taper, increased total REM sleep and suvorexant were each associated with reduced SOWS (both p 's < 0.05), with a marginally significant interaction between suvorexant and total REM sleep ($p = 0.051$). Similarly, increased REM percent was associated with reduced SOWS (both p 's < 0.05). A significant interaction between total REM percent and suvorexant ($p = 0.013$) indicated that suvorexant attenuated the association between REM percent and withdrawal severity.

In the post-taper phase, the pattern reversed. Increased REM and total sleep time were associated with increased SOWS ($p < 0.05$), and suvorexant mitigated this effect ($p < 0.05$). Suvorexant also had a significant effect on mitigating withdrawal in the post-taper phase after accounting for REM sleep ($p < 0.05$).

Conclusions: Suvorexant may reduce withdrawal severity both directly and by moderating associations between sleep architecture and withdrawal during a buprenorphine taper. REM sleep including rebound REM might be biomarkers of different phases of opioid withdrawal. Improving our mechanistic understanding of the role of the orexin neurotransmitter system during early OUD treatment can lead to medication development and ultimately improved treatment for OUD.

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Efficacy of non-pharmacological approaches to improve sleep in patients with post-traumatic stress disorder: systematic review and meta-analysis

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Introduction: Exposure to violence and adversity during childhood has been identified as a significant risk factor for the later development of both psychiatric conditions and sleep disturbances, with post-traumatic stress disorder (PTSD) frequently emerging as a consequence. While current evidence-based guidelines advocate for trauma-focused psychotherapies (e.g., Imagery Rehearsal Therapy, Cognitive Processing Therapy) as first-line treatments for PTSD, two main challenges persist. First, sleep-related dysfunction, manifesting as maladaptive cognitions about sleep and irregular sleep behavior, is often insufficiently addressed by these therapeutic approaches and frequently remains as a residual symptom post-treatment, impairing quality of life and increasing the risk of relapse. Second, access to psychotherapy is not universally available, underscoring the need to explore alternative interventions. Non-pharmacological strategies, such as physical exercise and mindfulness-based approaches, have shown beneficial effects on both sleep and mental health, and may thus be helpful for individuals with PTSD. Considering the bidirectional relationship between sleep and psychological functioning, we conducted a systematic review and meta-analysis to evaluate the efficacy of non-pharmacological interventions in improving sleep outcomes among individuals diagnosed with PTSD. We included non-psychotherapeutic interventions, trauma-focused psychotherapies, non-trauma-focused psychotherapies, and combined psychotherapies.

Materials and methods: This systematic review and meta-analysis (PROSPERO: CRD42022318904) examined randomized controlled trials (RCTs) investigating the effects of non-pharmacological treatments on sleep in adults diagnosed with PTSD. Studies were included if they were peer-reviewed, published in English, involved adult participants with a PTSD diagnosis, and reported at least one sleep-related outcome. Eligible trials compared non-pharmacological interventions (e.g., psychotherapy, yoga, exercise, acupuncture) with other non-pharmacological treatments, treatment-as-usual, waitlist control,

or no treatment. Standardized mean differences (SMDs) were calculated, and subgroup and meta-regression analyses were conducted to explore potential sources of heterogeneity.

Results: Across 34 studies, with a total pooled sample of 3,688 participants ($n = 2,070$ in experimental groups and $n = 1,618$ in control groups), active treatments significantly improved sleep quality compared to control conditions, with a large overall effect size ($SMD = 0.77$, $p < .001$) and significant heterogeneity ($I^2 = 88.89\%$). The effect remained robust after excluding studies at high risk of bias ($SMD = 0.90$, $p < .0001$). Subgroup and regression analyses revealed no significant effects of participants' age, percentage of male participants, or baseline severity of negative symptoms. No evidence of funnel plot asymmetry was found ($p = 0.107$), suggesting a low risk of publication bias. Additional analyses are ongoing and will be reported as defined in the protocol.

Conclusions: Our findings suggest that non-pharmacological interventions, including psychotherapies and behavioral strategies, are associated with significant improvements in sleep quality among adults with PTSD, with a robust and clinically meaningful effect. These results support the integration of sleep-focused, non-pharmacological approaches into treatment plans for PTSD. Addressing sleep disturbances in PTSD is essential, as persistent sleep problems contribute to symptom maintenance and increased risk of relapse. Targeted sleep interventions may enhance emotional regulation, facilitate fear extinction, and improve overall treatment outcomes. Further analyses are underway to clarify the specific characteristics and mechanisms of the most effective interventions.

Exploratory Study of Sleep-wake Patterns in People with Schizophrenia Residing in the Community

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Introduction: Disturbances in circadian and sleep-wake rhythms are frequently observed in individuals with schizophrenia and other psychiatric disorders. However, their lifestyles and sleep patterns, particularly in community-dwelling settings, remain insufficiently explored. This study investigated the sleep-wake rhythms of individuals with schizophrenia living in non-urban communities, and receiving home nursing care, using both subjective and objective measures.

Materials and methods: This study population comprised of nine individuals (aged 28–52 years) who were using home nursing care. Demographic data (age, employment history, smoking history, sports experience, and the presence of chronic constipation) were collected through interviews. Subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Objective sleep parameters were collected via an actigraphic device consistently worn on the participant's lumbar region for 7 d, excluding bathing time. Sleep variables were determined using SleepSign Act 2 (KISSEI COMTEC Co., Ltd.). Additionally, a chi-square periodogram was used to evaluate the 24-h cycle and note any deviations. Life functioning was evaluated using the World Health Organization Disability Assessment Schedule (WHODAS) 2.0. This study was approved by the Research Ethics Review Committee of Iryo Sosei University (Approval No. 22-04), and written informed consent was obtained from all individuals.

Results: Eight participants (seven males and one female) enrolled in this study. One was excluded because of poor attachment. The mean PSQI score was 8.17 and WHODAS 2.0 score was 22.88. Spearman's rank correlation analysis showed a moderate positive correlation trend ($\rho = 0.673$, $p = 0.067$) between PSQI and WHODAS 2.0 scores, suggesting a potential link between sleep quality and self-reported life function scores. Furthermore, when self-reported total sleep time was compared with the actigraphic measurements, a discrepancy of >1 h was observed in four individuals, indicating a potential misperception of sleep duration. Four participants showed a deviation in the peak of the chi-square periodogram of >30 min from the 24-h (range: -42 to $+48$ min). Actigraphic sleep parameters revealed that most participants showed a decline in sleep quality, characterized by reduced total sleep time, lower sleep efficiency, longer sleep latency, and increased wake time after sleep onset.

Conclusions: These results suggest a meaningful relationship between subjective sleep quality and life functioning among community-dwelling individuals with schizophrenia. Approximately half of the participants also deviated from a standard 24-h activity rhythm, which is consistent with previous findings. These results underscore the importance of promoting better sleep habits to improve lifestyle and mental functioning. Future support strategies should include individualized and comprehensive sleep interventions such as utilizing Cognitive Behavioral Therapy for Insomnia, alongside lifestyle modifications. Continued evaluation incorporating both subjective complaints of the individual and objective data will reinforce these findings.

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Exploring Sleep Disturbances Among Trauma-Exposed Psychiatric Populations

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Introduction: Sleep disturbances are complex, encompassing a range of disruptions to quality, quantity, and timing (Altman, Knauert & Pisani, 2017; Cormier, 1990). A well-established bidirectional relationship exists between poor sleep and mental health issues, with psychological distress increasingly recognised as impacting sleep health (Brindle et al., 2019). Hence, sleep issues are common among those with psychosis, where trauma exposure is prevalent (Kamphuis et al., 2013). However, little research has explored the relationship between life experiences and sleep among this population (Greenwood, 2020). The current study, therefore, explored the nature of sleep disturbances in psychiatric patients at a high-secure forensic mental health hospital in the UK.

Materials and methods: Semi-structured interviews, informed by measures such as the Pittsburgh Sleep Quality Index (Buysse et al., 1989) and the Morning Eveningness Questionnaire (Horne & Östberg, 1976), were conducted with 30 psychiatric inpatients with both active and residual psychosis symptoms. Participants discussed sleep patterns, preferences, and behaviours, as well as past experiences and night-time cognitions. Interviews were recorded and transcribed using Winscribe and thematically analysed using NVivo software.

Results: Five major themes emerged from the data, emphasising sleep behaviours characteristic of this population. Firstly, participants consistently reported evening chronotypes, alongside delayed sleep patterns, highlighting the impact of misaligned circadian rhythms on unhealthy behaviours, such as poor diet and disrupted routines. Secondly, negative night-time cognitions, such as ruminations of past violence and regrets, were common, often causing physical distress and pre-sleep arousal, further driving sleep disturbances. Thirdly, there was a persistent overlap between nightmares and trauma flashbacks, with participants discussing the two interchangeably, emphasising the impact of intrusion symptoms on sleep. Another prevalent theme was a long history of sleep issues, with participants identifying a 'tipping point' where both sleep and psychosis symptoms had significantly worsened. This appeared to be used as a reference point from which current sleep perceptions were measured. Finally, trauma therapies, such as eye-movement desensitisation and reprocessing (EMDR), were praised for improving sleep outcomes by reducing post-trauma nightmares and psychological distress.

Conclusions: Overall, findings highlight the relationship between trauma and sleep in those with psychosis, suggesting that circadian misalignment, negative cognitions, such as rumination, and intrusion symptoms, drive sleep disturbances. These findings emphasise the importance of exploring patient perspectives, recognising trauma as a target for improving sleep outcomes across secure settings.

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From genetic variants to genes: dissecting shared genetic architecture and biological mechanisms linking sleep traits and suicide attempt

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Introduction: Suicide attempt is a serious public health concern with complex causes involving both environmental and genetic factors. Sleep traits have emerged as promising targets in suicide prevention efforts. Epidemiological studies support associations between sleep traits and increased risk of suicide attempt, independent of psychiatric comorbidities. Moreover, both sleep traits and suicidality are moderately heritable. These lines of evidence suggest a potential shared polygenic architecture underlying both phenotypes. However, the genetic underpinnings linking the two remain not been fully elucidated. This study aimed to systematically identify shared genetic variants, genes, and biological mechanisms between 11 sleep traits and suicide attempt using a comprehensive multi-layered analytic framework.

Materials and methods: We conducted a genome-wide pleiotropic association study using GWAS summary statistics from European-ancestry cohorts, covering 11 sleep traits—7 self-reported (e.g., insomnia, short/long sleep, chronotype) and 4 accelerometer-derived traits—and suicide attempt. We first assessed genome-wide genetic correlations using linkage disequilibrium score regression (LDSC) and overall genetic overlap via genetic analysis incorporating pleiotropy and annotation (GPA). Then, pleiotropic single nucleotide variants (SNVs) were identified using the PLACO method, followed by functional annotation with FUMA and Bayesian colocalization analysis. MAGMA was used to identify pleiotropic genes, which were further evaluated through phenotype enrichment (MGI), GO/KEGG pathway analysis, and cell-type specificity analysis. Drug-gene interactions and druggability of pleiotropic genes were assessed using DGIdb. Finally, bidirectional Mendelian randomization (MR) was performed to examine potential causal relationships.

Results: Six trait pairs exhibited significant genetic correlations, while all 11 showed significant genetic overlap (Bonferroni-corrected $p < 4.54 \times 10^{-3}$). The PLACO analysis identified 2,224 pleiotropic SNVs (1,640 unique), mapped to 50 genomic risk loci, including two novel loci not previously reported. Colocalization analysis further supported shared causal variants at 15 loci (PP.H4 > 0.7). MAGMA identified 44 significant pleiotropic genes (32 unique), enriched in metabolic and neurodevelopmental pathways. Gene set enrichment revealed significant involvement in synaptic structure, immune signaling, and H3K27me3-mediated repression. DGIdb analysis highlighted several pleiotropic genes as druggable targets, notably DRD2 with extensive approved drug interactions. MR analysis indicated a significant protective effect of morning chronotype on suicide attempt (OR = 0.25, $p = 0.003$), and nominally significant risk associations for insomnia, short sleep, daytime napping, and reduced sleep duration.

Conclusions: This multi-layered pleiotropic analysis provides robust evidence of shared genetic mechanisms linking sleep traits and suicide attempt. The identified loci and genes uncover novel biological pathways including synaptic function, immune regulation, and epigenetic repression. Importantly, several candidate genes are druggable, offering promising therapeutic targets for translational research and targeted interventions to reduce suicide risk via modulation of sleep-related pathways.

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From Sleep to Diagnosis: A Novel Nomogram for Identifying Major Depressive Disorder Using Comprehensive Sleep Metrics

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Introduction: Sleep impairment is a one of the most common symptoms of Major depressive disorder (MDD). The stigma of MDD causes patients to conceal their core MDD symptoms, resulting in missed diagnosis. We aimed to develop a predictive model integrating self-report sleep, objective sleep architecture and EEG activity to estimate the probability of MDD in individuals with sleep complaints.

Materials and methods: Ninety-one patients with MDD and ninety-one age and sex-matched controls were included. All subjects were assessed by overnight polysomnography, electroencephalogram (EEG) relative power during sleep, Pittsburgh Sleep Quality Index (PSQI), Flinders Fatigue Scale (FFS) and

Epworth Sleepiness Scale (ESS). The Beck Depression Inventory (BDI) was used to assess depressive symptoms. Predictive factors were identified using random forest analysis and logistic regression. A nomogram was created based on the logistic regression results. Area under the receiver operating characteristic curve (AUC) was used to evaluate the discrimination of the nomogram. Bootstrapping was used for internal validation, and accuracy of the model was evaluated using the Hosmer-Lemeshow test. Decision curve analysis (DCA) of the nomogram was conducted.

Results: The prediction model included total scores for PSQI and FFS, wake after sleep onset, and EEG theta power during rapid eye movement sleep as predictors, and gave an AUC of 0.924 (95% confidence interval: 0.887 - 0.961). The Hosmer-Lemeshow test showed a $\chi^2=4.36$ ($p = 0.823$), and DCA showed a higher net benefit for the nomogram compared to the BDI.

Conclusions: This predictive model provides a reliable tool for identifying MDD in individuals with sleep complaints, which may help to decrease missed diagnosis rate of MDD.

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Genetic association of depression and antidepressant targets with α -synucleinopathy spectrum disorders

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Introduction: Observational studies have suggested the associations between depression, antidepressant use, and α -synucleinopathy spectrum disorders, including rapid eye movement sleep behavior disorder (RBD), Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). However, their genetic associations remains unclear. This Mendelian randomization (MR) study aimed to investigate the genetical associations between depression, antidepressant targets, and α -synucleinopathy spectrum disorders.

Materials and methods: We obtained summary statistics of genetic variants associated with depression and α -synucleinopathy spectrum disorder phenotypes from respective genome-wide association studies (GWAS). Expressive quantitative trait loci (eQTL) for antidepressant target genes were extracted from the eQTLGen Consortium. Antidepressant targets expression in blood with significant associations with α -synucleinopathy spectrum disorder phenotypes were further examined in brain tissues. Sensitivity analyses including stringent linkage disequilibrium (LD) criteria, summary-based Mendelian randomization (SMR), colocalization, and shared genetic architecture analyses were conducted to ensure the robustness of the findings.

Results: No significant effect of depression on overt α -synucleinopathies was confirmed. Conversely, RBD was suggested to be causally associated with depression (OR[95%CI] = 1.04[1.02 to 1.06], $p = 5 \times 10^{-5}$), driven by the 3'-SNCA variant rs3756059. Expression of three target genes—SLC29A4, SIGMAR1, and CYBA—in blood showed associations with PD, MSA, and DLB, respectively. However, these associations were not replicated in brain tissue nor supported by sensitivity analyses. No significant shared genetic architecture or colocalization was identified between depression or antidepressant targets and α -synucleinopathy spectrum disorders.

Conclusions: Our findings do not provide conclusive evidence for a genetic causal relationship between depression or antidepressant target genes and α -synucleinopathy spectrum disorders. Nonetheless, the observed association between RBD and depression, potentially mediated by the rs3756059 variant in the SNCA gene, suggests that depression may serve as a prodromal marker rather than a risk factor for RBD. These insights underscore the importance of considering depression in the early identification and management of individuals at risk for α -synucleinopathies.

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How are insomnia and sleepiness complaints influenced by use of tobacco, alcohol, cannabis and screens ?

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Introduction: Addiction is one of the most prevalent psychiatric disorders in the general population. It is characterized by impaired control over substance use and the occurrence of repeated relapses. The co-occurrence of addiction and sleep disorders is highly prevalent and exhibits a bidirectional relationship: while substance use can lead to poorer sleep quality, sleep disorders are also associated with an increased risk of developing substance use and addiction.

Materials and methods: The KANOPEE smartphone application offers interactions with a virtual companion to assess insomnia complaints using the Insomnia Severity Index (ISI), excessive daytime sleepiness (EDS) using the Epworth Sleepiness Scale (ESS), and to screen for problematic use of substances and screens: tobacco (CDS-5), alcohol (CAGE), cannabis (CAGE), and screens (CAGE). Mental health symptoms are evaluated using the PHQ-2 for anxiety and the PHQ-9 for depression. Then, a 7-day prospective sleep diary was used to measure sleep behaviors, including, sleep duration (total sleep time), sleep timing (mid-sleep point, defined as the middle between the sleep time and wake time), and sleep regularity (sleep regularity index, defined as the consistency of being asleep or awake at any two time points 24 hours apart).

These secondary analyses were conducted within the Kanopée cohort. Each participant was categorized into mutually exclusive primary addiction groups based on the substance/screens use identified as most problematic (i.e., scoring positive on the relevant screening tool and indicating the highest severity or complaint when multiple), or into a control group if they reported only non-problematic use(s).

Results: Since April 2020, 14,512 participants (61.7% women; mean age: 49.3 years) have been screened and classified in primary addiction groups as follows: Alcohol: 18.4% (n=2676), Tobacco: 12.0% (n=1739), Screens: 10.0% (n= 1458), Cannabis: 1.7% (n=247), and Control: 57.5% (n=8350). Sleep complaints were frequent, with 48.9 % reporting moderate to severe insomnia, and 42.0 % with reporting moderate to severe EDS.

In multivariate models accounting for socio-demographic characteristics and sleep behaviors, insomnia was significantly more frequent in the tobacco ($\beta=0.64$, $p < .001$), screens ($\beta=0.38$, $p < .001$), and alcohol ($\beta=0.28$, $p = .002$) groups, compared to the control group. EDS was significantly more frequent in the screens group ($\beta=0.55$, $p < .001$), but notably less frequent in the cannabis group ($\beta=-0.96$, $p = .002$) compared to the control group. When psychopathological variables were included in the models, the associations with insomnia were no longer significant, although the direction and significance of associations for EDS remained unchanged.

Conclusions: Sleep complaints and problematic substance/screens use are common among Kanopée users. The link between insomnia and problematic use of tobacco, alcohol, and screens appears to be largely mediated by underlying depression/anxiety symptoms. In contrast, the association between problematic screens use and EDS seems to be independent of psychopathology, insomnia, or total sleep time. Interestingly, the seemingly protective effect of being in the cannabis group for EDS contrasts with existing literature. Future studies should explore the direction and temporality of these relationships.

Impact of Alcohol Dependence on Sleep Patterns: A Polysomnographic Analysis of Detoxified Patients

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Introduction: Chronic alcohol use significantly disrupts the circadian rhythm, impairing the central nervous system and biological systems, which often leads to sleep disturbances such as insomnia. These disturbances can complicate the detoxification process and contribute to relapse, underscoring the importance of understanding and addressing sleep issues in alcohol-dependent individuals. The objective of this study was to objectively assess sleep disturbances in alcohol-dependent patients using polysomnography (PSG), a gold standard in sleep assessment, after the detoxification process.

Materials and methods: Twelve alcohol-dependent patients were recruited after obtaining ethics approval. The patients were detoxified and ensured to be free of withdrawal symptoms. Benzodiazepine effects were also accounted for to avoid confounding factors. The sleep parameters were recorded using Polysomnography (SOMNO HD PSG with camera compact wS) , a level 1 recording was done the reporting done.

Results: The mean age and BMI of recruited patients was 41.5 years and 20.7. The average sleep efficiency was 79.32%, which indicates that the patients spent a significant portion of time in bed awake, a common symptom in alcohol-dependent individuals. The mean sleep onset latency was 24.9 minutes, showing a moderate delay in falling asleep.

Stage Distribution:

- **N1:** 15.15% (Light sleep)
- **N2:** 56.3% (Light sleep)
- **N3:** 8.9% (Deep sleep)
- **REM:** 19.4% (Rapid Eye Movement sleep)
- A noticeable finding is reduced N3 (deep) sleep, essential for restorative sleep. This reduction could contribute to physical and psychological exhaustion and may be linked to the increased likelihood of relapse during detoxification.

Conclusions: Alcohol-dependent individuals showed moderate sleep disturbances, characterized by slightly reduced sleep efficiency, delayed sleep onset, and significantly reduced N3 (deep) sleep. These disruptions could contribute to the cognitive and physical impairments commonly observed in alcohol-dependent individuals during the withdrawal process.

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Narcolepsy, Depression, and REM Suppressing Antidepressants: Comorbidity & Confound Impacts on Sleep Architecture and Diagnostic Sensitivity

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Introduction:

Systematic reviews and meta-analyses showed a 32%-57% prevalence of Depression or depression symptoms in patients with Narcolepsy disorders. MSLT protocols recommend a drug washout period of ≥14-days for antidepressants and other medications known to confound sleep architecture and REM sleep. Patient noncompliance with washout protocols for REM-suppressing antidepressants (REMS-AD) was found to reduce the incidence of SOREMP observations in MSLTs by ≥89% compared to washout-compliant patients. Prior studies demonstrated potential for improvements in Narcolepsy diagnostic sensitivity and reproducibility by exploiting more comprehensive analysis of full-night polysomnography (PSG) signals, through deep learning-based AI models (ROC-AUC 0.96) and algorithmic approaches. Prior research characterized Narcolepsy-specific microarchitectural sleep EEG abnormalities that manifest in Sleep Latency (SL), REM (Latency (REML), median/minimum duration, density, prevalence), N3 (time/prevalence), hypnodelta characteristics, and separately, Depression-

specific state and trait EEG markers including low Delta Sleep Ratio (DSR), high/oscillatory Gamma, and high/asymmetric Alpha. Few works examine the extent of confounds to Narcolepsy diagnostic parameters from Depression comorbidity with and without the specific influence of REMS-ADs.

Materials and methods:

A nonrandomized, observational, de-identified cohort of N=282 PSGs were collected from subjects that underwent MSLT immediately following the PSG. Excluding subjects without drug-screen and/or medication questionnaire results, the final cohort (N=133) was composed of 59.6% Narcolepsy(+) subjects (N=35 NT1, N=44 NT2), and 40.4% Narcolepsy(-) Clinical Controls (CC) subjects. 47.9% of subjects had a documented Depression diagnosis, 52.1% with verified absence of Depression diagnostic history, and a 49.3% rate of comorbid Depression in Narcolepsy. The sample included N=39 subjects that were Narcolepsy(+)/Depression(+) for comparison to N=40 Narcolepsy(+)/Depression(-) subjects. Among Narcolepsy(+)/Depression(+), N=29 were REMS-AD(+) and N=10 REMS-AD (-). Mean latency, density, and prevalence were calculated for sleep stages (N1, N2, N3, REM, Wake, All-Stages), mean power spectral densities and ratios were calculated (Delta, Theta, Alpha, Beta, Gamma), then evaluated for differences and statistical significance in mean diagnostic parameter values based on two-sided 95% bootstrap median-percentile method Confidence Intervals (R=2,000).

Results:

In NT1, NT2, and CC, Mean REML was shortest in MDD(+)/REM-AD(-) subjects (NT1/NT2: 67mins (54mins, 77mins), CC: 118mins (97mins, 125mins)), the longest in MDD(+)/REM-AD(+) subjects (NT1/NT2: 156mins (115mins, 203mins), CC: 190mins (133mins, 247mins)), with MDD(-) subjects falling between (NT1/NT2: 108mins (93mins, 125mins), CC: 120mins (94mins, 152mins)). In both Narcolepsy and CC, Mean REM density was highest in MDD(+)/REM-AD(-) subjects (NT1/NT2: 111mins (88mins, 128mins), CC: 97mins (91mins, 105mins)), and substantially reduced in MDD(+)/REM-AD(+) subjects (NT1/NT2: 101mins (87mins, 113mins), CC: 82mins (62mins, 104mins)). Mean DSR was lowest in CC MDD(+)/REM-AD(-) subjects (CC: 0.96), and normalized in MDD(+)/REM-AD(+) (CC: 1.45) relative to MDD(-) (CC: 1.28). Mean DSR was lower in Narcolepsy MDD(+)/REM-AD(+) and MDD(+)/REM-AD(-) subjects than MDD(+)/REM-AD(+) and MDD(-) CCs (NT1/NT1: REM-AD(-): 1.19, REM-AD(+): 1.14, MDD(-): 1.39). Mean SOREMPs were lowest for MDD(+)/REM-AD(+) both in Narcolepsy (NT1/NT2: MDD(+)/REM-AD(+): 1.00, MDD(+)/REM-AD(-): 1.71, MDD(-): 1.50) and CCs (CC: MDD(+)/REM-AD(+): 0.21, MDD(+)/REM-AD(-): 0.33, MDD(-): 0.42).

Conclusions:

Comorbid Depression patients with and without REM-ADs showed substantial alterations in key Narcolepsy disorder diagnostic and sleep architecture parameters. Given significant rates of comorbidity, these findings highlight needs to better understand the interactions and impact of Depression on Narcolepsy diagnosis.

Network Controllability of rTMS Targets Predicts Improvement in Depression and Comorbid Sleep Disturbances

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Introduction: Sleep disturbances, as one of the most prevalent somatic symptoms of depression, manifest as difficulties in falling asleep, sleep maintenance problems, or early awakenings, severely impairing patients' quality of life. Repetitive transcranial magnetic stimulation (rTMS), a non-invasive neuromodulation technique, has demonstrated efficacy in alleviating depressive symptoms in patients with comorbid sleep disturbances. However, significant individual variability exists in treatment response, with some patients showing limited improvement to conventional protocols. Brain network

controllability theory provides a novel framework for understanding neuromodulation mechanisms, yet its application in sleep disturbances and comorbid depression remains unexplored. This study investigates whether the controllability of rTMS target regions can serve as a neuroimaging biomarker for predicting treatment response and examines its potential role in modulating sleep-related neural circuits.

Materials and methods: Totally 64 depression patients with clinically significant sleep disturbances were enrolled. All patients underwent individualized target localization following the Stanford Neuromodulation Therapy protocol, based on resting-state functional MRI (fMRI) and functional connectivity analysis. Clinical assessments (HAMD-17 for depression) and fMRI scans were conducted pre- and post-treatment. We evaluated local neural activity changes using amplitude of low-frequency fluctuations (ALFF) analysis and computed average controllability from functional connectivity matrices to quantify network regulatory capacity. Correlations between controllability and clinical improvement were analyzed.

Results: Firstly, the local neural activity of the core brain regions related to emotion and sleep changed significantly ($p < 0.05$) after treatment, as well as the control characteristics of the switching of the patient's brain network. Secondly, when stratified by treatment response (responders vs. non-responders based on HAMD-17 reduction), responders exhibited significantly lower baseline average controllability at stimulation targets ($p < 0.05$). Finally, pretreatment target controllability showed a significant negative correlation with clinical improvement ($r = -0.4227$, $p = 0.0314$), whereas the strength of targeted functional connections showed no predictive value.

Conclusions: This study pioneers the application of network controllability theory to rTMS treatment for depression with comorbid sleep disturbances. We identify network controllability as a predictive biomarker for dual symptom improvement, suggesting that low-controllability targets may be more susceptible to neuromodulation, thereby inducing beneficial network reorganization that concurrently alleviates depressive symptoms and sleep disturbances. These findings provide novel insights into the neural mechanisms of rTMS effects on sleep-related somatic symptoms and establish a theoretical foundation for developing personalized neuromodulation strategies based on network dynamics.

Neural activation reveals affective processing during sleep and correlates with depression symptoms in humans

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Introduction: While we sleep, neural networks supporting cognition and emotion are activated, driving subsequent behavior. Based on converging evidence showing that depression is linked with abnormal sleep and that affective networks are activated during sleep, we hypothesize that the activity of affective networks during sleep governs mental well-being in health and disease. We propose that maladaptive activation of brain networks supporting emotional processing during sleep is implicated in the etiology and progression of major depressive disorder. Negative biases in emotional processing (e.g., during ruminations) are a hallmark of wake-processing in mood disorders. Excessive ruminations lead to prolonged depression episodes and predict future depressed mood. We suggest that these biases perpetuate during sleep and play a causal role in the progression of depression symptoms.

Materials and methods: We examined the connection between affective processing during sleep and depression symptoms in a cohort of healthy young participants ($N = 52$). We first used EEG to identify neural patterns engaged in processing negative and positive images during wakefulness. Participants ($N = 52$) were fitted with a 64-electrode EEG system. They completed questionnaires, napped in the lab, and were presented with images taken from the International Affective Picture System. Stimuli were split evenly between positively and negatively valenced images. Locking to stimulus onset, we used the EEG data to train time-dependent support vector machine classifiers to label each trial's valence (positive vs. negative), using individual electrodes as features. These patterns were used as templates for analyzing data collected during sleep, essentially yielding individualized indices reflecting the valence of neural affective processing (positive vs. negative) during sleep. These indices were then correlated across participants with mental health indices, including Beck's Depression Inventory 2 (BDI-2) scores.

Results: During wakefulness, classification accuracy between negative and positive images was high throughout the first 2 s of image display ($p < 0.001$, corrected). EEG data therefore reflect affective processing during wakefulness. We applied each participant's wake-based classifiers to their sleep data. For each time point over sleep and each classifier, the models assigned a label (positive or negative). This revealed a ubiquitous, participant-specific pattern of activity that persisted throughout the nap and pre-nap rest, with little differences across sleep stages. The valence assigned by the classifier during this time period correlated with BDI-2 scores, so that more negative valence correlated with higher symptom severity ($r = 0.46$, $p < 0.001$; $p < 0.01$ after cluster correction).

Conclusions: Our results indicate that, during sleep, brain activity patterns expose affective processing and correlate with depression symptoms. These findings provide evidence that spontaneous affective processing during sleep contributes to waking mental well-being, with potential implications for identifying sleep-related biomarkers of affective disorders.

NeuroACT: Skills training for adolescents with neurodevelopmental disorders and symptoms of insomnia

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Introduction:

Adolescents with neurodevelopmental disorders, such as Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD), often experience significant sleep disturbances, including difficulties with sleep initiation and sleep maintenance (i.e., insomnia). These sleep issues may exacerbate existing challenges related to emotional regulation, stress, and daily functioning. Despite the high prevalence of sleep disorders in this population, few studies directly address both neurodevelopmental challenges and sleep-related problems. This study evaluates the feasibility and preliminary effects of NeuroACT, a skills training program based on Acceptance and Commitment Therapy (ACT) principles, among adolescents with neurodevelopmental disorders and symptoms of insomnia.

Materials and methods:

The study employs a within-group design and is conducted at child and adolescent psychiatry services in Karlstad, Sweden. Participants (current: $n=4$; target: $N=34$) are adolescents aged 13-19 diagnosed with autism and/or ADHD, and symptoms of insomnia, recruited through clinical services. Inclusion criteria include fluency in Swedish, stable medication regimen (if applicable), and informed consent from both participants and guardians for those under 15 years. Exclusion criteria comprise ongoing substance abuse, suicidality, psychosis, intellectual disability, or severe mood disorders. The NeuroACT intervention consists of 12 weekly sessions, each lasting 120 minutes, involving groups of 4–8 participants. Two licensed psychologists, with at least one having formal NeuroACT training, lead the sessions. The training covers key themes such as stress management, emotional regulation, mindfulness, social interactions, and goal setting. Quantitative data are collected using validated measures of insomnia (Insomnia Severity Index), stress (Perceived Stress Scale), psychological distress (Hospital Anxiety and Depression Scale), mindfulness (Five Facet Mindfulness Questionnaire), and overall functioning (Strengths and Difficulties Questionnaire) at pre-, mid-, and post-intervention. Additionally, qualitative feedback is gathered through semi-structured interviews to capture participants' subjective experiences of the skills training.

Results:

The initial results indicate that the intervention is feasible and promising for this patient group in terms of perceived stress (pre $M=38.00$, $SD=14.00$; post $M=27.25$, $SD=6.45$), and mindfulness (pre $M=66.00$, $SD=33.96$; post $M=80.25$, $SD=22.59$). Measures of insomnia (pre $M=9.75$, $SD=4.27$; post $M=10.50$, $SD=3.42$), psychological distress (pre $M=16.75$, $SD=10.97$; post $M=22.33$, $SD=6.03$), and overall

functioning (pre $M=21.67$, $SD=5.03$; post $M=20.00$, $SD=8.19$) have not shown improvements at this stage, highlighting areas for further investigation. Attendance rates are relatively high, and no significant adverse effects have been reported thus far. Preliminary themes from the interviews: (1) Overcoming initial hesitation and vulnerability; (2) Group support and tailored treatment as enablers of change; and (3) Improvements within a complex reality.

Conclusions: Early findings suggest that NeuroACT is a feasible and potentially beneficial intervention for adolescents with neurodevelopmental disorders, particularly in reducing stress and enhancing mindfulness. These results support continued evaluation of Acceptance and Commitment Therapy-based approaches addressing the complex interplay between neurodevelopmental symptoms and sleep problems in youth.

Neurometabolic Alterations in the Anterior Cingulate Gyrus and Putamen: Insights from Adolescents with Insomnia and Depression

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Introduction: Previous research has established that sleep disorders are prevalent among individuals with major depressive disorders (MDD), particularly in adolescents, with an incidence rate surpassing that of low mood. Nonetheless, the effects of sleep disorders on brain function in depressed adolescents remain inadequately understood.

Materials and methods: We recruited 97 right-handed, untreated adolescent patients with MDD, and 68 demographically matched healthy controls (HCs) and underwent the proton magnetic resonance spectroscopy (1H-MRS) scan in the anterior cingulate gyrus (ACC) and putamen. Differential and association analysis was performed to investigate the relationship between sleep quality and the severity of depression and neurometabolism ratios of ACC and putamen in MDD groups.

Results: The study identified 64 patients as Insomnia (IS) group, characterized by an insomnia item score of ≥ 1 on the 24-item Hamilton Depression Rating Scale (HDRS) and a Pittsburgh Sleep Quality Index (PSQI) total score of ≥ 6 , while 33 patients were categorized into the Non-Insomnia (NIS) group. The IS group exhibited significantly lower choline-to-creatine (Cho/Cr) ratios in the right ACC compared to both the NIS and HCs, as well as lower Cho/Cr ratios in the left ACC relative to the HCs. Furthermore, the NIS group showed reduced N-acetylaspartate-to-creatine (NAA/Cr) ratios in the right putamen compared to the IS and HC groups. The 24-item HDRS scores were negatively correlated with Cho/Cr ratios in the bilateral ACC ($r = -0.354$ and $r = -0.246$, respectively; both $p < 0.05$), and insomnia item scores were correlated with Cho/Cr ratios in the right ACC ($r = -0.294$, $p = 0.018$) within the IS group.

Conclusions: A substantial proportion of adolescents with depression experience clinically significant sleep disturbances. The observed brain dysfunction is influenced by the cumulative effects of previous severe mood episodes and sleep disturbances. Therefore, incorporating therapeutic interventions for sleep disorders should be an integral component of antidepressant treatment strategies for depressed adolescents.

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Obstructive Sleep Apnea and Psychiatric Co-morbidities: A Territory-Wide Study in Hong Kong

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Introduction: The bidirectional relationship between obstructive sleep apnea (OSA) and psychiatric disorders is increasingly recognized. However, most existing studies rely on convenient clinical samples, focus on symptoms rather than formal psychiatric diagnoses, and are typically limited to adult populations. There is a lack of large-scale, population-based studies examining OSA and its associated psychiatric co-morbidity across the lifespan.

Materials and methods: We conducted a retrospective study using the data from Clinical Data Analysis and Reporting System (CDARS), covering over 90% of health services in Hong Kong. Patients of all ages with at least one psychiatric diagnosis (ICD-9-CM codes 290–319) between 2014 and 2023 were included. Those with missing or implausible data (age < 0 or death before diagnosis date) were excluded. OSA was identified by ICD-9-CM codes 780.51, 780.3, and 780.57. Each OSA patient (OSA group) was matched with a non-OSA psychiatric control (Controls) by sex and age at first psychiatric diagnosis using propensity score matching. An "archive date" was set as the date of the first OSA diagnosis. Psychiatric diagnoses within ± 2 years of the archive date were captured as the psychiatric comorbidity surrounding the diagnosis of OSA. For the Controls, we match the time interval between the archive date to the first psychiatric diagnosis with the OSA group to ensure comparable observation windows. Age at archive date was stratified into child (<18), adult (19–64), and senior (65+) groups. Diagnoses were grouped into anxiety, depression, bipolar disorder, psychosis, dementia, substance-related disorders, insomnia, sexual/gender identity disorders, eating disorders, ADHD/hyperkinetic disorders, autism, and others. Group differences were tested using chi-square, Fisher's exact, or t-tests with False Discovery Rate correction (significance: adjusted $p < 0.05$).

Results: We identified 11400 patients in the OSA group (64.3% male; mean age = 50.3 ± 21.3), of whom 14% were children, 61.5% adults, and 24.5% seniors. Insomnia was significantly more prevalent in the OSA group across all ages (children: 1.6 vs. 0.2%; adults: 2.8 vs. 0.8%; seniors: 5.5 vs. 1.3%). In children, OSA was associated with higher rates of intellectual disability (19.8 vs. 10.6%) and eating disorders (3.6 vs. 0.8%). Among adults and seniors, anxiety (21.3 vs. 17.3%; 17.0 vs. 12.2%) and depression (15.1 vs. 10.0%; 12.9 vs. 8.4%) were more common in the OSA group. Bipolar disorder (2.8 vs. 1.8%) was also significantly higher in adults with OSA. Conversely, co-morbid substance-related disorders and psychosis were significantly lower in the OSA group. Dementia appeared lower in seniors with OSA (21.2 vs. 23.9%), though became insignificant in a sensitivity analysis limited to diagnoses after the archive date (13.0 vs. 11.9%).

Conclusions: This study provides an age-stratified description of psychiatric diagnostic patterns associated with OSA in a real-world psychiatric population. Our findings confirm well-established associations between OSA and mood or sleep disorders. In contrast, substance-related disorders and psychosis were significantly less prevalent in the OSA group, which may reflect underdiagnosis due to help-seeking behaviors, diagnostic overshadowing, or assessment barriers specific to these populations.

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Out of Bed, Out of Reach: Sleep Disruption in a Marginalized Patient with Dual Diagnosis

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Introduction: In patients with psychiatric comorbidities and chronic alcohol use, nocturnal disturbances may stem from various overlapping phenomena. Diagnostic clarity is often impaired in socioeconomically vulnerable individuals, particularly when poor adherence and limited health literacy interfere with investigation and treatment. We present a diagnostically challenging case of a man with profound sleep disruption in the context of chronic alcohol misuse and complex psychopathology.

Materials and methods: Clinical data were collected through interviews, chart review, and collateral reports. Patient consent was obtained.

Results: A 56-year-old man with alcohol dependence (consuming 15–20 beers/day) and poor social support (unemployed, lives alone, illiterate) presented with auditory hallucinations, depressed mood, irritability and long-standing nocturnal disturbances. He reported vivid, action-filled dreams with themes of pursuit and threat (e.g., helicopters, cemeteries, tanks), often awakening disoriented, out of

bed, or with bedding disarranged. Episodes were accompanied by intense autonomic arousal, fear, and urgent flight responses, sometimes described as “waking up screaming” and “needing to escape” or episodes in which he was awakened by others due to be “jumping in bed”, which he did not recall afterward. These symptoms raised multiple diagnostic possibilities, including RBD, sleep-related panic attacks, PTSD and alcohol-induced hallucinosis. He was started on sertraline 150 mg, olanzapine 15 mg and gabapentin 300mg, which led to improvement in mood and resolution of auditory hallucinations; however, sleep disturbances persisted despite psychiatric stabilization. The patient was admitted to a residential alcohol rehabilitation unit, where he maintained abstinence for three months. Notably, despite the cessation of alcohol use, his sleep disturbances remained unchanged, undermining a purely substance-related etiology. Formal polysomnography was scheduled but not completed due to nonadherence. Blood tests, neuroimaging and ECG were otherwise unremarkable.

Conclusions: This case exemplifies the diagnostic complexity of sleep disturbances in individuals with dual diagnosis. Chronic alcohol use exerts a profound impact on sleep architecture, promoting REM rebound, increasing vulnerability to parasomnias, and exacerbating emotional dysregulation. More broadly, it underscores the challenges of diagnostic clarification in real-world, resource-constrained settings and the imperative to adapt sleep medicine practices to better address the needs of socioeconomically disadvantaged populations. Factors such as limited health literacy, precarious living conditions, and fragmented mental health care systems may significantly compromise the feasibility and effectiveness of gold-standard assessments such as polysomnography.

Physiological dynamics surrounding trauma-related nightmares: Differentiating REP, PREP, and NREP awakenings in patients with PTSD

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Introduction: Trauma-related nightmares (TRNs) are vivid, distressing nocturnal episodes tied to trauma-specific imagery and high emotional recall. They differ from idiopathic nightmares through their strong trauma anchoring and tendency to cause prolonged awakenings, perpetuating hyperarousal, anticipatory anxiety, and chronic sleep disruption. Clinically, TRNs vary in replicativity: replicative (REP) closely mirror the trauma, partially replicative (PREP) mix symbolic and trauma content, and non-replicative (NREP) retain only thematic traces. While this typology may reflect trauma integration levels, its physiological correlates remain poorly understood. This study examined autonomic dynamics before, during, and after TRN-related awakenings to determine whether they differ by subtype.

Materials and methods: We included 74 French former military personnel with PTSD (PCL-5 > 44) from a cohort of 131. Sleep was recorded at home over seven nights using the Dreem V2 EEG headband and Empatica E4 wristband. Across the final five nights, 412 TRN-related awakenings were identified (mean 2.13/night) and classified as REP (n = 160), PREP (n = 183), or NREP (n = 68) using the TRNS-FR questionnaire. For each event, 17 physiological parameters (electrodermal activity [EDA], heart rate [HR], heart rate variability [HRV], movement) were extracted for three windows: 10 minutes before awakening, 2 minutes after, and 10 minutes after returning to sleep. Group comparisons used Kruskal–Wallis tests.

Results: **Ten minutes before awakenings**, REP TRNs showed the highest sympathetic activation with elevated EDA ($p < 0.001$), greater SCR activity, increased HR, and decreased HRV indices (SDNN, RMSSD, pNN50; all $p < 0.001$), indicating parasympathetic withdrawal. PREP values were intermediate, while NREP displayed the lowest pre-awakening arousal. **Two minutes post-awakening**, REP and PREP remained in heightened sympathetic states: REP showed elevated EDA ($p < 0.001$), blunted HRV (LF, HF, SDNN; all $p < 0.001$), and delayed SCR recovery ($p < 0.01$). NREP showed lower EDA and faster HR/HRV return to baseline. **Ten minutes after falling back asleep**, only REP TRNs retained significant physiological deviation from baseline (EDA $p < 0.001$; HRV suppression $p < 0.001$), while PREP trended toward baseline and NREP was indistinguishable from baseline.

Conclusions: TRN subtypes are associated with distinct autonomic activation profiles during the peri-awakening period. REP TRNs are linked to higher and more persistent sympathetic arousal, particularly elevated EDA and sustained HRV suppression. These findings support the utility of temporal physiological monitoring—especially EDA and HRV—to differentiate TRN subtypes and potentially inform personalized interventions targeting TRN-related autonomic dysregulation in PTSD.

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Pre-Infusion EEG Vigilance Dynamics as Predictive Indicators of Ketamine Response in Major Depression: A Placebo-Controlled Study

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Introduction: Ketamine has gained increasing attention as a rapid-acting intervention for treatment-resistant forms of major depressive disorder (MDD). Accumulating evidence suggests that neurophysiological markers derived from EEG-based vigilance regulation may serve as early predictors of antidepressant outcomes.

Materials and methods: A placebo-controlled, single-blind, within-subject trial was conducted involving two patient cohorts diagnosed with MDD (combined n = 48). Each participant received an intravenous ketamine infusion (0.54 mg/kg), with brain arousal fluctuations quantified using the Vigilance Algorithm Leipzig (VIGALL). EEG was recorded at multiple intervals: baseline, infusion onset, midpoint, termination, and 24 hours post-infusion. The primary clinical endpoint was a ≥33% reduction in the Montgomery–Åsberg Depression Rating Scale (MADRS) score after 24 hours. Resting-state EEG data were segmented into 1-second epochs for vigilance stage classification.

Results: Ketamine administration, in contrast to saline placebo (0.9% NaCl), produced a notable increase in stage B1 (reduced vigilance) by the end of the infusion. This alteration showed a significant correlation with serum ketamine concentrations, independent of clinical outcome. However, patients classified as responders—regardless of the intervention—exhibited a marked shift in EEG profile: decreased time in high-vigilance stage A1 and increased time in stages B2/3. Pre-infusion EEG characteristics differed meaningfully between responders and non-responders, with responders displaying a substantially higher baseline proportion of stage A1 (53% vs. 21%). Predictive modeling using logistic regression and leave-one-out cross-validation yielded an area under the ROC curve of 0.7, supporting the prognostic value of initial vigilance stage distribution.

Conclusions: This study supports the utility of EEG-derived vigilance metrics as potential biomarkers for predicting the clinical efficacy of ketamine in depression. Elevated baseline stage A1 may indicate increased likelihood of treatment response, suggesting a stratification approach for optimizing antidepressant interventions based on neurophysiological profiling.

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Psychiatric comorbidities associated with obstructive sleep apnea

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Introduction: Over the past 2 decades, sleep researchers have made significant advances in understanding sleep disorders including obstructive sleep apnea (OSA). OSA commonly coexists with

psychiatric disorders encompassing mental health issues like depression, anxiety, bipolar, schizophrenia and others. This study aims to assess the comorbidity of OSA with depression and anxiety disorders among Egyptian patients.

Materials and methods: During the study, we conducted a cross-sectional study involving 92 adults diagnosed with OSA. Those patients were interviewed using a checklist to gather information regarding their chief complaints and other associated symptoms. The psychological status was assessed utilizing the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I), Beck Anxiety Inventory (BAI), and Beck Depression Inventory (BDI) scoring. The severity of the breathing disorder was classified as mild, moderate, or severe based on the respiratory disturbance index (RDI), which was confirmed through overnight polysomnography. Daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS).

Results: The sample of patients as a whole shows that witnessed apneas represent the highest percentage (70.7%), followed by fatigue (69.6%), then non-refreshing sleep (67.4%), and snores (63.0%). The least frequent presenting symptom is frequent naps.

The majority of OSA patients have a comorbid psychiatric disorder (65.0%). Among these, depressive disorders are the most prevalent (31.5%), followed by anxiety disorders (23.9%) and psychoses (6.5%). It is worth noting that 38% of OSA patients do not have any psychiatric disorders.

In terms of anxiety disorders, the most common subtype observed is OCD (8.7%), followed by GAD (6.5%), panic (5%), and PTSD (3.3%). As regards depressive disorders, the predominant subtype present is depressive disorder not otherwise specified (11.9%), followed by dysthymic disorder and major depressive disorder (8.7% for each), and then bipolar disorder (depression) at 2.2%.

Conclusions: We conclude the following:

1. OSA patients are likely to present with comorbid depression and/or anxiety disorder(s).
2. Fatigue was found to be the most prevalent presenting symptom in OSA patients with comorbid anxiety compared to those without anxiety.

rTMS Modulation of Sleep-Related Brain Networks in Major Depressive Disorder: Multisite Identification and Therapeutic Validation

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Introduction: Sleep disturbances (SD) represent a core symptom of major depressive disorder (MDD), affecting up to 90% of patients. Critically, SD exhibits a strong bidirectional relationship with MDD and significantly elevates the risk of suicidal behavior. While antidepressant pharmacotherapy can improve SD and subsequently alleviate associated symptoms like suicidal ideation and mood dysregulation, its utility is often limited by prolonged treatment duration and significant side effects. Repetitive transcranial magnetic stimulation (rTMS), an FDA-approved rapid-acting intervention for MDD, offers a promising alternative. However, despite its established antidepressant efficacy, the specific impact of rTMS on the core symptom of SD and the neural mechanisms underlying any potential sleep improvement remain poorly characterized. Crucially, it is unknown whether successful mood modulation via rTMS reliably translates to concurrent SD amelioration, potentially undermining long-term outcomes. Elucidating the core brain regions implicated in MDD-related SD based on multisite datasets and investigating how rTMS modulates these regions is critical.

Materials and methods: Resting-state fMRI data from the REST-meta-MDD Project (988 MDD patients across 16 sites) were analyzed. Neural activity was quantified via mean amplitude of low-frequency fluctuations (mALFF). SD severity was assessed using HAM-D sleep sub-scores (items 4-6). Correlation analyses identified SD-associated brain regions. An independent randomized controlled trial (RCT) cohort received 2-week rTMS with multimodal MRI at baseline/post-intervention. Clinical assessments occurred at baseline, post-treatment, and 6-week follow-up. Paired t-tests evaluated rTMS-induced neural changes. Altered mALFF in identified regions was correlated with sleep improvement to determine rTMS efficacy for SD.

Results: Multicenter analysis revealed that MDD patients with severe sleep disturbances showed increased activation in the putamen, insula, thalamus and supplementary motor area, alongside decreased activation in the subgenual anterior cingulate cortex, posterior cingulate gyrus, precuneus,

superior frontal gyrus and superior temporal gyrus. In the clinical trial, patients receiving active rTMS demonstrated significantly greater improvement in both depressive symptoms and sleep disturbances compared to the sham group. Neuroimaging analysis indicated that rTMS activated multiple regions related to sleep disturbances, including the subgenual anterior cingulate cortex and superior frontal gyrus. Furthermore, rTMS-mediated inhibition of putamen and supplementary motor area activity correlated with sleep improvement.

Conclusions: This study identified the brain activation patterns associated with sleep disturbances in MDD using multisite neuroimaging data. The randomized controlled trial demonstrated that rTMS effectively alleviates both depressive symptoms and sleep disturbances in MDD patients. rTMS modulated key brain regions implicated in sleep pathology, particularly through suppressing overactive areas including the putamen and supplementary motor area. These findings support rTMS as a targeted intervention for MDD-related sleep disturbances and provide neurophysiological insights into its therapeutic mechanisms.

Sleep and Circadian Predictors of Depression Outcomes: A Systematic Review

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Introduction:

Major depressive disorder (MDD) is a debilitating psychiatric disorder, affecting 5% of individuals yearly. Only approximately 30% of patients will remit with their first antidepressant treatment, and another 20-30% with a medication switch or augmentation. As further treatment steps are required, response rates decrease substantially. Similarly, bipolar disorders (BD) affect 1-2% of individuals, and patients with bipolar I disorder remain depressed for up to 35% of long-term follow-up. In both disorders, relapse is common. Changes in sleep and circadian (SC) rhythms are also common to both disorders, and are associated with worse outcomes.

There are currently no well-validated biomarkers to predict response to antidepressants in MDD or BD; there are also no clinically applicable models to predict relapse in depression. SC factors represent potential operationalizable predictors of treatment outcomes; to our knowledge, there has been no previous comprehensive review investigating this question. Our study systematically reviews and synthesizes current literature investigating whether SC factors predict response, remission, and relapse in depression.

Materials and methods: Our systematic review followed PRISMA guidelines. Search concepts included *depression* and *sleep or circadian rhythms*. Prognosis/prediction methodology were further selected for using validated search filters. Searches were conducted on January 22, 2025, of Embase, Ovid Medline, PsycINFO, CINAHL, and Cochrane databases. Records were then exported to Covidence. Title/abstract and full-text screening were performed by two authors independently. Included articles were required to be full-text empirical studies of human participants with depressive symptoms in the context of existing diagnoses of MDD or BD. Studies must have investigated SC factors as predictors of depression outcomes.

Results:

28,650 records were initially retrieved, with 7,074 excluded via de-duplication. 20,778 articles were excluded through title/abstract screening, advancing 798 for full-text screening. 513 articles were excluded at this stage, with 285 preliminarily included in our review. Risk of Bias assessment and data synthesis are ongoing and nearing completion. Primary outcomes will include prediction of response, remission, and relapse in depression; we anticipate that these measures may have heterogeneous definitions (e.g., what constitutes 'response' versus 'remission'). Wherever possible, we will standardize these outcomes, or will report study-specific definitions. Similarly, effect measures for our main

outcomes may vary. We will report study-specific measures of effect, and where possible, mathematically convert to standardized effects. For all predictors for which meta-analysis is possible, a random-effects meta-analysis will be carried out.

Conclusions: To our knowledge, there has been no prior comprehensive review characterizing sleep and circadian factors as potential biomarkers of response, remission, or relapse in depression. By summarizing existing literature on this topic, our review can potentially help to identify biomarkers of personalized treatment response in depression. If such biomarkers could be identified, this could help to improve patient functioning and quality of life, and enable more effective depression management strategies.

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Sleep and Pharmacotherapy in Treatment-Resistant Late-life Depression: Findings from the OPTIMUM Clinical Trial

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Introduction: Adults with treatment-resistant late-life depression (TRLDD) have high rates of sleep problems. However, little is known about the occurrence and change in sleep during pharmacotherapy of TRLDD or how sleep affects treatment response. We investigated the bidirectional relationship between sleep and treatment outcomes in the Optimizing Outcomes of Treatment-Resistant Depression in Older Adults (OPTIMUM) study, the largest comparative effectiveness trial of pharmacotherapy for TRLDD to date.

Materials and methods: This analysis examined: (1) occurrence of reduced sleep in 634 participants in the OPTIMUM randomized controlled trial; (2) how their sleep changed during pharmacotherapy; and (3) whether treatment outcomes differed among participants with consistent insufficient sleep [$n = 164$], worsened sleep [$n = 62$], or with improved sleep [$n = 158$]. We used item #4 (scale 0 – 6) from the Montgomery-Asberg Depression Rating Scale (MADRS) to assess insufficient sleep, representing reduced sleep duration or depth compared to usual sleep pattern. Scores >2 indicate a meaningful reduction in duration or sleep depth. Patients who scored >2 on item #4 throughout the trial were classified as having consistent insufficient sleep; patients who reported an increased score (and >2 at trial end) were classified as having worsened sleep; and patients who reported a decreased score (and ≤ 2 at trial end) were classified as having improved sleep. Treatment response was defined as a $> 50\%$ reduction in the total MADRS score (minus item #4) at trial end.

Results: About half (51%, $n = 323$) of participants with TRLDD reported reduced or insufficient sleep before treatment. At trial end, consistent insufficient sleep and worsened sleep were each associated with treatment non-response. Improved sleep was not a significant predictor of treatment response, however participants with consistent sufficient sleep or improved sleep were three times more likely to experience treatment response compared to patients with insufficient sleep and worsened sleep.

Conclusions: Insufficient or reduced sleep are modifiable factors that may improve treatment outcomes in TRLDD. Given that sleep complaints including insomnia are associated with greater risk of depressive relapse and treatment non-response, a tailored treatment plan for those at greatest risk of sleep disturbance with concomitant depression may facilitate better outcomes.

Sleep and PTSD Symptom Severity in Military Personnel: Insights from Multi-Night Ecological Recordings

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Introduction: Sleep disturbances—especially insomnia and trauma-related nightmares—are prominent features of post-traumatic stress disorder (PTSD) in military populations. These nocturnal symptoms are not only persistent but also deeply intertwined with daytime impairment, psychiatric comorbidities, and the chronicity of PTSD. Despite accumulating evidence of altered sleep architecture in PTSD, most existing studies rely on single-night laboratory assessments, which fail to capture the natural variability of sleep. The current study aimed to examine the relationship between PTSD severity and intra-individual fluctuations in sleep using multiple consecutive nights of home-based EEG recordings.

Materials and methods: We conducted a prospective controlled study involving 130 military personnel with diagnosed PTSD and 65 healthy military controls. Participants recorded their sleep at home for five nights using a validated EEG headband device. Key sleep metrics included total sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency index (SEI), and sleep architecture parameters. PTSD symptoms were assessed using standardized clinical tools, including the PTSD Checklist for DSM-5 (PCL-5). Mixed-effects models were used for between-group comparisons, and sleep-symptom associations were tested using Spearman's rank correlations.

Results: Compared to controls, individuals with PTSD showed significantly longer SOL and WASO, reduced SEI, and diminished N3 and REM sleep durations ($p < 0.001$). Night-to-night variability in SOL and WASO was markedly higher in the PTSD group. Sleep fragmentation—particularly during non-REM sleep—was strongly correlated with overall PTSD severity ($\rho = 0.42$, $p < 0.001$), with the most robust associations found for intrusive and avoidance symptom clusters.

Conclusions: This study emphasizes the clinical value of multi-night, home-based sleep assessment in capturing the instability of sleep in PTSD. The observed links between symptom severity and fragmented, variable sleep suggest that night-to-night instability may be a key modifiable target. Future research should explore whether improving sleep regularity and reducing fragmentation could contribute to better clinical outcomes in PTSD.

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Sleep and Suicide: The Influence of Sleep Quality on Suicide Risk in Adults

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Introduction: Suicide is a serious global public health problem, causing between 700,000 and 1 million deaths annually. Identifying modifiable risk factors and developing prevention strategies is essential. Sleep disorders (SD), such as insomnia, nightmares, and poor sleep quality (PSQ), have been highlighted as important risk factors for suicide, as they increase suicidal ideation, planning, and attempts, regardless of the presence of depression. This study aims to evaluate the relationship between sleep quality and suicide risk (SR) using validated instruments.

Materials and methods: Cross-sectional study nested within a birth cohort from Ribeirão Preto, with data collected from 1,775 participants between 2016/2017 on mental health, sleep quality, and sociodemographic information, using the Mini International Neuropsychiatric Interview and the Pittsburgh Sleep Quality Index. For the analyses, 1,702 individuals with complete information on sleep and SR were included; after controlling for major depressive disorder (MDD), the sample comprised 372 participants, and, after adjustment for melancholia, 236 remained. There was not a sufficient

sample for analysis of bipolar disorder. Statistical tests such as Chi-square and logistic regression were applied, with significance defined as $p < 0.05$.

Results: Among participants with good sleep quality (GSQ) (PSQI < 5), 93% did not present SR, compared to 77.5% in the PS group (PSQI > 5). Individuals with PS showed significantly higher percentages of both low (15.1% vs. 5.5%) and high SR (7.3% vs. 1.5%) compared to the group with GSQ ($\chi^2 = 88.86$; $p < 0.001$).

In the PS group, 73.7% of individuals presented with MDD, compared to 50.7% in the GSQ group ($\chi^2 = 20.14$; $p < 0.001$). This represents a 2.7 times greater chance of having MDD among those with PS (OR = 2.72; 95% CI [1.75–4.25]).

After adjustment for current MDD, individuals with PS had 2.4 times greater chance of presenting high SR (OR = 2.38; 95% CI [1.02–5.56]; $p = 0.045$). When adjusted for current melancholia, this risk increased to 3.3 times (OR = 3.3; 95% CI [1.29–8.45]; $p = 0.01$).

Conclusions: The study demonstrated a statistically significant association between PS and increased SR, corroborating previous evidence linking PS to worsening suicidal ideation, planning, and attempts. Critically, this association remained robust and independent after adjustment for MDD, confirming that PS quality may be an autonomous predictor of high SR, not merely a depressive symptom.

These findings highlight that inadequate sleep increases suicidal vulnerability. Thus, we can suggest as possible clinical implications the urgent need to assess and monitor sleep disorders in patients with suicidal behavior, integrating this approach into prevention strategies.

The study has limitations. The lack of sample size for analysis in patients with bipolar disorder indicates the need for future research with this population. Additionally, as this is a cross-sectional study, it is not possible to establish causality, reinforcing the importance of further studies to deepen this relationship.

The study highlights that PS quality is associated with SR, even after controlling for depression and melancholia. We emphasize the importance of healthcare professionals including the assessment and treatment of sleep disorders in suicide prevention strategies.

Sleep Complaints in Children and Adolescents with Major Depressive Disorder: Early Markers of Illness Severity

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Introduction: Affective disorders are among the most prevalent forms of mental illness in youth, and they can impose a substantial and often long-lasting burden on development if left unaddressed. Evidence suggests that sleep disturbances not only increase the risk of developing depression within five years but are also associated with a higher incidence of suicidal behavior in youth. This study aimed to investigate whether children and adolescents with depression and multiple sleep complaints present higher depression severity and how these complaints may impact their global functioning.

Materials and methods: Our sample included 142 children and adolescents with Major Depressive Disorder (MDD) and reporting sleep complaints, according to DSM-IV criteria assessed by Diagnostic Interview for Children and Adolescents (DICA IV). The participants were consecutively referred to an outpatient clinic. Depression severity was measured using the Children's Depression Rating Scale (CDRS), a 16-item clinician-rated scale. Global functioning over the past month was assessed using the Children's Global Assessment Scale (CGAS) for individuals under 18 years old. A one-way ANOVA was used to compare CDRS T-scores and CGAS scores across youth presenting with 1 to 4 different sleep complaints. The significance level was set at 0.05 in this study.

Results: All participants had sleep complaints (mean of age = 11 ± 8.1 ; 55% boys) and 57% were under 12 years old ($n=142$). The severity of disease were obtained by the mean CDRS T-score: 78.7 ± 7.1 ,

indicating clinically significant depressive symptoms. Prevalence of specific sleep complaints: 88.7% had initial insomnia, 54.2% had night awakenings, 34.5% showed early awakening, and 31% exhibited hypersomnia. Youth with three or more sleep complaints had significantly higher depression scores with CDRS T-score: $[F(3,138)=5.7, p=0.001]$, and particularly among adolescent boys: $[3,138]=3.1, p=0.027]$. Having more sleep complaints in depressive youth, these patients did not worsen the overall CGAS score $[F(3, 138)=.96, p=0.41]$.

Conclusions: Sleep complaints in youth with depression are associated with greater severity of depressive symptoms, specially in adolescent boys. Interestingly, this was not reflected in overall global function scores, suggesting that sleep disturbances may serve as early clinical markers of illness severity rather than indicators of broader functional impairment. A comprehensive evaluation of sleep disturbances is crucial in managing depressive episodes in youth. Future studies should clarify the specific role of different types of sleep complaints and their potential link to suicidal risk and treatment outcomes in this population.

Sleep in schizoaffective disorder: a systematic review and meta-analysis

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Introduction: A systematic review and a meta-analysis of sleep studies in schizoaffective disorder were conducted using published articles researched in major databases within the period since inception to June 15, 2025. Sleep parameters of drug-free schizoaffective patients (SZA) were analyzed and, where available, compared with case-control data of healthy controls (HC), drug-free schizophrenics patients (SCZ) and drug-free depressed patients (MDD).

Materials and methods: A total of 9 studies with 67 SZA, 88 SCZ, 79 HC and 131 MDD were included in the meta-analysis. Further 23 studies with 87 SZA, 143 SCZ, 1038 HC and 31 MDD were included in the systematic review. Data were extracted regarding 15 sleep parameters: total sleep time (TST), sleep latency (LAT), wakefulness time during sleep (WAKE), REM time (REMT), REM percentage (%REM), REM latency (REMLT), REM density (REMD), stage 1, 2 and 4 sleep time (ST1, ST2, ST4) and percentage (%ST1, %ST2, %ST4), delta sleep time (DELTAT) and percentage (%DELTA). All the patients were drug-free for a minimum of two weeks in all but one study, where they have been drug-free for two days. A minimum of three studies was required to perform a meta-analysis for each parameter. The primary outcome was the standard mean difference. Data were fitted with a random-effects model. Publication bias assessment was checked by means of Egger's Regression and funnel plot asymmetry.

Results: SZA showed reduced TST ($p<0.001$), increased LAT ($p<0.001$) and WAKE ($p<0.001$) compared to HC. SZA showed reduced REMT ($p=0.006$) and shortened REM latency ($p=0.007$) compared to HC. SZA showed reduced stage ST4 ($p<0.001$) and %ST4 ($p<0.001$) compared to HC. SZA did not differ from HC regarding %REM and DELTAT.

SZA showed increased LAT compared to MDD ($p<0.001$). SZA did not differ from MDD regarding TST, WAKE, REMT, %REM, REML, REMD, ST4, %ST4, DELTAT, %DELTA.

SZA did not differ from SCZ regarding any sleep parameter.

Conclusions: Drug-free SZA sleep does not seem to differ from that of drug-free SCZ and drug-free MDD (except for SLAT in this last comparison). SZA patients show a shorter and more fragmented sleep, with difficulties falling asleep, compared to HC. SZA show a shortened REML and a reduced REMT compared to HC, with slow-wave sleep time deficits like that of SCZ and MDD. Literature regarding sleep in SZA is very limited, therefore meta-analysis could not be performed for some parameters (REMD and %DELTA in SZA vs HC; ST1, %ST1, ST2, %ST2 in SZA vs HC and in SZA vs MDD). Heterogeneity of 40% of meta-analyses in this study was substantially high ($>70\%$). Further studies, preferably involving drug-naïve patients, are needed to clarify whether SZA sleep is more similar to that of SCZ or MDD. Specific attention should be allocated to the investigation of REMD in SZA, for this data could help clarifying the significance of REMD in human sleep and its usefulness as a marker of affective and/or psychotic disorders.

Sleep Profiles in Schizophrenia Inpatients: A Cross-Sectional Study of Clinical and Genetic Associations

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Introduction: Schizophrenia is frequently accompanied by sleep disturbances that persist beyond acute psychotic episodes. Up to 80% of patients report dyssomnia, which correlates with poorer outcomes. While insomnia dominates during psychosis, emerging evidence suggests circadian rhythm disruptions become prominent in non-acute schizophrenia, potentially linked to genetic variations in clock genes. This study hypothesized that sleep disturbance in schizophrenia is clinically heterogeneous, circadian sleep-wake abnormalities are prevalent and associated with polymorphisms in circadian system genes.

Materials and methods: Design and Participants

A cross-sectional study (2021–2023) enrolled 391 inpatients with paranoid schizophrenia (ICD-10: F20.0) from psychiatric hospitals in Omsk and Ufa, Russia. Exclusion criteria included comorbid diagnoses, active psychosis, or recent benzodiazepine use.

Assessments

- **Sleep Quality:** Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI).
- **Psychopathology:** PANSS (Positive and Negative Syndrome Scale) and Calgary Depression Scale (CDSS).
- **Genetic Analysis:** RT-PCR genotyping of *CLOCK* (rs1801260), *MTNR1A* (rs34532313), and *MTNR1B* (rs10830963).

Statistical Approach

Non-parametric tests, ROC analysis, and two-step cluster analysis (IBM SPSS 27). Propensity Score Matching (PSM) balanced groups with/without sleep disturbances (155 patients each) for therapy heterogeneity.

Results: Prevalence and Characteristics of Sleep Disturbances

Among 391 patients, 58.9% (n=236) exhibited poor sleep quality (PSQI ≥ 5). Strikingly, 48.7% reported subjective sleep dissatisfaction (e.g., prolonged latency, fragmentation) despite normal sleep duration (ISI < 7). This discordance highlighted the inadequacy of duration-based metrics alone for assessing sleep dysfunction in schizophrenia.

Propensity Score Matching (PSM)

To control for confounding effects of therapy, PSM created matched groups (n=155 each) with comparable antipsychotic treatment. Post-matching analysis confirmed no significant differences in treatment profiles ($p > 0.05$), enabling unbiased comparisons.

Cluster Analysis: Three Sleep Phenotypes

Cluster 1 (44.6%): Minimal Sleep Issues – lowest PANSS-Positive scores (15,00 [12,00; 18,00]) and no depression (CDSS: 1,00 [0,00; 3,00]).

Cluster 2 (29.6%): Insomnia Phenotype – highest PANSS-Positive (16,00 [13,00; 20,00]) and CDSS scores (6,00 [3,00; 10,50]), with severe sleep fragmentation and shortened sleep time.

Cluster 3 (25.7%): Circadian Phenotype – delayed sleep onset (latency: 60 ± 22 min) with preserved total sleep duration, interrupted sleep, difficult awakening, and daytime dysfunction. In this group there were practically no patients with depressive symptoms (3,00 [1,00; 5,00]) and P subscale scores (15,00 [12,00; 18,00]) were average for the sample.

Genetic Correlates

- *CLOCK* CC homozygotes had prolonged sleep latency ($p = 0.005$).
- *MTNR1A* CC ($p = 0.043$) and *CLOCK* TT ($p = 0.017$) variants were linked to frequent nocturnal awakenings.

Conclusions:

1. Sleep disturbances in schizophrenia are heterogeneous, with distinct phenotypes: insomnia-dominant (linked to positive symptoms/depression) and circadian-rhythm disruption (genetically driven).
2. The *CLOCK* and *MTNR1A* polymorphisms highlight circadian system dysregulation as a therapeutic target.

3. Clinical Implications:

- Insomnia requires personalised antipsychotic-antidepressant therapy.
- Circadian interventions may benefit 25% of patients.

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Sleep regularity, actigraphic rest-activity rhythms and light exposure patterns in patients with bipolar depression and evening chronotype

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Introduction: Sleep and circadian rhythm disturbances, which are closely related to light exposure, are closely related to bipolar disorder (BD). Eveningness, fragmented and irregular sleep are common features in BD. A lower Sleep Regularity Index (SRI) score has been reported in euthymic BD patients compared to healthy controls, particularly among those with phase delay. This study focuses on a vulnerable group of patients with bipolar depression and eveningness and we hypothesized that a lower SRI correlates with greater delays in sleep and light exposure.

Materials and methods: This study analysed the baseline data obtained from an ongoing randomized controlled trial (ClinicalTrials.gov ID: NCT05357313) involving patients with non-seasonal bipolar depression and eveningness (defined as a Morningness-Eveningness Questionnaire, MEQ score < 42). The assessments included 1-week prospective sleep diary and actigraphy, and one sample of overnight urinary 6-sulfatoxymelatonin (aMT6s). In addition to basic sleep parameters, non-parametric analyses were applied to both rest-activity rhythm (RAR) and white light (WL) exposure actigraphic data. Key actigraphic metrics included: SRI (range 0-100, higher scores indicating greater regularity), intradaily variability (IV; range ≥ 0 , higher values indicating increased activity-rest fragmentation), and L5/M10 start times (onset of the 5-hour/10-hour periods with minimal/maximal average activity or light exposure). The associations between SRI and the sleep/light metrics were explored by Pearson (r) or Spearman (r_s) correlation, where appropriate.

Results: Thirty-two patients with bipolar depression (mean age = 42.0±11.4 years, female: 84.4%) and evening chronotype (MEQ score mean ± SD = 34.3±8.2) were included in the analysis. The SRI scores ranged from 44.6 to 95.0, with a mean of 71.1±14.7. A lower SRI score correlated with a later rest start time ($r = -0.481$, $p = 0.005$), a later sleep start time ($r = -0.491$, $p = 0.004$), shorter time in bed (TIB; $r = 0.418$, $p = 0.017$), and reduced total sleep time (TST; $r = 0.413$, $p = 0.019$). Regarding light exposure, a lower SRI correlated with a later light exposure L5 start time ($r_s = -0.562$, $p = 0.001$) and a higher IV ($r = -0.475$, $p = 0.006$). No correlation was found between SRI and the creatinine-adjusted urinary aMT6s levels ($r = 0.162$, $p = 0.459$).

Conclusions: In patients with bipolar depression and evening chronotype, a lower sleep regularity, as measured by SRI, correlated significantly with delayed sleep timings, shorter sleep duration, and an increased variability of light exposure. Our study underscores the intricate relationship among sleep regularity, timing, and light exposure. The findings suggest the potential to integrate therapeutic interventions that target improving sleep regularity, aligning sleep timing, and optimizing light exposure patterns to enhance outcomes in patients with bipolar depression and eveningness.

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Sleep Revolution: The Interplay between Mental Health and Sleep in Untreated Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder, affecting nearly one billion individuals globally, and is associated with substantial cardiovascular and neurocognitive morbidity. In addition to its well-established physiological impacts, growing evidence points to a link between OSA and psychological distress, including symptoms of depression, anxiety, and stress. Despite these associations, the relationship between psychological symptoms and both objective sleep architecture and subjective sleep experience in untreated OSA remains insufficiently understood. This study aims to examine how psychological distress—specifically levels of depression, anxiety, and stress—is associated with objective sleep parameters assessed via polysomnography (PSG) and with subjective sleep quality in individuals with untreated OSA. Additionally, the study will explore whether these associations vary by OSA severity.

Materials and methods:

This exploratory, cross-sectional study includes N = 143 untreated OSA patients (≥18 years) recruited through the Sleep Revolution project (WP8, ISRCTN17539031) across three sleep centers in Germany (Berlin, Mainz, Solingen). Each participant completed a full overnight PSG and a battery of standardized questionnaires assessing psychological distress and subjective sleep parameters. Exclusion criteria included prior OSA treatment, respiratory failure, cardiac instability, and recent substance use disorder.

Key Variables:

- **Objective sleep:** PSG-derived measures (TST, SE, SOL, WASO, REM/NREM stages, arousal index, SpO₂)
- **Subjective sleep:** Insomnia and fatigue scales (ISI, PSQI, ESS, FSS)
- **Mental Health:** DASS-21 subscales for depression, anxiety, and stress

Results: Descriptive and inferential analyses (Pearson/Spearman correlations, multivariable linear regressions) will assess the associations between distress scores and both sleep physiology and perceived sleep quality. Models will be adjusted for age, sex, and BMI. Severity-stratified subgroup analyses (based on OSA severity) will explore potential severity-dependent relationships. Results are currently being analyzed and will be presented at the congress.

Conclusions: By identifying patterns between psychological distress and sleep characteristics in untreated OSA, this study aims to enhance understanding of the mental health implications of sleep-disordered breathing. Findings may inform more personalized diagnostic and therapeutic strategies, integrating mental health support alongside standard OSA treatments.

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Stimulant Medications and Sleepiness in ADHD: Insights from a Sleep Deprivation Study

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Introduction: Individuals with attention-deficit hyperactivity disorder (ADHD) often experience heightened levels of sleepiness compared to the general population, particularly under conditions of sleep deprivation. This study investigates the impact of stimulant medications (Methylphenidate and Amphetamine) on the sleepiness curve of young men diagnosed with ADHD, during and following an extended period of sleep deprivation.

Materials and methods: Fifty-nine young men (age 18 – 35) participated in this study. Among them, 39 participants had been diagnosed with ADHD combined type and were regular users of stimulant medications (ADHD group), while 20 served as a control group without ADHD (control group). The ADHD group was further divided into two subgroups: a medicated ADHD group (n = 17), who took

their regular doses of either Methylphenidate (n = 13) or Amphetamine (n = 4) during the experimental session: at 8:00 a.m. and again at midnight (ADHD medicated group), and an unmedicated ADHD group (n = 22), who refrained from medication during the experimental session (ADHD unmedicated group). Participants were required to maintain a regular sleep schedule for five consecutive nights prior to the experimental session, ensuring at least seven hours of sleep per night (from 23:00/24:00 to 7:00/8:00), verified via actigraphy. The experimental session began at 8:00 a.m. and included 25 hours of sleep deprivation, during which participants were kept awake in a controlled environment. During this period, Sleepiness was measured hourly using the Karolinska Sleepiness Scale (KSS).

Results: No significant differences were observed in sleep duration, sleep onset latency, or sleep efficiency between the two ADHD subgroups (the ADHD unmedicated group and the ADHD medicated group) during the pre-experimental period. However, during the sleep deprivation session, the unmedicated ADHD group exhibited significantly higher sleepiness scores compared to the control group, particularly during the post-midnight hours. In contrast, the medicated ADHD group displayed sleepiness scores similar to those of the control group throughout the experimental session.

Conclusions: Stimulant medications, such as Methylphenidate and Amphetamine, effectively mitigate excessive sleepiness experienced by young men diagnosed with ADHD, even under conditions of extended sleep deprivation. These findings have important clinical and theoretical implications. Given the negative effects of sleepiness on cognition and emotional regulation, these results suggest that the beneficial effects of stimulant medications in ADHD may partially stem from their effect on sleepiness.

Systematic Review and Meta-analysis of Nonpharmacologic Interventions for Sleep Disorders in Individuals with Attention-Deficit Hyperactivity Disorder (ADHD)

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Introduction: Sleep disturbances are highly prevalent among both children and adults with ADHD, contributing to increased symptom severity and can negatively affect psychosocial functioning and quality of life for individuals with ADHD and their families.

Materials and methods: We conducted a systematic review of studies evaluating nonpharmacological interventions for sleep and ADHD interventions evaluating the effects on sleep. We searched PubMed, CINAHL, Embase, Web of Science, Scopus, and PsycINFO; and we reference-mined systematic reviews indexed in PubMed, Cochrane Database of Systematic Review (CDSR), Campbell Collaboration, and PROSPERO. We also searched guideline and research repositories, reference-mind reviews, and consulted a technical expert panel. Two independent reviewers screened citations and full text. We used random effects meta-analyses and explored multiple potential effect modifiers. We assessed risk of bias, applicability, and strength of evidence (SoE).

Results: In total, 44 studies met inclusion criteria. This included 32 studies evaluating an intervention that addressed sleep as well as 12 studies reporting on the effect of sleep of an ADHD intervention not explicitly targeting sleep. Nonpharmacological sleep interventions showed positive effects on sleep (SMD 0.47; CI 0.14, 0.80; 15 studies; RR 1.10; CI 0.59, 2.08; 5 studies; moderate SoE) and ADHD symptom scores (SMD 0.61; CI 0.26, 0.95; 11 studies; moderate SoE). We did not detect systematic effects of nonpharmacological ADHD interventions on sleep. No direct comparisons of two competing interventions has been replicated. Identified studies rarely tested the effects of specific nonpharmacological sleep intervention components and the evidence was insufficient. Studies reported on the potential effect modifiers for age, sex, and ADHD presentation but the evidence was insufficient for concrete evidence statements.

Conclusions: Targeted nonpharmacological interventions focusing on sleep have the potential to improve both sleep quality and ADHD symptoms. Addressing ADHD symptoms alone may not lead to improvements in sleep. These findings may inform clinician and patient decisions regarding incorporation of sleep-focused interventions in comprehensive treatment strategies for ADHD.

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The Bidirectional Association Between Sleep and Affect: Evidence from the Budapest Sleep, Experiences, and Traits Study

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Introduction: Sleep and mood are closely linked, but findings more consistently show that sleep predicts next-day mood than vice versa. Prior research often relies on subjective measures and cross-sectional designs, limiting insight into their dynamic, bidirectional relationship. We aimed to examine the bidirectional associations between sleep and daily affect and to identify which trait-level moderators influence these links.

Materials and methods: We analyzed data from the Budapest Sleep, Experiences, and Traits Study (BSETS), a 7-day observational study involving 269 participants and 1,901 nights of data, combining psychological assessments with daily mood and sleep tracking. Participants completed a baseline test battery assessing personality traits and affective dispositions, followed by 7 days of diary-based PANAS mood ratings and sleep monitoring using the Dreem2 portable EEG device. Subjective sleep quality was measured with the Groningen Sleep Quality Scale. Within-person associations were examined using random intercept and random slopes models.

Results: Higher daily positive affect (PA) predicted later bedtime ($p < 0.001$). In the reverse direction, earlier bedtime ($p < 0.001$), earlier wake-up time ($p < 0.001$), shorter sleep latency ($p < 0.01$), and better subjective sleep quality ($p < 0.001$) predicted higher next-day PA. Extraversion, sociability, and depression moderated the association between sleep timing and PA.

Conclusions: Our findings confirm that sleep and mood influence each other bidirectionally. Earlier sleep timing and better subjective (but not objective) sleep quality are associated with improved next-day mood, particularly in individuals high in extraversion and sociability. In contrast, participants with higher depression scores showed weaker sleep–mood links. These findings suggest that targeting sleep timing may be especially effective for mood enhancement in socially engaged individuals, while alternative approaches may be needed for those with elevated depressive traits.

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The Impact of Sleep Quality on Prefrontal Hemodynamic Response during Verbal Fluency Task in Depression: An fNIRS Study

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Introduction: Major depressive disorder (MDD) is frequently accompanied by significant sleep disturbances. Sleep quality critically impacts cognitive functions, including verbal fluency, and neurovascular activity. Functional near-infrared spectroscopy (fNIRS) provides a non-invasive method for investigating task-evoked cortical hemodynamic responses. This study aimed to investigate how sleep quality in individuals with MDD influences hemodynamic responses, primarily indexed by changes in oxygenated hemoglobin (HbO) concentration, in target brain regions during a verbal fluency task (VFT).

Materials and methods: This study enrolled 196 patients with MDD fulfilling DSM-5 diagnostic criteria. Participants' sleep status was assessed using Item 4 of the Self-Rating Depression Scale (SDS). Depressive symptoms, anxiety, and anhedonia were evaluated with the SDS, Self-Rating Anxiety Scale (SAS), and Snaith-Hamilton Pleasure Scale (SHAPS) respectively, while ruminative symptoms were measured using the Ruminative Response Scale (RRS). During performance of a standardized Verbal Fluency Task (VFT), participants underwent hemodynamic monitoring via a 48-channel fNIRS system. Statistical analysis was performed using SPSS 26.0. Functional near-infrared spectroscopy (fNIRS) data underwent dedicated preprocessing with NirSpark software. Primary analytical methods employed included the chi-square test, analysis of variance (ANOVA), and Pearson/Spearman correlation analyses.

Results:

1. No significant differences were observed between groups in age, gender, or educational level (all $P > 0.05$).
2. Significant differences were observed between MDD patient groups stratified by sleep problem severity on measures of anhedonia ($F = 4.274$, $p < 0.05$), depression ($F = 32.234$, $p < 0.05$), anxiety ($F = 106.413$, $p < 0.05$), and rumination ($F = 64.367$, $p < 0.05$).
3. During the VFT, MDD patients with severe sleep problems, compared to other groups, demonstrated significantly increased HbO concentration activation in the temporal pole (Brodmann Area 38, BA38) and Broca's area (BA44), alongside significantly reduced HbO concentration activation in the dorsolateral prefrontal cortex (BA46). Furthermore, the dorsolateral prefrontal cortex demonstrated the weakest haemodynamic response intensity during the 60-second task activation period."

Conclusions: This study demonstrates that poorer sleep quality in MDD patients is associated with more severe symptoms of anxiety, depression, anhedonia, and rumination. Furthermore, compromised sleep quality may alter patterns of task-evoked cerebral hemodynamic responses. These findings provide novel evidence supporting the neurophysiological mechanisms underlying the sleep-cognition-emotion interactions in depression. Improving sleep quality represents a promising intervention target for optimizing cognitive function and enhancing the efficacy of neuromodulatory treatments in MDD.

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The Mediating Role of Depressive Symptoms in the Association Between Dysfunctional Sleep Cognition and Insomnia Severity Among Chinese Students

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Introduction: Insomnia is prevalent among students and is often influenced by both cognitive and emotional factors. Dysfunctional beliefs about sleep (DBAS) have been linked to poor sleep outcomes, but the underlying mechanisms remain underexplored in young populations. This study aimed to investigate whether depressive symptoms mediate the relationship between dysfunctional sleep-related cognition and insomnia severity among Chinese students.

Materials and methods: A cross-sectional survey was conducted among 161 student participants (mean age = 16.99 years, 73.2% female). Participants completed the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16), the Patient Health Questionnaire (PHQ-9), and the Insomnia Severity Index (ISI). Mediation analysis was performed using regression-based methods and Sobel test to examine the indirect effect of DBAS on ISI through PHQ-9 scores.

Results: Dysfunctional beliefs about sleep significantly predicted both depressive symptoms ($\beta = 0.25$, $p < .001$) and insomnia severity ($\beta = 0.21$, $p < .001$). When controlling for depressive symptoms, the direct effect of DBAS on ISI remained significant but reduced ($\beta = 0.11$, $p = .025$). The Sobel test confirmed a significant mediation effect ($Z = 3.73$, $p < .001$).

Conclusions: Depressive symptoms partially mediate the association between sleep-related dysfunctional cognition and insomnia severity in students. Targeting both cognitive distortions and emotional distress may enhance the effectiveness of sleep interventions in this population.

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Therapeutic Education Targeting Sleep in Military PTSD: Design and Progress of the EDUSOMMEPT Study

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Introduction: Sleep disturbances are highly prevalent in military post-traumatic stress disorder (PTSD), notably insomnia and trauma-related nightmares. Despite their clinical significance and prognostic value, no standardized program in France specifically targets these nocturnal symptoms. Building on preliminary qualitative assessments and prior psychoeducational workshops, we developed a therapeutic patient education (TPE) module addressing sleep-related issues in PTSD, inspired by core principles of cognitive behavioral therapy for insomnia (CBT-I) and adapted to the specific constraints of military populations.

Materials and methods:

The EDUSOMMEPT study aims to evaluate the effectiveness of this therapeutic module on insomnia severity, trauma-related sleep symptoms, quality of life, and sleep physiology, using a multimodal assessment strategy.

This ongoing, prospective, multicenter study (National Military Teaching Hospital Begin and Percy) involves 50 active or former military personnel diagnosed with PTSD (PCL-5 > 38). The TPE module integrates cognitive-behavioral principles, psychoeducation, and relaxation techniques. Outcomes are assessed pre- and post-intervention (1 and 6 months) using validated instruments, including the Insomnia Severity Index (ISI), WHOQOL-BREF, PCL-5, BDI, PSQI, and the TRNS-FR—recently validated in our team (*Military Medicine*, 2024). Sleep is also monitored via actigraphy and home EEG (Zmax®).

Results: Initial feedback reveals high patient adherence and perceived relevance. To illustrate the program's clinical utility, we propose to present individual patient cases, showing pre/post intervention changes in subjective and objective sleep parameters.

Conclusions: EDUSOMMEPT is the first structured TPE program in France designed to address sleep disturbances in PTSD. It offers a promising model for personalized, scalable interventions in trauma-exposed populations.

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Trauma-related nightmares: From nosography to physiology, bridging Mind-Body dynamics in sleep

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Introduction: Trauma-related nightmares (TRNs) are vivid, specific sleep phenomena tightly anchored to traumatic experiences and occurring during both REM and non-REM sleep. Unlike idiopathic nightmares, TRNs display a repetitive structure and can precede or persist long after PTSD remission. They are typically classified as replicative, partially replicative, or non-replicative, reflecting different

levels of symbolic transformation. TRNs exemplify mind–body dynamics in sleep through strong autonomic activation and distressing, often abrupt awakenings.

Materials and methods: We synthesized current evidence across nosography, physiology, and clinical management to build an integrative, mind–body model of TRNs. We organized findings from clinical observations and ecologically valid home-based recordings—combining subjective reports with wearable physiological measures (e.g., heart rate, electrodermal activity)—into five blocks: trauma-linked triggers, pre-TRN sleep conditions, sleep-stage mechanisms, TRN-associated awakenings, and post-TRN consequences, leading to treatment implications.

Results: TRNs are triggered by internal/external cues (environmental factors, psychiatric stress, sleep disorders) and converge with sleep instability (arousal, fragmentation, REM/NREM instability) before awakening. They arise from either REM (more symbolic, often late-night) or NREM sleep (more realistic content, higher sympathetic arousal and skin conductance). Awakenings involve panic, hypervigilance, and emotional distress—especially after NREM TRNs—and contribute to chronic sleep fragmentation and daytime impairment. Long-term consequences span psychiatric, cognitive, sleep, and somatic domains, creating a self-reinforcing cycle linking trauma exposure, nocturnal arousal, and health deterioration. Management options supported in this framework include sleep-focused interventions (CBT-I; CPAP for OSA), imagery-based therapies (IRT, ERRT, EMDR, TPE), and pharmacological agents (prazosin, propranolol), within tailored, multimodal care.

Conclusions: TRNs represent a distinct, systemic condition that necessitates personalized, multimodal strategies. Integrating environmental modulation and physiological monitoring with behavioral and pharmacologic treatments is a promising path to disrupt the TRN cycle and reduce their mental and physical health burden.

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Trauma-related nightmares: how to stop losing sleep over subjective complaints!

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Introduction: Trauma-related nightmares (TRNs) are a core symptom of post-traumatic stress disorder (PTSD), characterized by trauma-specific imagery, vivid recall, and sudden arousals. They often cause severe sleep fragmentation and extended awakenings, perpetuating hyperarousal and anxiety. While validated questionnaires such as the Trauma-Related Nightmare Survey – French Version (TRNS-FR) quantify frequency, intensity, and distress, they cannot capture the physiological dynamics of TRNs. Ecological momentary assessment (EMA) enables real-time symptom tracking, while neurophysiological recordings may detect brain and autonomic activity surrounding TRNs. This study explores current methods for bridging subjective reports and objective markers of TRNs.

Materials and methods: We conducted a literature review on psychometric assessments, EMA, and polysomnographic or wearable-based physiological monitoring of TRNs. We also present original findings from our team using TRNS-FR in French-speaking military PTSD patients, combined with home-based sleep recordings. Participants wore a push-button EEG headband (Dreem V2) and an EDA wristband (Empatica E4) over seven consecutive nights to signal TRNs. Sleep stage scoring, electrodermal activity (EDA), and fragmentation indices were computed to examine temporal relationships between nightmare events and autonomic activation. All events were reviewed by a psychiatrist and certified sleep physician to confirm TRN-related awakenings.

Results:

Existing literature confirms that TRN frequency and distress can be reliably measured subjectively, but variability limits objective event capture. Our recordings showed that 65.5% of TRN-related awakenings occurred during NREM sleep, challenging the predominance of REM-related TRNs. EDA analyses revealed significantly higher autonomic reactivity preceding NREM TRNs, with greater EDA

peak frequency than during REM awakenings. These findings support integrating psychometric data with physiological monitoring to address discrepancies between reported symptoms and objective markers.

Conclusions: Current TRN assessment methods face limitations, with persistent gaps between subjective complaints and objective measures. Combining validated questionnaires, EMA, and wearable-based physiological recordings improves TRN characterization and may help refine diagnoses and interventions. Our findings highlight the need to integrate brain and autonomic data into TRN evaluation to better capture instability beyond REM sleep and support advanced analytic methods for PTSD populations.

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Umbrella Review of Pharmacological and Behavioural Sleep Interventions in ADHD Across the Lifespan

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Introduction: Sleep disturbances are highly prevalent in individuals with attention-deficit/hyperactivity disorder (ADHD) and can exacerbate core symptoms and impair quality of life, yet evidence-based guidance on effective sleep interventions across the lifespan remains limited and fragmented. This umbrella review synthesizes findings from systematic reviews of pharmacological and behavioural sleep interventions for individuals with attention-deficit/hyperactivity disorder (ADHD) across the lifespan.

Materials and methods: Following PRISMA guidelines, 1243 studies published up until November 9th, 2024 were identified across five databases. (Embase: 817, MEDLINE: 183, PubMed: 164, Web of Science: 69, Scopus: 10). After exclusions (909 at title/abstract review; 52/67 full-text assessments), 15 systematic reviews were included. Methodological quality was assessed using AMSTAR 2.

Results: Melatonin demonstrated the strongest evidence, particularly when combined with sleep hygiene strategies, improving sleep onset latency (21-27 minutes) and total sleep time (TST) (20-23 minutes) in paediatric ADHD populations. Clonidine showed subjective improvements in sleep latency and evening restlessness with mild side effects (e.g. sedation/fatigue) reported in 31%. Guanfacine was associated with high somnolence rates (up to 73%) and worsening of several sleep parameters. Zolpidem offered minimal objective benefits with frequent mild side effects, while L-theanine improved sleep efficiency but not latency or TST. Behavioural interventions, including CBT for insomnia (CBTi), showed preliminary promise but were limited by methodological heterogeneity and inadequate bias reporting.

Conclusions: Melatonin shows the strongest evidence for managing ADHD-related sleep disturbances in children. Other pharmacological and behavioural interventions show promise but require further evaluation. Notably, dual-orexin receptor antagonists (DORAs) and CBTi, which have robust evidence for treating insomnia in the general population, are relatively underexplored among those with ADHD despite their potential to address circadian dysregulation and comorbid insomnia. Significant research gaps also persist in adult ADHD populations, who are underrepresented in the ADHD and sleep literature despite comprising most new diagnoses. Future studies should adopt standardized methodologies and objective sleep assessments while prioritizing high-quality trials of DORAs and ADHD-specific adaptations of CBT-I to expand evidence-based treatment options across the lifespan and not just in paediatric populations.

Uncovering hidden depression: the critical role of depression screening in sleep disorders at U.S. sleep centers

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Introduction: Depression and sleep disorders are strongly linked, with sleep centers (SCs) reporting depressive symptoms in up to 63% of patients and depression diagnoses in 22%. Despite this, routine depression screening is not standard in SCs. This study aimed to identify patients meeting criteria for a current major depressive episode (cMDE) among those self-reporting clinically significant depressive symptoms (CSDS) in U.S. SCs.

Materials and methods: This retrospective sub-analysis of an ongoing multicenter trial included 147 adults (22-75 years) referred for sleep disorder evaluation. Participants underwent psychiatric assessments using the Mini-International Neuropsychiatric Interview and Patient Health Questionnaire-9 (PHQ-9), with CSDS defined as PHQ-9 ≥ 10 . Descriptive statistics were compared between patients with/without a confirmed cMDE using non-parametric tests. Additional Mann-Whitney U tests assessed sleep characteristics by cMDE, major depressive disorder (MDD), and bipolar disorder (BD) (statistical significance, $p < 0.05$).

Results: Of 147 patients, 57 (38.8%) had a PHQ-9 score ≥ 10 . Among them, 23 (40.3%) were diagnosed with cMDE: 17 (29.8%) met cMDD criteria, and 6 (10.5%) had BD, type I. A significantly lower cMDE prevalence was observed in patients without CSDS. Sleep characteristics showed no significant differences except for a lower N3 percentage in cMDE. BD, type I was associated with higher obstructive sleep apnea comorbidity compared to cMDD.

Conclusions: Our findings suggest major depression prevalence in SCs is five times higher than in the general population, highlighting the need for routine depression screening and psychiatric confirmation. This also aids in identifying comorbidities and fostering tailored interventions to improve outcomes.

REM Behavior Disorders

Altered Interhemispheric Excitability in Patients with REM Sleep Behavior Disorder: An Exploratory TMS Study

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Introduction: REM Sleep Behavior Disorder (RBD) is characterized by the loss of normal muscle atonia during REM sleep, leading individuals to act out their dreams, often violently. RBD is a well-recognized predictor of neurodegenerative diseases, particularly alpha-synucleinopathies such as Parkinson's disease and Lewy body dementia. Understanding the brain changes that occur in RBD, even years before the onset of an overt alpha-synucleinopathy, is crucial for early diagnosis and potential therapeutic interventions. Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique offering a translational window into the brain's electrocortical activity, allowing to detect subtle, even preclinical, alterations in intracortical and intercortical excitability. Previous TMS studies in RBD revealed specific changes supporting the theory of a "retrograde neurodegeneration" spreading from the brainstem upwards to the cortex. However, a key aspect of brain connectivity, i.e., the GABA-mediated interaction between the two hemispheres, largely through by the corpus callosum, had not yet been explored to TMS in this patient group, which is the aim of this exploratory study.

Materials and methods: 10 right-handed individuals with RBD (70.0 years, IQR 65.0-76.0; 6 males) and 10 healthy individuals (65.5 years, IQR 59.0-69.5; 5 males) underwent screening for cognitive function to the Montreal Cognitive Assessment, quantification of depressive symptoms through the Geriatric Depression Scale (short form), and excessive daytime sleepiness to the Epworth Sleepiness Scale. To assess transcallosal functioning, both latency and duration of the ipsilateral silent period (iSP) was

assessed by stimulating the left primary motor cortex at an intensity of 130% of each participant's resting motor threshold (rMT). Motor responses were recorded from the First Dorsal Interosseous muscle from the same side as the stimulation, during active contraction.

Results: Patients and controls were well-matched for sex, age, and years of education. There was no significant difference between the groups for cognitive performance, depressive symptoms, and daytime sleepiness. Similarly, they did not differ for the rMT and iSP latency; conversely, the iSP duration was significantly shorter in patients than in controls (15.0 ms, IQR 13.0-23.5 vs. 27.0 ms, IQR 26.0-28.5; $p < 0.001$). Moreover, a significant positive correlation between the iSP duration and cognitive scores was found; namely, a more pronounced reduction in interhemispheric inhibition was associated with poorer cognitive performance ($r = 0.5349$; $p < 0.05$), although overall cognitive scores remained within the normal limit.

Conclusions: These findings provide the first evidence of interhemispheric disinhibition to TMS in individuals with RBD at risk for alpha-synucleinopathies. This might potentially contribute to the abnormal motor behavior experienced by these patients during REM sleep and support the involvement of GABA-mediated interhemispheric circuits in the pathophysiology of RBD, even when overt motor and/or cognitive symptoms are still not evident. This also aligns with recent imaging studies identifying both structural and functional changes in the corpus callosum of RBD patients. Future studies on larger samples will help to confirm the role of interhemispheric disinhibition to TMS as a potential biomarker for RBD and its progression, ultimately contributing to a better understanding of RBD pathophysiology and improving assessment strategies and therapeutic options.

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Artificial Intelligence in REM Sleep Behavior Disorder: A Systematic Review of Machine and Deep Learning Methods

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Introduction: Rapid Eye Movement (REM) sleep behavior disorder (RBD) is increasingly recognized as a prodromal stage of alpha-synucleinopathies, including Parkinson's disease and dementia with Lewy bodies. Machine learning (ML) and deep learning (DL) hold promise for improving RBD diagnosis, predicting phenoconversion, and enabling large-scale population screening. However, the quality and transparency of ML/DL research in RBD has not been systematically assessed. This systematic review aims to evaluate the reporting quality of ML/DL studies in RBD using the APPRAISE-AI tool.

Materials and methods: PubMed and Web of Science were searched up to April 30, 2025, for studies applying ML/DL where RBD was either the primary outcome or a key input feature. Studies were included if they focused on RBD, confirmed diagnosis using video-polysomnography, and employed ML/DL models. Two reviewers independently screened studies, with disagreements resolved by a third. Reporting quality was assessed using the APPRAISE-AI tool, which scores 24 items across six domains: clinical relevance, data quality, methodological conduct, robustness of results, reporting quality, and reproducibility.

Results: A total of 75 studies met the inclusion criteria. Most studies included cohorts of 20–100 iRBD participants and control groups. Regarding aim, 73.3% focused on RBD detection, 16% on phenoconversion prediction, and a minority on disease subtyping. Most studies relied on traditional ML

approaches while DL models were used in 12% of studies. APPRAISE-AI scoring revealed that 80% of studies demonstrated moderate reporting quality (40–59 points), and 20% had high reporting quality (60–79 points). Key deficiencies included low average scores for transparency (23.3%), hyperparameter tuning (17.1%), bias assessment (26.9%), and error analysis (0.7%). Data leakage was identified in 32% of studies, typically through inappropriate feature selection or overlap of subjects in training and test sets.

Conclusions: ML/DL applications in RBD research are expanding and show encouraging progress. To enable robust development and clinical translation of AI tools, future studies must adopt open science practices, report model development in detail, and avoid critical errors such as data leakage. Clinical journals, in collaboration with sleep and ML societies, should implement stricter reporting standards for evaluation of ML.

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A Sleep-Stage-Independent Framework for Automatic Detection of REM Sleep Behavior Disorder Using Single-Channel EEG

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Introduction:

Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) is a parasomnia characterized by the loss of the physiological REM sleep muscle atonia. In its idiopathic form, it can be considered a prodromal neurodegenerative stage, thus serving as an early marker of neurodegenerative disorders such as Parkinson’s Disease. State-of-the-art diagnostic criteria for RBD are visual-based and require manual scoring of polysomnography (PSG), a labor-intensive and time-consuming process. Various Machine Learning (ML) approaches, based on the automated analysis of PSG-derived signals, have been proposed to support RBD diagnosis. However, they significantly rely on sleep staging and hand-engineered features to characterize N3 and REM phases. This work presents an ML-based, stage-agnostic framework for the automatic detection of RBD individuals through single-channel EEG sleep data, facilitating minimally-invasive sleep investigations while improving diagnostic robustness and scalability.

Materials and methods: PSG scored recordings from 58 patients (6.91 ± 1.19 hours), encompassing 26 Healthy-Control (15 males, 36.8 ± 17.6 years) and 32 RBD (27 males, 62.2 ± 6.4 years), were included. Single-channel EEG data (C3-A2, or C4-A1) were selected to extract features further used to characterize sleep. Specifically, in two approaches: (1) first only NREM segments were considered to assess the impact of N1 and N2 inclusion on RBD classification, compared to N3 alone, (2) then, all sleep was taken as a whole, stage-independent segment, to evaluate the robustness of the approach, which constitutes the main novelty of the current study. Features were extracted separately on the two EEG segments in an epoch-wise fashion; multi-domain features (time, frequency, time-frequency, and nonlinear) were extracted, taking into account key attributes found in topic-related studies. Supervised ML models (Support Vector Machine, K-Nearest Neighbors, Random Forest, Logistic Regression, and XGBoost) were employed to automatically detect RBD subjects by focusing on the top-10 most important features (p -value < 0.001). They retained clinically relevant information, hence highlighting the high interpretability of the proposed framework.

Results: In the NREM-based classification approach, the Logistic Regression emerged as the best model, correctly classifying 84.4% of RBD subjects. The classifier exhibited an 81% Accuracy, 76.9% Specificity, 83.1% F1 score, and 0.91 AUC. On average, all tested models yielded moderately high accuracy, with an average AUC value of 0.86 ± 0.03 on a Leave-One-Subject-Out validation approach. In the stage-independent classification, the XGBoost was the best classifier, with a 86.2% Accuracy,

90.6% Sensitivity, 87.9% F1 score, and 0.91 AUC. The stage-independent approach proved good predictive performance, with an average AUC value of 0.89 ± 0.02 across all models, and valuable overall balance, also compared to previous studies on the same database.

Conclusions: The proposed analysis framework revealed effective diagnostic support capabilities, with moderately high automatic detection performance of RBD subjects. The promising results of the stage-independent analysis point to scalable and accessible RBD screening studies, with clinical implications also in decision-making applications for early identification of neurodegenerative states.

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Association Between Iron Metabolism Biomarkers and REM Sleep Behavior Disorder: A Mendelian Randomization Study

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Introduction: REM sleep behavior disorder (RBD) is a parasomnia characterized by loss of muscle atonia during REM sleep, often preceding neurodegenerative diseases such as Parkinson's disease. Emerging evidence suggests that iron metabolism may play a role in neurodegenerative processes, but its association with RBD remains unclear. This study investigates the causal relationship between iron metabolism biomarkers and RBD using Mendelian randomization (MR).

Materials and methods: We performed a two-sample MR analysis to evaluate the effects of genetically predicted iron metabolism biomarkers, including ferritin, iron, total iron-binding capacity (TIBC), and transferrin saturation (TSAT), on RBD risk. Genetic instruments were obtained from genome-wide association studies (GWAS) of iron metabolism traits, and summary-level RBD data were sourced from a large publicly available GWAS. Several MR methods were applied, including inverse variance weighted (IVW), MR-Egger, weighted median, weighted mode, and simple mode, to ensure robust findings. Sensitivity analyses, including Cochran's Q test, MR-Egger intercept, and leave-one-out analysis, were conducted to assess pleiotropy and heterogeneity.

Results: Our MR analysis demonstrated that genetically predicted higher ferritin levels were associated with a lower risk of RBD (IVW: $\beta = -0.15$, SE = 0.25, $p = 0.57$; MR-Egger: $\beta = -1.22$, SE = 0.46, $p = 0.01$; Weighted median: $\beta = -0.47$, SE = 0.29, $p = 0.11$). For serum iron levels, the IVW method showed a negative association with RBD risk ($\beta = -0.03$, SE = 0.14, $p = 0.83$), while the MR-Egger method suggested a stronger negative effect ($\beta = -0.48$, SE = 0.30, $p = 0.12$). TIBC exhibited a weak positive association with RBD (IVW: $\beta = 0.07$, SE = 0.12, $p = 0.55$; MR-Egger: $\beta = 0.16$, SE = 0.28, $p = 0.57$). For TSAT, no clear association with RBD was observed (IVW: $\beta = -0.02$, SE = 0.08, $p = 0.79$; MR-Egger: $\beta = -0.18$, SE = 0.14, $p = 0.21$). Sensitivity analyses indicated no substantial heterogeneity (Cochran's Q test: $p > 0.05$ for all exposures) and no significant horizontal pleiotropy (MR-Egger intercept $p > 0.05$).

Conclusions: Our findings suggest a potential protective role of ferritin in RBD, with a stronger effect observed in MR-Egger analysis. While other iron metabolism markers, including iron, TIBC, and TSAT, did not show strong causal evidence, the direction of effect estimates warrants further investigation. Future studies are needed to explore the underlying mechanisms linking iron metabolism to RBD and its progression to neurodegenerative diseases.

Automated analysis of home video for screening REM sleep behaviour disorder

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Introduction: Isolated REM sleep behavior disorder (iRBD), a prodromal syndrome of alpha-synucleinopathy neurodegeneration is characterized by vivid and often action-packed dream enactment behaviors (DEBs) during REM sleep. Early detection of iRBD benefits in preventing the progress of neurodegeneration, and sleep-related injuries caused by DEBs. With the availability of ambulatory home-PSG measurement, emerging studies have supported the validity of screening and diagnosing varieties of sleep disorders, including iRBD, at home setting. In corroborating a diagnosis of iRBD, the use of video-polysomnogram (vPSG) will help to document sleep related movement during REM sleep. However, the detailed manual analysis of vPSG recording is time-consuming and labor-intensive. There has been increasing number of studies exploring the automated video analysis method in distinguishing iRBD from healthy controls, albeit most of them were conducted in laboratory settings. Here we aimed to explore the automated video analysis for screening RBD at the home setting.

Materials and methods: This study included 35 patients with iRBD and 35 non-RBD controls, with the diagnoses confirmed (or excluded) by prior in-laboratory vPSG monitoring, respectively. All subjects underwent home vPSG (Nox A1s) with time-synchronized infrared-night-vision video recording (XIAOMI C700/TP-Link C212). Sleep-wake stages were scored by certified polysomnographic technologists. For the automated video analyses, pixel-value differences between adjacent 2-seconds-frames were calculated to quantify the intensity of movements from REM sleep videos, generating a temporal motion signal. Motion signals were compared with manually score movements results (based on criteria proposed by Frauscher B, 2009). Then, following features of motion signal were compared between iRBD and controls: movement counts (counts of motion signal larger than 1.2/1.4/1.6/1.8 times median of motion signal's peaks [baseline, indicating a "static status" of sleep]) per minute, movement duration percentage (duration of motion signal larger than 1.2/1.4/1.6/1.8 times baseline), and averaged normalized intensity.

Results: We firstly compared motion signals versus manually scored movements during REM sleep. A total of 95 major jerk/movements (e.g., whole body jerk, gross body movement, raising the arm, isolated elevation of one leg) were manually identified from five iRBD patients (66.4 ± 7.4 years, 80.0% male), while the motion signal threshold of 1.2/1.4/1.6/1.8 times baseline identified these movements with sensitivities of 100.0/96.3/91.3/87.9% and specificities of 35.63/83.21/92.31/95.67%, respectively. Then, we compared the motion signals between iRBD patients (67.9 ± 6.6 years, 71.4% male) and controls (66.7 ± 6.8 years, 31.4% male), whose results showed that iRBD group exhibited significantly higher values than controls in movement counts (e.g., 1.6 times: median [IQR]: 2.03 [1.25-3.33] vs 0.23 [0.13-0.50] per minute, $P < 0.001$), movement duration percentage (e.g., 1.4 times: 8.7% [6.1-13.1%] vs 1.2% [0.7-3.7%], $P < 0.001$), and averaged normalized intensity (1.61 [1.45-1.96] vs 1.25 [1.16-1.47], $P < 0.001$).

Conclusions: This study suggested that automated video analysis method would be able to identify epochs with possible behavioral events and differentiate iRBD patients from controls. The findings may highlight the feasibility of using ambulatory home-PSG measurement with infrared-night-vision camera to screen RBD at home settings.

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Brain Connectivity Alterations in Idiopathic REM Sleep Behavior Disorder: A Multi-Cohort Study

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Introduction: Isolated REM sleep behavior disorder (iRBD) is a parasomnia characterized by abnormal movements during REM sleep and is strongly associated with the development of synucleinopathies. As a prodromal condition, iRBD provides a unique window for investigating early neurodegenerative processes preceding Parkinson's disease (PD) and dementia with Lewy bodies (DLB). While disruptions in brain structural connectivity have been well-documented in PD and DLB, their presence during prodromal phases such as iRBD remains unexplored. In this study, we used the largest international multicenter neuroimaging dataset of polysomnography-confirmed iRBD participants to characterize the presence of white matter alterations and their impact on brain architecture. We evaluated global and local efficiency in iRBD, which are key metrics for detecting network disruptions in pathology. Additionally, we explored how other network properties influence local efficiency. We hypothesized that participants with iRBD would show reduced global efficiency, alongside decreased local efficiency in regions implicated in PD or DLB, compared to controls.

Materials and methods: We analyzed Diffusion-Weighted Imaging data from 198 polysomnography-confirmed iRBD patients and 174 controls across seven cohorts. Structural connectivity maps were generated using advanced tractography and connectivity pipelines to reconstruct the white matter architecture between 448 cortical and 14 subcortical regions. Global and local efficiency metrics were calculated to quantify network efficiency and compared between iRBD and control groups, with FDR correction applied for multiple comparisons. W-scores were used to control for age and sex, and ComBat was applied to regress out scanner effects. Additionally, we investigated the association between changes in local efficiency and global efficiency, and other local network features, namely clustering coefficient (interconnectedness of a region's neighbors), connection strength, and degree (number of connections per region).

Results: Structural connectivity in iRBD patients showed significant disruptions compared to controls, with reduced global and local network efficiency. Local efficiency was decreased in 18 cortical and 3 subcortical regions, including the left putamen and bilateral thalamus, and increased in 9 cortical regions, many of which are associated with PD or DLB. Decreased global efficiency was associated with decreased local efficiency in the left putamen, bilateral thalamus, and left lateral orbitofrontal gyrus, as well as increased local efficiency in the left inferior and superior parietal cortices, left insula, and right orbitofrontal cortex. Additionally, local efficiency was positively correlated with clustering coefficient ($r=0.98$, $p\text{-value}_{\text{spin-FDR}} = .001$) and negatively correlated with connection strength ($r=-0.63$, $p\text{-value}_{\text{spin-FDR}} = .001$) and degree ($r=-0.66$, $p\text{-value}_{\text{spin-FDR}} = .001$).

Conclusions: This study reveals global and local efficiency changes in iRBD, aligned with what is observed in PD and DLB. Our results indicate that both decreased local efficiency in subcortical regions and increased local efficiency in specific cortical regions are associated with decreased global efficiency. Additionally, higher-efficiency regions in iRBD have more clustered neighboring regions, and are defined by weaker and fewer connections, potentially reflecting greater tissue damage. Overall, these findings highlight networks reorganization in iRBD, offering insights into white matter alterations preceding DLB and PD, and the mechanisms driving the progression towards these diseases.

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Causal Associations Between Tea Consumption and REM Sleep Behavior Disorder: A Mendelian Randomization Study

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Introduction: Previous studies have shown that tea consumption may have a protective effect against neurodegenerative diseases. However, the exact causal relationship between tea consumption and the precursor stages of certain neurodegenerative diseases, namely REM sleep behavior disorder (RBD), remains unclear. To evaluate the causal association between tea consumption and RBD, we employed a Mendelian randomization study.

Materials and methods: We identified genetic instrumental variables that are significantly associated with tea consumption through genome-wide association studies (GWAS) in European populations. Bidirectional two-sample Mendelian randomization was utilized to determine the causal relationship between tea consumption and RBD, while sensitivity analyses were further employed to evaluate the robustness of the results. The multivariate Mendelian randomization method was used to assess the influence of relevant confounding factors on the results.

Results: In the MR analysis using the inverse variance weighting method, a significant causal relationship between tea consumption and RBD was observed (OR=0.046, 95% CI 0.004- 0.563, $p=0.016$). The consistency of findings across maximum likelihood, MR PRESSO, and multivariate MR after adjusting for potential confounding further supports this causal association. Sensitivity analyses revealed no evidence of heterogeneity or pleiotropy.

Conclusions: The findings of our study demonstrate a robust causal association between tea consumption and RBD, indicating that tea consumption may serve as a protective factor against the development of RBD.

Acknowledgments: The datasets were derived from sources in the public domain: GWAS (<https://gwas.mrcieu.ac.uk>).

Circadian dysregulation in probable isolated REM sleep behaviour disorder: actigraphy insights from the Tasmanian ISLAND Sleep Study

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Introduction: Circadian rhythm disruption is increasingly implicated in the prodromal stages of alpha-synuclein-related diseases, such as Parkinson's disease and dementia with Lewy Bodies. Isolated REM sleep behaviour disorder (iRBD) is one of the earliest symptoms of these diseases, often occurring 10 years or more before a clinical diagnosis. There is an urgent need to develop new methods of detecting iRBD and associated circadian changes early in the disease process. Wearable devices offer a non-invasive, easily accessible means to capture these changes. This study examined whether actigraphy-derived measures of sleep and circadian rhythms could distinguish individuals with 'probable' iRBD (pRBD) from controls.

Materials and methods: 263 participants aged 50+ years from the Tasmanian ISLAND (Island Study Linking Ageing and Neurodegenerative Disease) Sleep Study completed the REM Sleep Behaviour Disorder Single-Question Screen to determine pRBD, and underwent wrist-worn actigraphy to assess sleep (total sleep time, wake after sleep onset, and number of overnight awakenings) and circadian metrics (sleep regularity, interdaily stability, intradaily variability, and timing and magnitude of daily activity). Cosinor analysis was performed to model circadian rhythms by fitting a cosine function to the activity data

Results: 122 participants with pRBD (mean (SD) age 68 (7.4) years; 62% male) and 161 controls (mean (SD) age 69 (7.5) years; 61% male) wore an actigraphy watch for two weeks and completed a sleep diary each day. General sleep metrics, including total sleep time, number of awakenings overnight, and moderate or vigorous activity during the sleep period did not differ between those with pRBD and controls. In contrast, circadian metrics revealed significant group differences. Individuals with pRBD showed decreased sleep regularity ($p < 0.01$), reduced interdaily stability ($p < 0.001$), increased intradaily variability ($p < 0.01$), altered timing of the least active 5 hours of the day ($p < 0.01$), and altered magnitude of activity during the most active 10 hours of the day ($p < 0.01$). Cosinor analysis further confirmed significant differences in circadian rhythm characteristics between the two groups, in both mesor (rhythm-adjusted mean activity; $p < 0.01$) and amplitude (half the difference between peak and nadir of the fitted cosine wave; $p < 0.001$).

Conclusions: In this community-based cohort, actigraphy metrics found significant circadian variation in those with pRBD compared to controls. This study highlights the utility of actigraphy-derived circadian metrics in detecting circadian dysregulation; a feature that has been strongly associated with the development and progression of neurodegenerative disease. These findings suggest that wearable

device data could be used more widely in the community to assist in identifying and monitoring those at-risk for alpha-synuclein-related diseases.

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Clinical, Physiological, and Behavioral Characteristics of iRBD Patients With Ambulatory Dream Enactment Behaviors

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Introduction: Isolated rapid eye movement (REM) sleep behavior disorder (iRBD) is characterized by dream enactment behaviors (DEBs) during REM sleep, accompanied by REM sleep without atonia (RWA). While most patients exhibit DEBs confined to the bed, a minority engage in ambulatory behaviors. This study aimed to investigate the clinical, physiological, and behavioral characteristics of patients exhibiting such ambulatory behaviors.

Materials and methods: This retrospective study reviewed the electronic medical records (EMRs) of 361 patients with video-polysomnography (v-PSG)-confirmed iRBD (mean age: 71.29 years; 213 males). Patients were classified as RBD-walkers if they or their witnesses reported at least one DEB episode involving ambulation, specifically exiting the room through a door; all others were categorized as non-walkers. Group comparisons of demographics, clinical assessments, and PSG metrics between RBD-walkers and non-walkers were conducted using Mann-Whitney U test and Fisher's exact test. Dream contents and related behaviors, obtained through structured sleep interviews, were qualitatively analyzed through thematic analysis.

Results: Among the 361 patients, 23 (6.4%) were classified as RBD-walkers. Clinically, RBD-walkers were more frequently female (60.4% vs. 39.1%, $p = 0.051$) and showed higher scores on Factor 1 of the RBDQ-KR (13.68 vs. 10.74, $p = 0.012$). They were more frequently prescribed a combination of clonazepam and melatonin (60.9% vs. 20.4%, adjusted residual = +4.46), and received higher doses of clonazepam (0.67 mg vs. 0.45 mg, $p = 0.006$).

Behaviorally, RBD-walkers exhibited more complex motor behaviors involving interaction with the sleep environment, such as opening doors (60.9% vs. 0.0%) or performing household tasks (17.4% vs. 0.0%). In contrast, non-walkers more often displayed vigorous bed-bound behaviors, including falling out of bed (43.5% vs. 21.7%). Among RBD-walkers, females more commonly engaged in chores, such as laundry or organizing clothes, than males (17.4% vs. 0.0%), whereas males more frequently exhibited aggressive behaviors, such as punching or kicking (88.9% vs. 42.9%) and weapon use (33.3% vs. 7.1%). Polysomnographic findings showed that RBD-walkers tended to have higher sleep efficiency (84.41% vs. 78.00%, $p = 0.054$) and reduced wake after sleep onset (55.03 min vs. 78.83 min, $p = 0.054$), along with significantly greater proportions of both deep (N3; 13.23% vs. 6.62%, $p = 0.006$) and REM sleep (23.42% vs. 20.69%, $p = 0.046$). Notably, EMG amplitude during REM sleep was higher in RBD-walkers compared to non-walkers (5.56 μV vs. 3.71 μV , $p = 0.031$), observed in both RWA epochs (10.64 μV vs. 8.04 μV , $p = 0.012$) and non-RWA epochs (3.46 μV vs. 2.68 μV , $p = 0.091$).

Conclusions: This study demonstrates that RBD-walkers represent a distinct clinical and neurophysiological phenotype within the iRBD spectrum. Their complex, environmentally interactive behaviors, elevated treatment requirements, and heightened baseline EMG activity during REM sleep suggest involvement of multifactorial mechanisms beyond simple motor disinhibition. These observations highlight the need for further research into the neural correlates and potential prognostic significance of this subgroup.

Cognitive and motor wobbling in isolated RBD: A multicentric study by the International RBD Study Group (IRBDSG)

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Introduction: Patients with iRBD often develop motor and non-motor signs and symptoms before phenoconversion to overt alpha-synucleinopathy. These may fluctuate (wobble) for a long time, making the exact time of the clinical diagnosis of phenoconversion difficult. Although such patients may be called prodromal PD, prodromal DLB or prodromal MSA, they do not yet fulfil diagnostic criteria for any overt synucleinopathy or other neurodegenerative disorder.

Aim of this study was to define and characterize clinically fluctuating transition phases from isolated RBD (iRBD) to possible overt alpha-synucleinopathy.

Materials and methods: IRBDSG centers included patients with over a 3-year follow-up period, who underwent ≥ 3 assessments at intervals ≥ 6 months apart. A wobble event was defined as an improvement at least once in at least one of the following: MDS-UPDRS III (≥ 4 points); MoCA (≥ 4 points) or MMSE (≥ 3 points) or MCI reverting to normal; orthostatic hypotension reverting to normal. PD, DLB or MSA criteria could not be fulfilled at any timepoint.

Results: 87 iRBD wobblers (17.2% female) from 15 centres (Europe, Canada, USA, Australia, Hong Kong, South Korea) were included. Mean age at iRBD diagnosis was 65.3 ± 7.2 y, with a time from diagnosis to first wobble event of 4.9 ± 4.3 y. At baseline the MDS-UPDRS-III was 3.7 ± 3.6 and MoCA 23.7 ± 3.2 . At baseline, 26.1% presented with MCI, 13.0% OH, 55.6% a cardiovascular disease, 29.6% a psychiatric disorder, and 12.0% diabetes mellitus. 50.0% of the patients were taking symptomatic treatment for RBD. 41 patients (48%) were classified as pure cognitive (C) wobblers, 22 (25%) as pure motor (M) wobblers, 19 (22%) as both cognitive and motor (C+M) wobblers. Age at RBD diagnosis, sex, time from diagnosis to first wobble event, presence of MCI, OH, comorbidities, and use of RBD symptomatic treatment did not differ among groups. At baseline, the MDS-UPDRS-III score was higher in the M wobblers and in the C+M wobblers, compared to the C wobblers. The MoCA score was lower in the C wobblers and in the C+M wobblers, compared to the M wobblers.

Conclusions: In iRBD, cognitive and motor symptoms can wobble over time, making the clinical diagnosis of phenoconversion difficult. Wobbling is a yet unreported phenomenon in iRBD and presents important clinical and research implications: if these measures are selected as outcomes in neuroprotective trials, wobbling could be misinterpreted as treatment efficacy. Further observations of wobblers are necessary to determine their final outcomes.

Data-Driven Subtyping of REM Sleep Behavior Disorder Using Sleep-Stage-Independent EEG and Unsupervised Learning

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Introduction:

Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) is a parasomnia characterized by the loss of physiological muscle atonia during REM sleep, often leading to dream-enactment behaviors. In its idiopathic form, RBD is widely recognized as a prodromal marker of alpha-synucleinopathies; longitudinal studies revealed a conversion rate of up to 73.5–96% within 12–14 years from the

diagnosis. Despite its clinical and prognostic relevance, RBD heterogeneity and intra-group disease progression remain underexplored. This work proposes an unsupervised learning framework based on sleep-stage-independent, single-channel EEG sleep data with the aim of identifying subgroups within the RBD population, potentially reflecting different stages or trajectories of disease evolution.

Materials and methods:

Polysomnographic (PSG) recordings of 32 patients diagnosed with RBD (27 males, 62.2 ± 6.4 years) were included in the analysis. A single EEG channel was selected from each recording; the whole sleep segment was employed in the analysis, without sleep stage distinction, to allow for a comprehensive view of sleep-related dynamics. The analysis pipeline is as follows. First, a comprehensive set of features was extracted, capturing overnight brain activity and signal morphology over time, frequency, and nonlinear domains. Second, features were standardized and Principal Component Analysis (PCA) was employed to reduce dimensionality and retain only the most informative variables for the analysis. Then, multiple unsupervised learning algorithms (K-means, Agglomerative, and Spectral Clustering) were applied to the reduced feature space, to identify patient subgroups. Finally, the REM Atonia Index (RAI) was extracted from the EMG signal during REM sleep and used as clinical reference for disease severity.

Results: The clustering analysis revealed two distinct subgroups across all applied algorithms, with K-means showing the highest internal validity (Silhouette score: 0.4), indicating moderate performance on real-world data. The PCA dimensions contributing to cluster separation primarily reflected differences in EEG signal complexity and spectral content, suggesting varying patterns of brain activity during sleep. Specifically, one cluster included subjects with higher EEG frequencies, lower signal regularity and lower values of RAI (0.1347 ± 0.208), while the other showed opposite trends, shifting towards lower EEG frequencies, higher regularity, and increasing values of RAI (0.246 ± 0.275). These findings suggest that the identified subgroups differ not only in electrophysiological features, but also in a clinical marker of severity. Although no single parameter is deemed responsible for cluster separation, the results support the presence of underlying neurophysiological and clinical heterogeneity within the explored RBD population.

Conclusions: This study demonstrates the feasibility of using unsupervised learning on sleep-stage-independent, single-channel EEG data to explore heterogeneity in RBD and identify latent subgroups. The clustering results support the presence of different trajectories in RBD and highlight varying electrophysiological profiles, potentially corresponding to different disease stages. These insights could contribute to the development of early diagnostic support tools and personalized interventions in the context of neurodegenerative disease prevention and management, offering a non-invasive, data-driven approach for stratifying patients and monitoring disease progression.

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Diagnosing idiopathic REM sleep behavior disorder, Parkinson's Disease with or without RBD using single-lead electrocardiogram of polysomnography

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Introduction: Rapid eye movement (REM) sleep behavior disorder (RBD) is recognized as a prodromal stage of alpha-synucleinopathies. Among individuals with Parkinson's disease (PD), the presence of RBD is associated with a more severe clinical phenotype and extensive cerebral pathology compared to those without RBD. This study aimed to differentiate idiopathic RBD (iRBD), PD with RBD (PDRBD), and PD without RBD (PDnoRBD) using heart rate variability (HRV) features derived from single-lead electrocardiogram (ECG) recordings during polysomnography (PSG).

Materials and methods: We retrospectively analyzed subjects who underwent both PSG and dopamine transporter positron emission tomography (PET) between January 2010 and December 2021. The study cohort comprised 4 individuals with iRBD, 9 with PDRBD, 8 with PDnoRBD, 9 clinical controls (NotRBD), and 15 healthy controls (HC). HRV features were extracted from PSG-derived ECG data, and group classification was performed using machine learning algorithms.

Results: Demographic variables and obstructive sleep apnea severity did not differ significantly across the groups, except for the HC group. Machine learning models effectively distinguished between iRBD, PDRBD, and PDnoRBD based on ECG-derived HRV metrics.

Conclusions: This study highlights the potential of single-lead ECG signals as a non-invasive tool to classify RBD and PD subtypes. These findings support the utility of autonomic biomarkers in differentiating neurodegenerative phenotypes and provide a basis for future prospective studies to predict phenoconversion from iRBD to overt synucleinopathy.

Diagnostic Cutoffs for REM Sleep Without Atonia in Isolated REM Sleep Behavior Disorder from a Korean Population

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Introduction: Isolated REM sleep behavior disorder (iRBD), characterized by REM sleep without atonia (RWA), is a prodromal stage of alpha-synucleinopathies. Although diagnostic cutoffs for RWA are established in Western populations, ethnic variations necessitate confirmation of these criteria in Asian cohorts. Previous Korean studies were limited by small sample sizes, manual scoring methods, and inconsistent quantification standards. Using advanced automated algorithms, this study aimed to establish reliable diagnostic cutoffs for RWA quantification for Koreans.

Materials and methods: Baseline polysomnograms were analyzed from 95 iRBD patients (aged 66.2 ± 7.4 years; 63.2% male) diagnosed at Seoul National University Hospital, free from secondary causes, neurological disorders, or severe obstructive sleep apnea. Controls consisted of 24 matched individuals (16 with restless leg syndrome, 8 healthy subjects), and an external validation cohort comprised 95 matched elderly Koreans without RBD. Single-night PSG included EEG, EOG, ECG, respiratory monitoring, mentalis (MT), and bilateral flexor digitorum superficialis (FDS) EMG recordings. MT electrodes were attached to all participants, whereas FDS electrodes were attached to all controls and 42 patients with iRBD. Automated RWA quantification utilized the validated in-laboratory algorithm (AURA), demonstrating high reliability compared to human scoring (PABAK: 0.736–0.945). RWA was assessed using SINBAR criteria, AASM criteria, cumulative RWA percentage (CRWA%), and REM atonia index (RAI). Diagnostic performance was assessed using receiver operating characteristic analyses, with bootstrap methods (1,000 iterations) for 95% confidence intervals (CI), determining cutoffs internally and validating externally.

Results:

Optimal and specificity=1 cutoffs for the MT channel included CRWA% (5.62% and 5.62%, AUC: 0.94 [0.91–0.98]), Tonic SINBAR (0.55% and 2.83%, AUC: 0.86 [0.80–0.91]), Phasic SINBAR (14.32% and 19.89%, AUC: 0.87 [0.79–0.93]), Any SINBAR (17.47% and 20.02%, AUC: 0.92 [0.87–0.96]), Phasic AASM (4.48% and 15.07%, AUC: 0.82 [0.73–0.91]), Any AASM (7.55% and 16.00%, AUC: 0.92 [0.87–0.97]), and RAI (0.90 and 0.78, AUC: 0.92 [0.85–0.96]).

For the FDS channels, cutoffs were CRWA% (4.50% and 13.16%, AUC: 0.90 [0.82–0.97]), Phasic SINBAR (18.72% and 33.22%, AUC: 0.86 [0.76–0.95]), Any SINBAR (23.92% and 34.95%, AUC: 0.91 [0.83–0.97]), Phasic AASM (8.84% and 27.75%, AUC: 0.84 [0.74–0.94]), and Any AASM (10.00% and 29.38%, AUC: 0.90 [0.82–0.96]).

For the combined MT+FDS channels were: CRWA% (9.21% and 16.40%, AUC: 0.97 [0.94–1.00]), Phasic SINBAR (28.30% and 34.91%, AUC: 0.92 [0.85–0.97]), Any SINBAR (MT) + Phasic SINBAR (FDS)

(36.24% and 36.24%, AUC: 0.97 [0.92–0.99]), Phasic AASM (9.80% and 26.67%, AUC: 0.88 [0.79–0.96]), and Any AASM (MT) + Phasic AASM (FDS) (13.86% and 27.52%, AUC: 0.97 [0.94–1.00]).

When the optimal and specificity=1 cutoffs for the MT channel were applied to the external validation cohort, both specificity and sensitivity fell within the CIs observed in the internal cohort, indicating no significant differences in performance.

Conclusions: Our findings showed that RWA diagnostic cutoffs in Koreans, especially for Phasic and Any RWA, were largely consistent with those reported in Western populations. Notably, the lower tonic RWA observed in our study may help explain the lower phenoconversion rate reported in Korean cohorts compared to Western populations.

Distinct gut microbial, brain gene expression and clinical progression profiles in REM sleep behavior disorder biotypes

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is a well-established prodromal stage of α -synucleinopathies. However, individuals with iRBD demonstrate considerable heterogeneity in clinical symptoms, disease progression, and neurodegenerative trajectories. Our previous work identified two distinct brain-clinical biotypes of iRBD: Biotype 1 (characterized by brain atrophy) and Biotype 2 (characterized by structural brain reserve) with unique neuroanatomical patterns, connectivity, and clinical profiles, while underlying mechanisms driving these divergent biotypes remain unclear. Given the growing evidence implicating the gut-brain axis in neurodegeneration, this study investigated whether these biotypes exhibit differential gut microbiome profiles. We further explored gene expression profiles associated with structural brain changes and clinical trajectories in each biotype.

Materials and methods: T1-weighted MRI and clinical assessments were obtained from 86 Biotype 1 and 86 Biotype 2 iRBD patients, along with 126 controls. Fecal samples were collected from a subset of these subjects, including 42 Biotype 1 and 50 Biotype 2 patients, and 75 controls. Shotgun metagenomic sequencing was performed on these samples to analyze gut microbial profiles, which were then compared between each iRBD biotype and controls. Gene set enrichment analysis (GSEA) was performed to examine transcriptomic pathways associated with neuroanatomical alterations in each biotype. A two-year clinical follow-up evaluated motor and cognitive decline among the two biotypes and controls.

Results: Biotype 1 displayed a severe dysbiosis pattern relative to controls, whereas Biotype 2 showed a microbiome profile more akin to controls after adjusting age and sex. Specifically, Biotype 1 demonstrated elevated abundances of proinflammatory species, including *Collinsella aerofaciens*, *Bacteroides fragilis*, *Eggerthella lenta*, and *Ruthenibacterium lactatiformans*, alongside reduced levels of short-chain fatty acid (SCFA)-producing bacteria, such as *Phocaeicola vulgatus* and *Faecalicatena fissicatena*. Multivariate analyses revealed significant associations between brain atrophy pattern in Biotype 1 and the presence of microbial species such as *Ruthenibacterium lactatiformans*, *Eggerthella lenta*, *Akkermansia muciniphila*, *Hungatella hathewayi* and *Bacteroides fragilis*. GSEA showed that brain atrophy in Biotype 1 was uniquely associated with pathways such as *Alzheimer's disease*, *vesicle-mediated transport in synapse*, *intracellular protein transport*, and *positive regulation of monoatomic ion transport*, converging on neuroinflammation and apoptotic processes. Increased brain structure in Biotype 2 was associated with pathways such as *regulation of postsynaptic neurotransmitter receptor activity* and *enzyme-linked receptor protein signaling pathway*, suggesting adaptive or potentially neuroprotective mechanisms. Longitudinally, Biotype 1 exhibited significantly more rapid progression of motor and cognitive decline compared to Biotype 2 and controls.

Conclusions: The two distinct brain-clinical biotypes identified in iRBD also exhibited divergent profiles in gut microbiota composition, brain gene expression, and clinical progression. These findings also highlight the gut-brain axis with integration of neuroimaging features as a critical contributor to disease

progression and suggest that microbiome-targeted interventions may hold promise as personalized and precision therapeutic strategies in prodromal neurodegenerative stage.

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Environmental Exposures, Clinical Characteristics and Gut Microbial Features in Patients with Early α -Synucleinopathies and Their Cohabiting Partners

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Introduction: Idiopathic REM sleep behavior disorder (iRBD), a prodromal stage of α -synucleinopathies, exhibits gut dysbiosis characterized by enriched pro-inflammatory bacteria and depleted short-chain fatty acids (SCFA)-producing bacteria. Previous studies have shown that microbiome is shaped by shared environment, with cohabiting spouses exhibiting strong similarities. However, whether iRBD-related microbiome dysbiosis exists in iRBD spouses (RS), and how lifestyle and clinical factors affect their gut microbiome remain unclear. This study aims to characterize clinical, lifestyle and gut microbial features in RS, and explore the underlying host-microbiome interplays.

Materials and methods: This cross-sectional study included 58 video-polysomnography-confirmed iRBD patients (69.5 $\pm$ 6.6 years, 87.9% male), 58 RS (66.1 $\pm$ 6.8 years, 12.1% male) and 58 unrelated controls (UC, 66.0 $\pm$ 6.9 years, 13.8% male). UC were 1) age- and sex-matched with RS; 2) not cohabiting with or genetically related to iRBD couples; and 3) had spouses free of RBD or neurodegeneration. Participants underwent clinical assessments, questionnaires, and fecal shotgun metagenomic sequencing. Dietary information was collected using a 20-item questionnaire. Data were analyzed using SPSS 29.0 and R 4.4.2.

Results: Compared to UC, RS trended toward a higher prevalence of possible RBD (defined as RBDQ-HK total score > 18: 8.9% vs. 1.8%, $p=0.098$). RS also exhibited higher prevalence of depression and upper gastrointestinal (GI) disorders. Additionally, the occurrence of injuries in iRBD patients was positively associated with depression in their spouses ($p=0.029$). In contrast, lower GI symptoms—as reflected by Rome-IV diagnosed constipation, bowel movement frequency, and SCOPA-AUT subscores—appeared to be milder in RS versus UC ($p=0.050$, $p=0.088$, $p=0.014$, respectively).

Regarding lifestyle, RS had significantly lower dietary diversity and higher consumption of salty snacks and animal fat than UC. Further analyses within iRBD couples showed positive correlations between patients and their cohabiting spouses in education level, consumption of most food groups (16/20, 80%), cognitive function, and upper GI symptoms.

Metagenomic analyses revealed comparable gut microbial composition between RS and UC, with no significant differences in alpha or beta diversity, or any individual taxa. However, compared to iRBD patients, RS showed significantly reduced observed species, as well as microbial dissimilarity after adjusting for age, sex and constipation. Nine species and five genera differed significantly between RS and iRBD patients, with RS displaying higher abundances of SCFA-producing genera *Agathobaculum*, *Faecalibacterium* and *Roseburia*. Host-microbiome interaction analyses showed that longer constipation duration was negatively correlated with all these SCFA-producing genera, while constipation was associated with reduced *Faecalibacterium* abundance. Additionally, higher consumption of unhealthful plant-based foods, including refined grains and bakery products, was negatively correlated with *Agathobaculum* abundance.

Conclusions: iRBD spouses exhibit higher prevalence of depression and upper gastrointestinal symptoms, alongside lower constipation rates and dietary diversity. Despite shared environmental and lifestyle factors, iRBD spouses did not display RBD-like gut dysbiosis; instead, their microbiota featured a possible enrichment of SCFA-producing bacteria, suggesting a "healthier gut" phenotype. Lifestyle factors, particularly fewer bowel disorders (e.g., constipation), are likely associated with these health-promoting bacteria.

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Evaluation of cardiac autonomic modulation via deceleration capacity during polysomnography in isolated REM sleep behavior disorder and Parkinsonian syndromes

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Introduction: Isolated REM sleep behavior disorder (iRBD) is considered a prodromal stage of alpha-synucleinopathies (aSYN), such as Parkinson's disease (PD) and multiple system atrophy (MSA). These neurodegenerative diseases present both motor and non-motor symptoms, including autonomic dysfunction, which can precede or accompany motor signs. Cardiac autonomic disturbances show syndrome-specific patterns and are also observed in iRBD. However, early clinical differentiation between iRBD converting to PD or MSA remains challenging due to overlapping motor features. Heart rate variability (HRV) offers a non-invasive assessment of cardiac autonomic function, with deceleration capacity (DC) emerging as a sensitive parasympathetic marker. This study investigates HRV and DC profiles in iRBD, PD, and MSA to explore their potential for early diagnosis and potential differential classification of aSYN.

Materials and methods: In this retrospective study, we analyzed full-night polysomnography recordings from 105 healthy controls (HC), 61 iRBD patients, 50 PD patients, and 28 MSA patients. HRV parameters were assessed across all groups, including DC as a marker of parasympathetic function, SDNN (Standard Deviation of NN intervals) reflecting overall HRV, and SDANN (Standard Deviation of the Average NN intervals) representing long-term heart period variability over consecutive 5-minute segments. HRV parameters were analyzed for each sleep stage (NREM stages 1-3, REM sleep), total sleep time, and total recording time.

Results: During the total recording time, HC showed the highest mean DC values (7.35 ms $\pm$ 0.52), followed by PD (7.26 ms $\pm$ 2.8) and iRBD (7.22 ms $\pm$ 1.97). During NREM1 sleep, PD patients showed the highest mean DC values (8.29 ms $\pm$ 3.37), followed by HC (8.13 ms $\pm$ 3.23) and iRBD (7.86 ms $\pm$ 2.51). MSA patients had significantly lower values during total recording time and NREM1 sleep (mean 5.21ms $\pm$ 2.07; 5.73 ms $\pm$ 2.91) compared to all other groups. During total sleep time, mean SDNN was significantly lower in MSA (53.39 ms $\pm$ 30.64) compared to HC (68.12 ms $\pm$ 27.98) and iRBD (67.14 ms $\pm$ 22.44), but not to PD (64.05 ms $\pm$ 1.97). These SDNN differences remained significant for NREM1, NREM2, and REM sleep, but not during NREM3. Mean SDANN was significantly lower in HC (50.68 ms $\pm$ 17.54) compared to iRBD (58.83 ms $\pm$ 15.27) and PD (67.33 ms $\pm$ 31.91) during the total recording time, but not MSA (54.68 ms $\pm$ 16.40). Regarding sleep stages, SDANN was significantly lower in HC compared to MSA in NREM1 and REM sleep, and compared to iRBD during NREM1.

Conclusions: DC may help differentiate MSA from PD and iRBD, complementing other more established HRV markers such as SDNN and SDANN. Reduced DC in MSA reflects pronounced cardiac parasympathetic dysfunction. Considering the impact of autonomic impairment on quality of life and mortality, comprehensive autonomic testing should be included in the diagnostic workup. Larger prospective studies and longitudinal follow-ups of iRBD patients are needed to validate these findings, identify prodromal markers predicting conversion to PD or MSA, and further characterize the progression of cardiac autonomic dysfunction over the diseases' courses.

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Free water imaging predicts phenoconversion in isolated REM sleep behavior disorder: a longitudinal, multicentre, prospective cohort study

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Introduction: Isolated REM sleep behavior disorder (iRBD) is the early manifestation most strongly associated with the development of synucleinopathies, with over 90% of patients eventually converting to dementia with Lewy bodies (DLB) or Parkinson's disease (PD). This makes iRBD a valuable window for early intervention and the evaluation of new neuroprotective therapies. However, there remains a lack of validated, objective, and quantitative biomarkers able to predict disease progression in iRBD, notably in distinguishing progression to DLB versus PD. This study aimed to evaluate the potential of extracellular free water (FW), a diffusion MRI-based proxy of neuroinflammation, as a prognostic biomarker in one of the largest polysomnography-confirmed iRBD neuroimaging cohorts to date.

Materials and methods: Diffusion-weighted imaging scans from 438 participants (261 iRBD patients and 177 controls) were included. Of these, 230 patients were followed longitudinally, for a median of 8.4 years, during which 64 (28%) converted to a neurodegenerative disease and 166 (72%) remained disease-free. FW fractions were computed with the FreeWater Flow pipeline and extracted from the left and right Nucleus Basalis of Meynert (NBM), and posterior substantia nigra (SN). Gray matter volume estimates were also extracted from the NBM regions. FW levels were compared between groups and correlated with motor and cognitive measures. Cox regression models were used to assess the relationship between FW fractions and the likelihood of conversion to PD, DLB, or remaining disease-free. Phenoconversion outcomes were also investigated with multinomial regressions including both FW and NBM volume as covariates.

Results: No significant differences were observed in FW levels between iRBD patients and controls in either the NBM or posterior SN overall. However, stratification by phenoconversion status revealed that iRBD converters showed increased FW values in the left and right NBM and left posterior SN compared to non-converters. Higher FW in the NBM was significantly associated with an increased risk of developing DLB. While NBM volume also predicted phenoconversion to DLB, only FW in the NBM remained a significant predictor when both metrics were included in the same model.

Conclusions: Free water measurement in the SN and the NBM has the potential of predicting the development of a synucleinopathy. Notably, FW in the NBM was specifically associated with the phenoconversion to DLB, but not to PD. Our findings also highlight the greater sensitivity and specificity of FW compared with volumetric measures.

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Free water is increased within the basal forebrain and suprachiasmatic pathways of isolated REM sleep behavior disorder

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Introduction: Cognitive impairments in dementia with Lewy bodies (LBD) and Parkinson's disease (PD) are associated with cholinergic dysfunctions and volumetric reductions within the nucleus basalis of Meynert (NBM). These patients also experience severe sleep-wake dysfunction whose mechanisms relate to dysfunctions within the suprachiasmatic nucleus (SCN). Tractography allows characterizing changes in white matter (WM) tracts, including those departing from the NBM and SCN. Increased free water (FW) within these tracts has been reported in PD. However, the presence of such changes in prodromal stages, such as in isolated REM sleep behavior disorder (iRBD), remains unknown. Here, we examined the presence of FW changes in the NBM and SCN pathways in a large multicenter cohort of polysomnography-confirmed iRBD individuals and controls.

Materials and methods: A total of 621 diffusion-weighted MRI scans (275 iRBD patients and 300 controls) were processed using Tractoflow-ABS followed by bundle-specific tractography using BST-flow. Selected bundles were extracted from 9 bilateral regions, namely the lateral and medial NBM, amygdala, retino-suprachiasmatic-hypothalamic nuclei, and corpus callosum-forceps (minor and major). Statistical differences in the bundles' FW values between iRBD and control groups were tested using binomial GLM models controlling for age, age squared, sex, site, diffusion-measure (DM), age and sex interaction (FDR correction).

Results: Increased FW in the NBM pathway was found in iRBD compared to controls. This increase was observed specifically within the left lateral projections from the NBM, notably the fibers projecting to the left amygdala. An increase in FW in SCN was also observed between iRBD vs controls suggesting that white matter microstructure alterations in iRBD may involve both cholinergic and neuroendocrine circuitry. Taking account of the NBM volume, FW changes in NBM pathways seem strongly associated with PD phenoconversion

Conclusions: These findings demonstrate that NBM and SCN pathways already display changes in iRBD, potentially indicating new early biomarkers of progression in synucleinopathies such as PD and LBD

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Glymphatic defect in isolated REM sleep behavior disorder is associated with phenoconversion to Parkinson's disease

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Introduction: Isolated rapid eye movement (REM) sleep behavior disorder (iRBD) is characterized by the loss of muscle atonia and abnormal, often violent, movements and vocalizations during REM sleep. It is the strongest prodromal marker for progression to synucleinopathies such as dementia with Lewy

bodies (DLB) and Parkinson's disease (PD). iRBD individuals already show brain changes consistent with manifest synucleinopathies, but their mechanisms remain poorly understood. Identifying brain biomarkers that predict disease progression and distinguish future phenoconversion trajectories remains a critical challenge. The glymphatic system is involved in the brain clearance of waste products and its defect has been associated with a higher likelihood of pathological burden and neurodegeneration. MRI-based diffusion tensor imaging along the perivascular space (DTI-ALPS) has been proposed as a noninvasive proxy of glymphatic function. This study aimed to determine whether iRBD patients exhibit a reduced DTI-ALPS index compared to healthy controls, and whether a lower DTI-ALPS index is associated with an increased risk of phenoconversion to PD or DLB.

Materials and methods: We analyzed diffusion-weighted brain MRI data from a large international multicentric cohort of 250 polysomnography-confirmed iRBD individuals (mean age 66.5 ± 6.8 years; 87% men) and 178 healthy controls (65.7 ± 6.8 years; 81% men), recruited across five international centers. Using advanced tractography pipeline (TractoFlow Atlas-Based Segmentation) to calculate the FA map from the ICBM_DTI-81 atlas, we created cubic binary masks (5mm) on bilateral associative and projection fibers at the level of the lateral ventricle. These masks were then aligned to the standard space of each participant using ANTs, followed by quality control. The masks were then multiplied by each directional diffusivity map (x,y,z) obtained from the Tractoflow (FA RGB) results in the subject space. Left and right DTI-ALPS indices were extracted, harmonized for scanner effects, and compared between groups. Cox regression models assessed the relationship between glymphatic index and the likelihood of conversion to PD, DLB or remaining disease-free.

Results: We found a significantly reduced left DTI-ALPS index in iRBD individuals compared to controls (mean difference = -0.034, 95% CI: -0.067 to -0.001; $P = 0.043$). Among the 224 iRBD individuals followed longitudinally (6.1 years, ± 3.5 years), 65 phenoconverted to a synucleinopathy. iRBD converters exhibited lower left DTI-ALPS index compared to non-converters (mean difference = -0.050, 95% CI: -0.098 to -0.003; $P = 0.038$). There was no significant difference between groups for the right DTI-ALPS index. Lower left DTI-ALPS index was associated with increased conversion risk to PD over time (hazard ratio = 2.43, 95% CI: 1.13 to 5.25; $P = 0.012$). Other diffusion metrics inside periventricular masks, namely fractional anisotropy, diffusivity metrics and free water, did not differ between groups.

Conclusions: iRBD patients exhibit reduced DTI-ALPS index, suggesting altered glymphatic function. This reduction was associated with future phenoconversion to PD, supporting the DTI-ALPS index as a potential prognostic MRI biomarker of progression in prodromal synucleinopathies.

Gut microbiota in major depressive disorders with rapid eye movement behavior disorder: tracing a subtype of depression with underlying neurodegeneration

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Introduction: REM sleep behavior disorder (RBD) is a parasomnia associated with α -synucleinopathy. RBD features are more common in major depressive disorder (MDD). While initially postulated as an antidepressant-induced phenomenon, emerging evidence suggests that MDD comorbid with RBD (MDD+RBD) represents underlying neurodegeneration. The gut-brain axis is increasingly recognized in both depression and neurodegeneration, with PD-like gut dysbiosis observed in idiopathic RBD (iRBD). This study aims to characterize gut microbiome in MDD+RBD to explore its potential as a distinct depressive subtype with neurodegenerative features for etiological understanding and intervention.

Materials and methods: This case-control study included four groups: patients with MDD+RBD, age- and sex-matched MDD without RBD (MDD-only), healthy control (HC), and iRBD without a psychiatric disease. RBD diagnosis was confirmed by video-polysomnography. MDD+RBD was defined as MDD onset preceding the appearance of RBD. Fecal samples were analyzed using metagenomic sequencing.

Results: A total of 420 participants were included: 124 HC, 80 MDD-only, 82 MDD+RBD and 134 iRBD. The mean age and sex distribution were comparable among HC (65.7 ± 7.0 years, 61.3% male), MDD-only (65.6 ± 6.5 years, 50.0% male), and MDD+RBD (66.3 ± 5.6 years, 62.2% male). However, iRBD group was slightly older (67.9 ± 6.1 years) and had a higher proportion of males (78.4%) compared to the HC group.

1. **Psychiatric and gastrointestinal features:** The psychiatric profiles of MDD-only and MDD+RBD were largely comparable. Regarding gastrointestinal features, lower Bristol stool scale scores (BSS, harder stool) were observed in iRBD and MDD+RBD, compared to MDD-only and HC (3.3 ± 1.2 vs 3.2 ± 1.5 vs 4.2 ± 1.3 vs 4.1 ± 1.1 , $q < 0.001$).
2. **Neurodegenerative biomarkers:** The total likelihood ratio for prodromal PD (excluding RBD) was higher in MDD+RBD than iRBD, MDD-only and HC (1.78 ± 1.11 vs 1.38 ± 0.97 vs 0.74 ± 0.70 vs 0.44 ± 0.55 , p -value < 0.001).
3. **Microbial profiles:** After adjusting for age, sex and BSS, MDD+RBD exhibited a distinct microbial composition compared to both HC ($R^2 = 0.012$, q -value = 0.003) and MDD-only ($R^2 = 0.011$, q -value = 0.013), while its microbiota composition was similar to that of iRBD ($R^2 = 0.0052$, q -value = 0.26). In contrast, MDD-only was similar to HC in terms of microbial clustering. Taxonomic analysis, adjusting for age, sex and BSS, revealed that MDD+RBD displayed a gut dysbiosis with both PD-associated species (e.g., enriched *Akkermansia muciniphila*, *Ruthenibacterium lactatiformans*, and depleted SCFA-producer *Faecalibacterium prausnitzii*) and depression-related (e.g., enriched *Eggerthella lenta* and decreased *Coprococcus eutactus*) alterations. Random Forest model showed that microbial species and GI features could effectively differentiate MDD+RBD from MDD-only (AUC = 0.78).

Conclusions: MDD+RBD exhibited a gut dysbiosis similar to that of iRBD, whereas MDD-only subjects resembled more closely to HC, suggesting that MDD+RBD is likely a variant of depression with underlying neurodegeneration. In addition, the gut microbiome might serve as a promising biomarker for early neurodegenerative risk stratification in psychiatric populations. Our findings offer novel insights into microbiota-gut-brain axis, highlighting its role in the intersection of depression and neurodegeneration.

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Habitual diet and gut microbiome correlates in isolated REM sleep behavior disorder

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Introduction: Accumulating evidence indicates that habitual diet, including plant-based dietary patterns, are associated with the risk of developing neurodegenerative alpha-synucleinopathy. However, the role of dietary pattern and its correlation with gut microbiome at prodromal alpha-synucleinopathy, i.e., among patients with isolated REM sleep behavior disorder (iRBD), are largely unclear. This study aims to evaluate the associations of dietary patterns with iRBD and their interactions with gut microbial dysbiosis. Additionally, the effect of dietary factors on neurodegenerative progression in patients with iRBD was further examined.

Materials and methods: A total of 287 iRBD patients (66.9 ± 7.1 years, 74.6% males) and 208 controls (66.6 ± 7.3 years, 68.3% males) were involved in the study. Plant-based diet indices (overall plant-based diet index, oPDI; healthful plant-based diet index, hPDI; and unhealthful plant-based diet index, uPDI) were derived from food frequency questionnaire based on 20 food groups. The shotgun metagenomic sequencing for microbiome was performed in 452 subjects (261 iRBD vs. 195 controls) for further diet-microbiome analyses. After a median of 4.1 years, 45 (15.7%) iRBD patients converted to alpha-synucleinopathies. The impact of habitual diet on neurodegenerative outcomes were analysed using Cox proportional hazards models.

Results: Multivariable logistic regression models showed that subjects in the highest quartile of hPDI experienced 52% lower odds of iRBD (OR [95% CI]: 0.48 [0.29, 0.80], $P = 0.005$) compared to the lowest quartile, whereas that of uPDI would increase the odds of iRBD by 73% (1.73 [1.03, 2.91], $P = 0.04$). In terms of individual food groups, iRBD patients had lower intake of whole grains and were prone to consume more refined grains. Notably, the association of uPDI with iRBD was significantly more pronounced in subjects with depression (OR [95% CI]: 1.93 [1.26, 2.95], $P = 0.002$) and those who were physically inactive ($P = 0.01$). Gut metagenomic analysis revealed that habitual diet was linked to the variations in microbial composition and changes in individual microbes among iRBD patients. Further mediation analyses suggested that 39.1% ($P = 0.006$) of the effects of uPDI on iRBD were mediated by iRBD-enriched microbial species *Ruthenibacterium lactatiformans*. During follow-up, iRBD with higher baseline coffee drinking had a decreased risk of converting to alpha-synucleinopathy (Multivariate-adjusted HR [95% CI] = 0.22 [0.06, 0.74], $P = 0.01$), especially parkinsonism-first conversion (0.11 [0.02, 0.66], $P = 0.02$), whereas increased whole grain consumption was associated with lower risk of dementia (0.06 [0.004, 0.87], $P = 0.04$).

Conclusions: Patients with iRBD consumed more unhealthful plant-based diet and a decreased intake of healthful plant-based foods, such as whole grains. The habitual diet in iRBD is closely associated with gut microbiome dysbiosis with predictive value for neurodegenerative progression. The findings suggest that diet, gut microbiome, and their interplay might hold potential value for future interventions in alpha-synucleinopathy neurodegenerative diseases.

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Harnessing Nocturnal Physiology and AI for REM Sleep Behavior Disorder Detection

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Introduction: REM Sleep Behavior Disorder (RBD), a parasomnia characterized by dream enactment and loss of muscle atonia during REM sleep, is one of the most specific prodromal markers of neurodegenerative synucleinopathies, including Parkinson's disease. Individuals with RBD often exhibit signs of autonomic dysfunction—including altered heart rate variability, abnormal respiratory patterns, and impaired blood pressure regulation—even in the absence of overt neurodegenerative disease. Despite its clinical significance, RBD remains underdiagnosed due to the reliance on resource-intensive video polysomnography (vPSG) for confirmation. Physiological signals such as respiration and heartbeat can now be collected continuously across multiple nights using wearable or nearable home-based devices, enabling scalable and non-invasive route for RBD screening. In this study, we developed and validated a novel artificial intelligence (AI) model for detecting vPSG-confirmed RBD based on such accessible nocturnal biosignals.

Materials and methods: This multi-center study comprised 1,323 nights of in-clinic PSG recordings, including 447 vPSG-confirmed RBD cases (72.9% male, mean age 66.3 ± 9.1 years) and age- and sex-matched controls (1:2 ratio, screened to exclude Parkinsonism and RBD). Data were sourced from six clinical centers: Chinese University of Hong Kong, Ruijin Hospital, Second Affiliated Hospital of Soochow University, Sir Run Run Shaw Hospital, Shanghai Sixth People's Hospital, and Inner Mongolia Mental Health Center. The dataset was split into training (70%), validation (15%), and testing (15%) subsets. Respiratory and cardiac signals were extracted from each night of PSG, focusing on features that are potentially measurable in non-laboratory environments. Our Transformer-based foundational model was pre-trained on 44,451 PSG recordings using heartbeat and abdominal-respiration signals. The model learned high-dimensional representations by predicting EEG spectrograms and oxygen desaturation events. It was then fine-tuned for RBD diagnosis using a multilayer perceptron. External validation was performed on an independent dataset from the Affiliated Brain Hospital of Guangzhou Medical University (39 cases, 41 controls).

Results: On the internal testing dataset, the model achieved an accuracy of 86.4%, recall of 80.0%, precision of 78.8%, specificity of 89.6%, and an area under the receiver operating characteristic curve (AUROC) of 0.921. On the external validation dataset, accuracy was 76.3%, with a recall of 84.6%, precision of 71.7%, specificity of 68.3%, and AUROC of 0.872. While there was a moderate decline in overall accuracy and specificity (68.3%) on the external cohort, the model maintained high sensitivity and strong discriminative performance, suggesting robustness in identifying true RBD cases across clinical populations using only respiration and heartbeat-derived features.

Conclusions: Our findings demonstrate the potential of nocturnal respiration and heartbeat signals as digital biomarkers for RBD detection. Their compatibility with wearable and nearable devices makes them well-suited for multi-night, home-based screening applications. The AI-based framework performed consistently across multiple clinical centers, highlighting its applicability as a non-invasive, scalable tool for RBD screening. Further research should assess its utility in home settings and longitudinal value for predicting neurodegenerative disease progression.

Integrated gut microbiome and metabolome analysis in isolated REM sleep behavior disorder

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Introduction: Isolated REM sleep behavior disorder (iRBD) is considered as the most specific prodromal marker of alpha-synucleinopathies, including Parkinson's disease (PD). Emerging evidences suggest similar gut microbiota dysbiosis between iRBD and PD. Fecal metabolomics provide a functional readout of microbial activity, and several key metabolites may play crucial roles in the pathophysiology of PD, including substrates of choline metabolism, amino acids (glutamate and tyrosine), bile acids and long chain saturated fatty acids. However, to date, fecal metabolomics of iRBD has not been thoroughly investigated. This study aims to explore the alterations in fecal microbiome and metabolome in patients with iRBD, along with their possible interactions.

Materials and methods: This is a cross sectional study, including 224 video-polysomnography confirmed iRBD (68.2 ± 7.3 years old, male 73.2 %) and 127 healthy controls (65.7 ± 7.5 years old, male 62.2 %). Fresh stool samples were collected from both groups. Gut microbiota was analyzed using shotgun metagenomic sequencing. Untargeted fecal metabolomics were performed using liquid chromatography–mass spectrometry.

Results: Fecal metabolomics analysis identified 296 metabolites distributed across 37 metabolic pathways. After adjusting for age and gender, 57 differential metabolites were identified (false discovery rate [FDR] < 0.1). Majority of the differential metabolites (N = 45) were more abundant in the iRBD group, including elevated fatty acids (Oleic acid, Myristic acid, traumatic acid) and lipid peroxidation products (15,16-DiHODE, 12(13)-DiHOME, 16-hydroxyhexadecanoic acid), suggesting the potential presence of an inflammatory state and oxidative stress in the gut of iRBD patients. Elevated levels were also observed for amines such as phenylethanolamine, anandamide (AEA), L-histidinol, as well as lithocholic acid, indole and its derivative 2-oxindole. For the metabolites which were decreased in iRBD, Leucine has the most significant depletion, which may indicate disrupted branched-chain amino acid (BCAA) catabolism in iRBD patients.

For the metagenomics, a total of 21 differential microbial species were found between iRBD and controls (false discovery rate [FDR] < 0.1 after adjusted age and gender). For example, the abundances of *Anaeromassili bacillus* sp An250, *Christensenellaceae* bacterium NSJ 63 and *Lachnospiraceae* bacterium NSJ 29 were increased, while *Clostridium fessum* and *Faecalibacterium prausnitzii* were depleted in the iRBD group. We then examined the correlations between differential metabolites and microbial species in both groups. Of note, iRBD-enriched species *Christensenellaceae* bacterium NSJ 63 was widely associated with fecal metabolites indole, leucine, lysophosphatidylglycerol (lysoPG) and lithocholic acid, while these associations were not found in the control group, suggesting that the pathogenesis of iRBD may be closely linked to gut microbiota-mediated metabolic reprogramming.

Conclusions: The gut metabolome, including BCAA degradation, bile acid biosynthesis, phospholipid biosynthesis and tryptophan metabolism, is altered in iRBD, providing important biological insights into the gut-brain pathophysiology of alpha-synucleinopathies. Gut microbiota imbalance may be a driving factor underlying the gut metabolic alterations. These findings support a role for microbial metabolites as potential targets for the development of new biomarkers and therapies in iRBD.

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Investigating Cognitive Performance in Isolated REM sleep Behavior Disorder Patients with Digital-based Cognitive Tests

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Introduction: Isolated rapid eye movement sleep behavior disorder (iRBD) is a well-recognized prodromal syndrome for a-synucleinopathy including Parkinson's disease (PD), associated with

progressive motor dysfunction and cognitive decline. Emerging evidence has indicated that digital measurements provide a sensitive and reliable means to characterize cognitive dysfunctions in PD. This study aims to assess the cognitive performance of iRBD patients with different levels of prodromal Parkinson's disease (pPD) risk using digital-based cognitive tests.

Materials and methods: A total of 354 subjects were enrolled in this study, including 160 controls (mean age 65.8 years, 48.8% males) and 194 video-polysomnography confirmed iRBD patients (68.5 years, 71.6% males). Probability of pPD was calculated according to the 2019 criteria of International Parkinson and Movement Disorder Society 2019 criteria (MDS). Patients with iRBD were stratified into low-to-moderate pPD risk (probability < 0.8, N = 66) and high pPD risk (probability $\geq$ 0.8, N = 128) groups. Cognitive data were collected via the self-developed mobile app SmartBrainApp™, which includes psychomotor vigilance task (PVT), clock setting test, color trails test (CTT), symbol digital modalities test (SDMT), 1-back and 2-back memory tasks, and color vision task. One marker from each task was analyzed to explore group differences using ANCOVA with age as covariate variable and Spearman's correlation was used to examine the relationship between the pPD risk scores and task performance.

Results: Those iRBD patients with high pPD risk showed significantly longer reaction time in SDMT when compared to controls (3.24 vs 2.47, $p < 0.001$) and low-to-moderate risk iRBD patients (3.24 vs 2.61, $p = 0.014$). In addition, the PVT overall reaction time ($p = 0.004$), CTT completion time ($p < 0.001$), and color vision incorrect counts ($p < 0.001$) were higher, while 1-back task d prime ($p < 0.001$) and 2-back task d prime ($p < 0.001$) were lower in high pPD risk iRBD when compared to the controls. No significant differences were found between low-to-moderate risk iRBD and control groups.

In iRBD patients, Spearman's correlation analysis showed weak positive correlations between pPD risk scores and SDMT reaction time ($r = 0.307$, $p < 0.001$). Weaker correlations were observed in CTT completion time ($r = 0.194$, $p = 0.007$), PVT overall reaction time ($r = 0.158$, $p = 0.028$), color vision incorrect counts ($r = 0.156$, $p = 0.03$). Mild negative correlation was also found in correct counts of clock setup test ($r = -0.154$, $p = 0.033$) and 1 back task d prime ($r = -0.25$, $p < 0.001$).

Conclusions: Digital cognitive assessment unveils impairment in working memory, color vision, attention, and executive function among iRBD patients with high pPD risk, whereas those with low-to-moderate pPD risk exhibit no significant deficits. CTT and SDMT are the digital cognitive markers most associated with pPD risk in patients with iRBD. These findings underscore the potential utility of digital biomarkers in stratifying prodromal PD risk and tracking neurodegenerative progression.

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Long-term Follow-up of Olfactory Function in isolated REM-Sleep Behaviour Disorder

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Introduction: The presence of hyposmia in isolated REM sleep behaviour disorder (iRBD) is known as a biomarker of short-term phenoconversion to overt alpha-synucleinopathy, in particular Parkinson's disease (PD). Yet, research about the longitudinal changes in olfactory function over time in iRBD is scarce. One cohort study reported a stable course of olfactory function in iRBD (Iranzo A et al. 2013), although these findings have not been replicated so far. This study aimed at investigating long-term changes in olfactory function in patients with iRBD.

Materials and methods: This long-term observational cohort study was conducted at the Centre for Sleep Medicine, Department of Neurology, Medical University Innsbruck, from 2006 to 2025. Patients with iRBD were consecutively included after polysomnography-based diagnosis and were followed up regularly. Follow-ups included clinical assessment to detect phenoconversion, and biomarker assessment including the Sniffin' Stick 16-item identification test. Olfaction scores were categorized into normosmia, hyposmia or anosmia according to age- and sex-based cut-offs. Olfactory function changes over time were compared among those with iRBD at the last follow-up versus those who phenoconverted during the follow-up time.

Results: A total of 88 patients (90.9% men) with ≥ 2 follow-ups were included. After a mean of 54.2 ± 46.4 months of follow-up, 15 patients phenoconverted (10 to PD, 4 to DLB and 1 to multisystem atrophy)[SA1]. The mean age at baseline was 65.1 ± 10.0 years[SA2]. The baseline olfaction score was

12 (3-16) in those with iRBD at follow-up (hyposmia/anosmia 45.0%), and 9 (5-16) (hyposmia/anosmia 60.0%) in phenoconverters, *p* ns. At follow-up, the median olfaction score was 11 (0-16) in the whole cohort, 12 (0-6) in iRBD (hyposmia/anosmia 51.0%) and 8 (4-14) in phenoconverters (hyposmia/anosmia 87.0%), *p*=0.020 for olfaction score and *p*=0.010 for olfactory dysfunction. The increase in hyposmia/anosmia over time was significant only in phenoconverters (*p*=0.046). The percentage of patients who normal olfaction over time was significantly lower in phenoconverters compared to patients with iRBD at last follow-up (13.0% versus 36.9%, *p*=0.032). Eight (9.1%) patients, all with iRBD at the last follow-up, presented an improvement in olfactory function over time [first score: 10.5 (5.0-11.0), last score: 13.0 (12.0-16.0), *p*=0.005].

[SA1]These must be DLB... Please remind me to check this with you during one of our meetings. In the meanwhile, keep them as DLB for the submission

[SA2]Not needed as you report FU time

Conclusions: The high percentage of olfactory dysfunction in phenoconverters in our cohort confirms hyposmia/anosmia as a marker of phenoconversion in iRBD. In contrast to previous studies, we found a worsening in olfactory dysfunction over time in phenoconverters, suggesting that longitudinal monitoring of olfactory function in patients with iRBD could improve the prediction of phenoconversion risk.

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Neural correlates of decisional impulsivity across early stages of α -synucleinopathy: a case-control functional magnetic resonance imaging study

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Introduction: Idiopathic rapid eye movement sleep behavior disorder (iRBD) is the strongest prodromal markers of α -synucleinopathy, including Parkinson's disease (PD), dementia with Lewy bodies, and multiple system atrophy. PD patients demonstrated altered impulsivity, usually attributed to dopaminergic agonists. Our previous study observed a complex construct of altered impulsivity in iRBD and early PD patients, manifested as decreased risk taking and increased reflection impulsivity. While corticostriatal circuits have been implicated in decisional impulsivity in healthy individuals, their precise role underlying decisional impulsivity across early α -synucleinopathy remains unclear. This study aims to investigate the neural correlates associated with the altered decisional impulsivity in early α -synucleinopathy.

Materials and methods: This was a case-control study conducted among controls, iRBD, and PD patients. Early PD patients were diagnosed with United Kingdom PD Brain Bank criteria with motor symptoms onset within five years. Participants underwent clinical assessments and 3T MRI scanning, including structural, resting-state, and task-based fMRI. Decisional impulsivity was measured using the Balloon Analogue Risk Task (BART) for risk taking and beads task for reflection impulsivity. Regions of interest (ROIs) were selected along corticostriatal circuits. Seed-based functional connectivity (FC) was computed with subcortical ROIs serving as seeds.

Results: A total of 97 patients, including 25 controls (mean age=67.7, male 57.7%), 40 iRBD patients (mean age=70.6, male 72.5%), and 32 PD patients (mean age=69.7, male 89.7%) were recruited. PD and iRBD patients exhibited elevated reflection impulsivity compared to controls, as evidenced by fewer extracted beads (PD vs. iRBD vs. controls: 3.6 ± 2.4 vs. 3.7 ± 2.1 vs. 4.9 ± 2.6 , *P*=0.03).

Meanwhile, risk taking level on the BART was comparable among groups. fMRI analyses revealed augmented neural activities in both ventral and dorsal striatum in iRBD patients during risky decision-making in the BART. Regarding the reflection impulsivity, PD and iRBD patients exhibited enhanced BOLD activations in mPFC during "beads-drawing" phase compared to controls, whereas iRBD patients

showed additional involvement of right ACC/OFC and left parietal lobe during the same phase ($P_{FWE} < 0.05$, TFCE). Further ROI analyses corroborated the findings and additionally revealed increased engagement in bilateral ventral striatum (VS) in PD patients (PD vs. control: right NAc: $0.07[-0.41, 0.70]$ vs. $-0.59[-1.55, -0.26]$, $P=0.002$; left NAc: $0.35[-0.21, 1.16]$ vs. $-1.13[-2.06, 0.05]$, $P=0.03$), whereas enhanced activation in right VS in iRBD patients (iRBD vs. controls: $-0.06[-0.66, 0.44]$ vs. $-0.59[-1.55, -0.26]$, $P=0.002$). Seed-based FC analyses revealed attenuated connectivity in PD patients between right NAc and multiple regions including the bilateral frontal and parietal cortex, striatum, thalamus, and cerebellum. Additionally, iRBD patients displayed decreased FC between the pallidum and both the putamen and OFC. ($P_{FWE} < 0.05$).

Conclusions: Alterations of decisional impulsivity, especially the reflection impulsivity, have already occurred in early α -synucleinopathies. Neuroimaging analyses revealed both the disrupted connectivity which potentially impaired reward networks and the recruitment of corticostriatal circuits contributing to decisional impulsivity deficits. Notably, altered decisional impulsivity in iRBD might reflect compensatory mechanisms following striatal dopamine neurons denervation, suggesting its potential utility as a phenoconversion marker.

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Neurodegeneration and Sleep Instability: A CAP-Based Comparison in RBD Patients

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Introduction: REM Sleep Behavior Disorder (RBD) involves dream enactment and loss of REM muscle atonia. Idiopathic RBD (iRBD) often precedes α -synucleinopathies such as Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB), and Multiple System Atrophy (MSA). Identifying early physiological changes in these patients is critical for intervention and monitoring. The Cyclic Alternating Pattern (CAP), a measure of sleep instability, and the Epworth Sleepiness Scale (ESS), a subjective measure of daytime sleepiness, may reflect early neurodegenerative changes. We conducted a pilot investigation to assess whether these markers differ between RBD patients with and without neurodegeneration.

Materials and methods: This cross-sectional case-control study included 8 patients recruited from a tertiary sleep and movement disorders clinic. All patients had PSG-confirmed RBD, with 4 classified as iRBD (no evidence of neurodegenerative disease after ≥ 12 months of follow-up) and 4 as nRBD (clinical diagnosis of PD, DLB, or MSA).

All participants were 18 years or older and underwent diagnostic overnight PSG demonstrating REM sleep without atonia (RSWA) and/or dream enactment behavior. The ESS was completed within one month of the PSG. Patients were excluded if they were taking medications that could significantly alter sleep architecture (e.g., sedatives, antidepressants) or had comorbid sleep disorders such as obstructive sleep apnea with an apnea-hypopnea index (AHI) ≥ 15 .

Sleep recordings were manually scored in accordance with AASM criteria. Sleep macrostructure parameters included total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency. CAP was scored visually and included CAP rate (percentage of NREM sleep containing CAP sequences), average CAP duration, and the distribution of phase A subtypes (A1, A2, A3). REM-related arousals and total nocturnal arousals were also recorded.

Descriptive statistics were used to compare groups. Given the small sample size, inferential statistical testing was interpreted with caution. Exploratory correlations between ESS scores and PSG features were examined.

Results:

The nRBD group demonstrated a higher CAP rate ($47.8\% \pm 9.1$) compared to the iRBD group ($36.2\% \pm 7.6$, $p < 0.001$). A2 and A3 subtypes were significantly more prevalent in the nRBD group ($p = 0.002$ and $p = 0.009$, respectively), while A1 subtype was lower. REM sleep in nRBD was more fragmented, with increased arousals (12.4 ± 4.1 vs. 7.9 ± 3.6 , $p < 0.001$), and macrostructure was also impaired, with greater WASO and lower sleep efficiency.

Conclusions: Our findings suggest that patients with RBD and neurodegenerative disease exhibit marked sleep instability, particularly reflected in CAP metrics and REM fragmentation. Subjective daytime sleepiness, as measured by ESS, also trended higher in the nRBD group and correlated with CAP-related disruptions, suggesting that these may serve as early physiological signals of underlying neurodegeneration. CAP analysis and ESS may serve as accessible and non-invasive markers to help identify RBD patients at elevated risk of neurodegeneration. Further validation in larger cohorts is needed to confirm these preliminary findings and refine their diagnostic utility.

Neurodegenerative quantification of the putamen in REM sleep behaviour disorder and its impact on brain connectivity architecture

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Introduction: Isolated REM sleep behaviour disorder (iRBD) is characterized by a loss of sleep atonia during REM sleep. It's considered a prodromal stage of synucleinopathies, with ~90% of individuals with iRBD developing Parkinson's disease (PD) or dementia with Lewy body (DLB) within 15 years. Synucleinopathies are characterized by a loss of dopaminergic neurons projecting to the putamen, responsible for movement coordination. Dopamine-binding tomography methods fail to measure dopaminergic loss in around 30% of iRBD patients.

MRI is particularly sensitive to brain changes in iRBD, with previous studies identifying atrophy in the putamen.

However, it remains unknown whether this atrophy follows a topographical pattern reflective of dopamine depletion and associated with the organization of structural connectivity networks. Our objective was to investigate using T1- and diffusion-weighted imaging how atrophy affects the morphology of the putamen in iRBD and its impact on architectural organization of brain connectivity.

Materials and methods:

This study includes 198 iRBD participants confirmed by video-polysomnography followed longitudinally and 121 age- and sex-matched healthy controls. All underwent T1- and diffusion-weighted brain MRI in 6 sites as part of an international multi-center initiative. T1 scans were processed using deformation-based morphometry in CAT12 to measure the extent of non-linear deformation required to fit a subject's brain to the template, yielding a map of local tissue deformation for each participant. The putamen was segmented on these maps and divided into segments along the medial-lateral, anterior-posterior, and ventro-dorsal axes to examine the spatial pattern of atrophy.

Diffusion-weighted MRI scans were processed to reconstruct via tractography each participant's structural connectivity matrix. Connectivity strength measured between every pair of regions (463 regions). BrainSpace was used to reduce the dimensionality of these matrices and derive the most significant connectivity gradients for each participant. Gradient expressions were compared between groups to identify whether the putamen was abnormally weighted in each gradient.

Linear mixed models were used on the deformation values to assess a group*segment effect in the putamen and linear regressions to assess a group effect on the putamen's weight on each connectivity gradient.

Time-to-event analyses were done to assess whether deformation in the putamen predicted phenoconversion to PD or DLB using Cox regression.

Results: There was a significant group*segment interaction effect, indicating that iRBD patients had more atrophy in the left hemisphere and that this atrophy followed a medial-lateral gradient. The lateral part showed significantly more atrophied; this atrophy significantly predicted phenoconversion into PD compared to any other progression phenotype. In iRBD patients and controls, 3 gradients of connectivity were identified. Gradient analysis revealed that the putamen's connectivity was impaired on the first gradient of connectivity (explaining the most variance), while it was preserved on the other gradients. This indicates that the putamen becomes disconnected in iRBD but not entirely segregated.

Conclusions: In iRBD, the putamen shows tissue deformation in the lateral segment and gradient-specific alterations in the brain's connectivity architecture.

Lateral tissue deformation in putamen predicts PD in iRBD.

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Neuroprotective Effect of Melatonin in Isolated Rapid Eye Movement Sleep Behavior Disorder

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Introduction: Over 90% of the patients with isolated rapid eye movement (REM) sleep behavior disorder (iRBD) will have a phenoconversion into a subtype of neurodegenerative diseases including Parkinson's disease and dementia over time. It remains unclear whether melatonin, a known hormone and one of the first-line symptomatic treatments of RBD, yields neuroprotective effect in iRBD.

Materials and methods: This study was conducted based on a longitudinal cohort of iRBD patients with naturalistic clinical follow-up of prescription, repeated neuropsychological assessments, and reevaluation on status of phenoconversion. To compare the potential neuroprotective effect of melatonin in iRBD, we first dichotomized the subjects into 'with melatonin' and 'without melatonin' by duration of melatonin use (e.g. 'with melatonin' was defined by using melatonin for at least one year and exceeding half of the follow-up duration). Generalized linear mixed models and Cox proportional regression models were fitted to compare the longitudinal change of neurodegenerative biomarkers, and the risk of conversion to neurodegenerative diseases between two conditions, respectively. Second, melatonin was treated as a time-varying covariate in the time-dependent survival analysis to investigate its effect by handling its varied dosage across the follow-up duration. Besides, the least optimal dosage of melatonin was also estimated for its neuroprotective effect.

Results: A total of 194 iRBD patients were included (66.2 ± 7.3 years, 72.2% male), with a mean follow-up duration of 5.5 years. Comparing with iRBD patients without melatonin (66.2 ± 7.9 years, 72.4% male), those with melatonin (66.2 ± 6.7 years, 71.9% male) showed a lower risk of phenoconversion (adjusted HR [95%CI] = 0.49[0.27, 0.87]), particularly for DLB (0.30[0.11, 0.82]). When considering the time-varying dosages of melatonin during follow-up, the neuroprotective effect of melatonin held (aHR [95%CI] = 0.91[0.84, 0.98]) with a least optimal dosage estimated at 7.25mg. At biomarkers level, iRBD patients with melatonin showed a slower decline of severity of RBD symptoms (group*time interaction, β [95%CI] = 0.94 [0.13, 1.74]) and cognitive performance (0.007 [0.001, 0.01]), and a slower deterioration in color vision (-0.020 [-0.022, -0.018]), visuospatial and attention (-0.018 [-0.033, -0.002]), and motor coordination function (-0.016 [-0.027, -0.006]).

Conclusions: Clinical prescription of melatonin for iRBD symptom management might also have a neuroprotective effect to delay the phenoconversion risk with a dose-response manner. Future research, especially randomized controlled trials and animal studies, is warranted to corroborate efficacy and mechanisms.

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Pathological α -synuclein in surplus biopsies and surgical resections of peripheral organs in idiopathic REM sleep behaviour disorder

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Introduction: α -Synuclein deposits (AS) have been found in transversal studies in peripheral organs in patients with idiopathic REM sleep behavior disorder (IRBD) with high specificity and variable sensitivity. When available, surplus biopsies or surgical resections previously obtained for the clinical practise could be leveraged for this detection avoiding side effects.

Materials and methods: unicentric case-control study with 161 blocks from 49 IRBD subjects and matched controls obtained from the pathology service biorepository between 1998-2023.

Immunohistochemistry studies were performed with two antibodies against phosphorylated and oligomeric AS (p-AS and o-AS) in the peripheral autonomic nervous tissue and evaluated positive or negative.

Results: 161 blocks from 49 IRBD patients were assessed. IRBD patients mean age at the time of block acquisition was 70.6 ± 8 years, and 89.4% were male. Samples were obtained in different clinical stages: presymptomatic RBD (n=34), symptomatic RBD stage before the diagnostic polysomnogram (n=38), polysomnography-proven IRBD (n=74), and Parkinson disease or Dementia with Lewy bodies (PD/DLB, n=15). Blocks were obtained from the gastrointestinal tract (49.7%), the genitourinary tract (35.4%), and the skin (14.9%). The p-AS and o-AS had a sensitivity of 6.8% and 11.2% respectively, and 99.4% specificity both, although their correlation was small (ϕ 0.23, $p < 0.001$). A trend of higher AS positivity with clinical progression of sinucleinopathy was found from 5.9% in the earliest presymptomatic RBD stage to 20% in PD/DLB. Unspecific background limited the evaluation of half of p-AS blocks. Eighteen percent of IRBD patients had a positive block with p-AS, and 28.6% with o-AS, compared to 0.8% with p-AS, and 0.8% with o-AS in controls (all $p < 0.001$); 30.6% of IRBD subjects had ≥ 1 positive block with any antibody (p-AS and/or o-AS) versus 1.6% of controls ($p < 0.001$).

Conclusions: The use of heterogeneous previous acquired surplus peripheral tissue blocks to identify AS deposits in IRBD has a low sensitivity but a high specificity. AS pathology can be present in the PANS even years antedating RBD symptoms and probably spreads throughout the PANS with disease progression. In selected cases that RT-QulC for misfolded AS detection is not available, AS immunohistochemistry studies using previous peripheral samples could be considered.

Prevalence of idiopathic REM sleep behaviour disorder in the Spanish community

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is a parasomnia with a typical age of onset over 50 years-old characterized by enacting dreams and the loss of REM sleep muscular atonia.

Diagnosing iRBD in the general population is challenging because it requires a video-polysomnography (PSG), a costly test that involves overnight monitoring in a sleep laboratory. Only two IRBD prevalence studies in the general population, both in South Korea, performed a PSG in all the subjects assessed. Kang et al. (2013) found in subjects of >60 years-old a prevalence of 1.15% [IC 95% 0.31-2.92], and Lee et al., (2023) in subjects between 50-80 years-old, of 1.4% [IC 95% 1-1.8]. In addition, five studies have evaluated the prevalence of iRBD using a two-step strategy, first using a questionnaire for RBD

and offering to perform a PSG only in those who tested positive, including: China in >70 years-old (2000), Spain in >60 years-old (2017), Switzerland in 35-75 years-old (2018), Japan in >65-years-old (2020) and Italy in 40-99 years-old (2021), with estimated prevalences ranging from 0.29% [IC 95% 0.06-0.85] in China, to 1.18% IC 95% 0.45-1.37], in Italy. The aim of our study was to study the prevalence and clinical characteristics of iRBD in a representative Caucasian sample from the elderly community of Barcelona, Spain, attending primary care centres.

Materials and methods: This study has been conducted in the primary care center CAP Casanova (Barcelona, Spain), which provides health care for a population of 35.165 inhabitants. Four general practitioners (MQ, ES, MFP, SC) responsible for a panel of approximately 7.000 patients participated in the study. Included subjects were consecutive individuals aged 60 years or older who underwent routine visits with the general practitioners between 7th February 2023 and 29th August 2024. Patients with the diagnoses of IRBD, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, mild cognitive impairment, Alzheimer's disease or any other neurodegenerative condition were excluded.

Included subjects underwent a two-stage study:

1) A validated screening single question for IRBD diagnosis (RBD1Q) followed by, in those who endorsed positive questionnaire

2) A visit in our sleep center for a clinical assessment by a neurologist offering a PSG.

Results: Of 332 individuals (62% women, mean age 71.8 ± 7.9 years, range 60-93), 33 (9.9%) endorsed positively the RBD1Q. All 33 were visited by a sleep neurologist, and 20 of these 33 accepted a v-PSG. V-PSG ruled out RBD in 16 subjects who had obstructive sleep apnea ($n = 10$), periodic limb movements of sleep ($n = 4$) and normal sleep ($n = 2$). IRBD was diagnosed in four individuals without motor or cognitive complaints, giving an estimated prevalence of 1.20% (95% CI = 0.03-2.37). They were three men and one woman between 64 and 76 years of age, with an interval between estimated RBD onset and V-PSG of 7.5 years (range 0.5-10 years). IRBD patients had constipation ($n=3$), hyposmia ($n=2$), apathy ($n=1$), and depression ($n=1$).

Conclusions: The prevalence of iRBD is 1.2% in the elderly community of Barcelona, similar than in other studies in the Caucasian and Asiatic elderly community.

Progression of prodromal markers of alpha-synucleinopathy neurodegeneration in the first-degree relatives of patients with REM sleep behavior disorder: a 7-year prospective study

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is the most specific prodromal phase of alpha-synucleinopathies, including Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Emerging evidence suggests a familial predisposition of iRBD, highlighted by the familial aggregation of RBD-spectrum features (e.g., dream enactment behaviors) and prodromal markers of alpha-synucleinopathies (e.g., motor dysfunction) in the first-degree relatives (FDRs) of iRBD patients. Building on these cross-sectional observations, this longitudinal 7-year follow-up study aims to further evaluate the progression of neurodegeneration markers and subsequent clinical neurodegenerative

development in the FDRs of patients with iRBD compared to the FDRs of controls, in the established Hong Kong family cohort.

Materials and methods: This prospective matched cohort study included 156 FDRs of patients with iRBD and 130 FDRs of controls as the referent individuals. Comprehensive clinical assessments were conducted, including interviews on sleep patterns and disorders, neuropsychiatric examinations, motor tests using the Unified Parkinson's Disease Rating Scale part III (UPDRS-III), and a series of questionnaires at baseline and follow-up. Additionally, 69 FDRs of iRBD patients and 40 control FDRs underwent video-polysomnographic assessments (v-PSG) at both time points. Linear and generalized linear mixed model analyses were employed to study the longitudinal changes.

Results: The mean follow-up duration for FDRs of iRBD patients and control individuals were 6.6 years and 6.8 years, respectively ($P = 0.28$). Baseline age (54.6 ± 9.0 vs. 55.3 ± 7.2 years, $P = 0.46$) and sex distribution (48.7% vs. 44.6% males, $P = 0.49$) were comparable between the two FDR groups. FDRs of iRBD patients consistently exhibited trends of increased RBD features at both baseline and follow-up, including self-reported dream enactment behaviors and electromyographic activity of chin mentalis evaluated by v-PSG. Over the observation period, six FDRs of iRBD (Cumulative incidence 4.0%) and one FDR of controls (Cumulative incidence 0.8%) were newly diagnosed with iRBD (group effect, $P < 0.001$; group*time effect, $P < 0.001$). Other prodromal markers, such as motor function assessed by UPDRS-III total score and sub-score for bradykinesia, showed greater impairment in FDRs of iRBD patients (group effects, $P = 0.02$ and $P = 0.01$), while gait instability demonstrated a significant group*time interaction effect ($P = 0.01$). However, global cognitive function did not differ significantly between the two groups. During the follow-up, two FDRs of iRBD patients were clinically diagnosed with PD (Cumulative incidence 1.3%), whereas no FDRs of control were diagnosed with PD. None of the FDRs in either group was diagnosed with dementia.

Conclusions: These findings further confirm the familial aggregation of RBD features and alpha-synucleinopathy neurodegeneration markers among FDRs of iRBD patients. Upon 7-year prospective follow-up, FDRs of iRBD patients exhibited higher incidences of RBD features (including iRBD diagnosis), progression of neurodegenerative features and clinical diagnosis of incident PD, highlighting FDRs of iRBD as high-risk populations for future neuroprotective interventions.

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Quantitative FP-CIT PET Analysis of Dopaminergic Degeneration in idiopathic RBD and Early Parkinson's Disease

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is regarded as a prodromal stage of alpha synucleinopathies such as Parkinson's disease (PD). This study aimed to identify changes in dopaminergic changes in patients with iRBD using FP-CIT PET.

Materials and methods: FP-CIT PET scans from 33 healthy controls, 77 iRBD patients, and 194 early PD patients were analyzed. Standardized uptake value ratios (SUVRs) were measured in 19 predefined brain regions, including detailed subregions of the striatum, caudate nucleus, and putamen. Asymmetry indices and anterior-posterior (A-P) gradients in the putamen were calculated. These quantitative markers were correlated with clinical parameters and also compared with expert visual interpretations.

Results: SUVRs exhibited a stepwise reduction (Normal > iRBD > early PD) in most regions, particularly in the striatum. Asymmetry indices were elevated only in early PD, while A-P gradients differed significantly across all groups. A-P gradient was significantly associated with depression scores, whereas asymmetry index correlated with UPDRS motor scores. Visual interpretation yielded positive findings in 100% of early PD and 54.5% of iRBD cases.

Conclusions: iRBD patients show intermediate dopaminergic degeneration between healthy controls and PD, with early involvement of the posterior putamen. Quantitative analysis may enhance early detection beyond visual assessment and provide novel insights into the pathophysiology of RBD and its progression to PD.

RBD and other sleep alterations in anti-CASPR2 encephalitis

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Introduction: Sleep disturbances, including RBD, are frequently observed in autoimmune encephalitis. Although V-PSG studies have been conducted in patients with Contactin-Associated Protein-Like 2 (CASPR2) antibody disease, RBD has not been previously reported. This study aimed to assess the presence of RBD and other sleep disturbances in patients with CASPR2-antibody disease using V-PSG and clinical evaluation.

Materials and methods: Patients diagnosed with CASPR2-antibody disease underwent clinical interviews, sleep questionnaires (PSQI, ESS, ISI), neuropsychological assessment, brain MRI, lumbar puncture and V-PSG following immunotherapy during a follow-up visit.

Results: Four male patients, with a median age of 67.75 years and a disease duration of 4.89 years, were included in the study. One patient was diagnosed with limbic encephalitis, while the other three had Morvan-like syndrome. Median questionnaire scores were: PSQI 5, ESS 4.5, and ISI 4.5. Two patients reported insomnia, with one also experiencing excessive daytime sleepiness. Bed partners observed dream-enactment behaviors (DEB) in two patients and sleep-talking in another. V-PSG revealed RBD with simple major episodes in the two patients displaying DEB. The remaining two patients showed increased tonic EMG activity in the chin during REM sleep, consistent with REM sleep without atonia (RWA). Two patients demonstrated executive function impairments. In all patients, brain MRI ruled out structural lesions, and CSF RT-QuIC for alpha-synuclein was negative.

Conclusions: RBD and RWA are common features in CASPR2-antibody disease and may be associated with autoimmune mechanisms, as structural brain lesions and synucleinopathy have been excluded, suggesting an autoimmune origin for these sleep disorders.

REM Density as a diagnostic indicator in patients with Dream-Enactment Behaviors: Insights into α -Synucleinopathy

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Introduction: Recurrent dream-enactment behaviors (DEB) and rapid eye movement (REM) sleep without atonia (RSWA) are two key diagnostic features of REM sleep behavior disorder (RBD), recognized as a prodrome of α -synucleinopathy¹. Increasing evidence suggests that prodromal features of RBD, in the form of isolated DEB, may exist, including those familial ones.²

REM density is defined as the number of REM events per minute during REM sleep, which serves as an important indicator of the intensity and quality of REM sleep, crucial for cognitive function, emotional regulation³ and memory consolidation⁴. Prior studies indicate that changes in REM density may correlate with the severity of dream enactment behaviors, highlighting a connection between the physiological characteristics of REM sleep and the clinical manifestations of the disorder. However, the exact relationship between isolated DEB among those prodromal RBD subjects and REM density is unknown. Furthermore, it is important to investigate how mood states may impact on REM density and DEB in view of close relationship between RBD and mental health.

Materials and methods: We recruited twenty-one subjects who reported dream-enactment behavior but without sufficient REM sleep without atonia (isolated DEB or prodromal RBD) and fourteen age and gender-matched controls. All participants underwent clinical assessment and video-polysomnography.

Results: Age and sex were comparable between the isolated DEB and control groups (Isolated DEB vs. Control: mean age: 58.1 $\pm$ 4.0 versus mean age: 58.9 $\pm$ 4.5, $p=0.60$, Male: 76% vs. 64% $p=0.45$). The

isolated DEB group exhibited had higher scores on the RBD Questionnaire-Hong Kong (RBDQ) (29.4 ± 16.5 vs. 11.1 ± 11.8 , $p=0.001$), Beck Depression Inventory (BDI) (9.1 ± 8.2 vs. 2.8 ± 6.2 , $p=0.038$) and Hospital Anxiety and Depression Scale (HADS) (16.0 ± 9.8 vs. 7.7 ± 6.0 , $p=0.021$) compared to control. Additionally, the isolated DEB group demonstrated significantly higher REM density than the control group (27.8 versus 16.3, $p=0.015$). Notably, 38% of the subjects in the Isolated DEB group were taking antidepressants, compared to 14.3% in Control group. After adjusting for antidepressant use, the REM density in the isolated DEB group remained significantly higher than that of the control group (GLM model, $p=0.014$). The levels of RSWA did not differ significantly between the groups (9.0 ± 7.0 versus 5.3 ± 3.1 , $p=0.073$).

Conclusions: Higher REM density is seen in high risk population with isolated DEB. Further study with larger sample size will be needed to investigate whether REM density may emerge as a reliable and easily accessible marker to enhance diagnostic accuracy of DEB among those with subsyndromal RWSA.

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Remote unsupervised tests of isolated REM sleep behaviour disorder in the community: results from the Tasmanian ISLAND Sleep Study

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Introduction: Isolated rapid eye movement (REM) sleep behaviour disorder (iRBD) may occur at least 10 years before a clinical diagnosis of an α -synucleinopathy, specifically dementia with Lewy bodies (DLB), Parkinson's disease (PD) and multiple system atrophy (MSA). Better understanding is needed around whether people with iRBD experience subtle, disease-specific symptoms and whether these changes can be detected in the community using remote (online and postal) assessment tools. Such tools could aid early detection and monitoring for people at risk of α -synucleinopathy. Here we aim to investigate remote tests of subjective and objective features of α -synucleinopathy in 'probable' iRBD (pRBD). We hypothesise that α -synuclein-related symptoms and signs will be more frequent in pRBD compared to healthy controls.

Materials and methods: 2,351 participants aged 50+ years from the Tasmanian ISLAND (Island Study Linking Ageing and Neurodegenerative Disease) Sleep Study completed the REM Sleep Behaviour Disorder Single-Question Screen to determine pRBD. They also completed several online subjective health and sleep questionnaires, along with unsupervised objective assessments of hand movement, cognition and olfaction. All questionnaires and assessments were completed online, apart from olfactory testing which was completed via post.

Results: People with pRBD ($n = 235$; mean (SD) age 63 (7.6) years; 53% female) reported more α -synuclein-related features than controls, especially for autonomic dysfunction, pain, sleep disturbance, and PD features (all $p < 0.001$). Specifically, they reported more slurred or softer speech, shaking in their lips, hands, arms and/or legs, difficulty with their feet getting stuck to the floor when walking or turning, trouble with balance, and more falls in the last year (all $p < 0.001$). People with pRBD also show objective impairments with greater olfactory dysfunction and slower non-dominant hand movements compared to controls.

Conclusions: This study highlights that people with pRBD exhibit a range of α -synuclein-related symptoms and signs, that can be detected using remote assessment tools. Remote monitoring of these features with a combined set of easily accessible, low-cost, online tools, along with remote olfactory testing may aid in identifying people in the community who are at high risk for developing an α -synucleinopathy. Early diagnosis of these diseases is vital for improving symptomology as well as recruiting those at-risk into clinical trials to explore potentially disease modifying treatments into the future.

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Resting-State fMRI Functional Connectivity Reveals Dual Network Disruption in REM Sleep Behavior Disorder: Diagnostic Insights from Multi-Metric Analysis

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is a prodromal phase of alpha-synucleinopathies such as Parkinson's disease. Functional changes may precede structural degeneration, making resting-state functional MRI (rs-fMRI) a valuable tool for early detection. This study aimed to investigate functional network changes in iRBD across multiple rs-fMRI metrics and evaluate their diagnostic and predictive utility using machine learning.

Materials and methods: We analyzed rs-fMRI data from 132 polysomnography-confirmed iRBD patients and 44 age- and sex-matched healthy controls. The brain was parcellated using the Shen 268-node atlas. Four rs-fMRI metrics—ALFF, fALFF, ReHo, and seed-based functional connectivity (FC)—were computed. Group comparisons were performed using ANCOVA controlling for age and sex. FC was corrected using family-wise error (FWE), and other metrics were thresholded at uncorrected $p < 0.01$. Classification performance was tested using machine learning models including SVM, XGB and MLP.

Results: FC showed the most robust and interpretable group differences. iRBD patients exhibited decreased FC in frontostriatal and default mode networks, and increased FC in cerebellar and motor circuits, suggesting early degeneration and compensatory reorganization. ALFF, fALFF, and ReHo showed scattered, inconsistent changes. SVM using FC features achieved the highest classification accuracy (87%), supporting the feasibility of prediction using rs-fMRI.

Conclusions: FC-based rs-fMRI revealed dual patterns in iRBD, with cognitive network disruption and motor network enhancement. These findings highlight FC as a sensitive marker of early pathological and adaptive changes. In combination with machine learning, FC-based rs-fMRI holds promise as a diagnostic and prognostic tool to stratify iRBD patients and track progression toward neurodegeneration.

Severe dream-enactment behaviors in isolated REM sleep behavior disorder: temporal clustering with sleep continuity and increased forearm EMG activity

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Introduction: REM sleep behavior disorder (RBD) is characterized by dream-enactment behaviors (DEBs), which can lead to injury to the patient and/or bed partner. While polysomnographic features of RBD have been widely studied, little is known about the temporal patterns and physiological correlates of DEBs.

Materials and methods: We analyzed video-polysomnography data from 27 patients with isolated RBD (mean age 66.4 ± 7.5 years; 2 women) at the Center for Sleep Medicine, Department of Neurology, Medical University of Innsbruck, Austria. Motor events were scored based on visual video analysis according to the 2022 International RBD Study Group guidelines, classifying events as mild, moderate, or severe. Severe events were defined as forceful or violent movements with potential to cause severe injury, e.g., kicking or punching. Motor event occurrence and duration were recorded at 1-second resolution.

We performed two analyses:

(1) To investigate when severe motor events occurred, we quantified their cumulative duration across

30-minute bins across the whole night and analyzed their timing within each REM sleep period as both absolute elapsed time from REM sleep period onset and normalized relative time.

(2) To identify factors associated with severe motor events, we compared REM sleep periods with and without severe motor events regarding prior NREM sleep duration (measured from the end of the prior REM period to REM onset, or from sleep onset to first REM). We also compared REM sleep without atonia (RWA) indices assessed by the SINBAR method. REM periods were compared using a linear mixed model accounting for within-subject clustering. The study was approved by the ethics committee, and written informed consent was obtained.

Results: We analyzed 88 REM sleep periods including 3,331 motor events, of which 28 were severe, with a total severe event duration of 934 seconds. Severe motor events showed a prominent clustering between 24:00 and 4:00, accounting for 70% of their total duration. Within REM sleep periods, 70% of severe event duration occurred after 20 minutes from REM sleep period onset, and 80% occurred after 50% of each REM sleep period had elapsed.

Severe motor events occurred in 18 REM sleep periods. REM sleep periods with severe motor events were preceded by longer total NREM sleep (median 84.0 [IQR 73.9–115.0] min), particularly longer N2 sleep (median 62.0 [IQR 56.9–73.5] min). Among RWA indices, the flexor digitorum superficialis (FDS) phasic index was higher in REM sleep periods with severe motor events (median 51.1 [IQR 36.3–59.2] %).

Conclusions: This study identified three key findings regarding severe motor events in isolated RBD: (1) severe events tended to occur after a certain elapsed time within each REM sleep period; (2) their occurrence was associated with prolonged NREM sleep prior to REM onset; and (3) their occurrence was associated with increased FDS phasic activity. Severe dream-enactment behaviors may occur under conditions of sustained sleep continuity and defective REM atonia in the arms.

Sex-Specific Challenges in REM Sleep Behaviour Disorder Identification: Insights from Clinical Data, Screening Questionnaires, and REM Sleep Without Atonia

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Introduction: Identifying REM sleep behavior disorder (RBD) is crucial due to the risk of injuries and the fact that its isolated form (iRBD) is an early alpha-synucleinopathy. Current validated RBD questionnaires assume uniform symptoms and clinical presentation in women and men despite existing literature on sex differences. Furthermore only few studies investigated sex differences in REM sleep without atonia (RWA). We aim To investigate sex differences in RBD identification by evaluating clinical data, three validated RBD screening questionnaires, and RWA measures.

Materials and methods: In this bicentric prospective study, 300 subjects referring to a sleep center for the first-time (159 men, 141 women) completed the RBD Screening Questionnaire (RBDSQ), RBD Single-Question Screen (RBD-1Q), and Innsbruck RBD Inventory (RBD-I) before a sleep expert interview and underwent 8-hour video polysomnography (v-PSG) to confirm or exclude RBD diagnosis. Clinical data, questionnaires, and RWA measures were compared between sexes.

Results: In the whole cohort, more women than men exceeded the cut-off for at least one RBD questionnaire (74.5% vs. 63.5%, $p=0.046$). In women, only exceeding the RBD-I cut-off was significantly associated with RBD diagnosis (log odds ratio (LOR) 1.812, $p=0.023$). In men, exceeding the cut-off for all questionnaires was associated with RBD (RBDSQ: LOR 3.076, $p=0.003$; RBD-1Q: LOR 2.837, $p<0.001$; RBD-I: LOR 3.076, $p=0.003$). The RBDSQ performed poorly in women compared to men (AUC 0.48 vs. 0.82, $p=0.001$). Among RBD patients ($n=30$; women:12, men:18), women were less likely to have bed partners (50% vs. 100%, $p=0.002$) and report abnormal sleep behaviors (58.3% vs. 100%, $p=0.006$). Expert suspicion of RBD was lower in women (50% vs. 83.3%, $p=0.102$). Exceeding cut-offs for chin-phasic, FDS, and SINBAR RWA-indices was associated with RBD diagnosis in both sexes ($p<0.005$); of note, exceeding chin tonic index cut-off was associated with RBD in women only ($p<0.001$).

Conclusions: Sex-related variability exists in RBD screening questionnaires, likely due to differences in RBD phenotype and related awareness affecting referrals. In our cohort, RWA measures better

identified RBD in women than questionnaires . These findings emphasize the need for sex-specific approaches for RBD screening and diagnosis.

Sleep Deprivation Accelerates α -Synuclein Pathology via Per2-Mediated Lysosomal Dysfunction in Mice with REM Sleep Behavior Disorder

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Introduction: Rapid eye movement sleep behavior disorder (RBD) is a well-recognized prodromal manifestation of α -synucleinopathies such as Parkinson's disease (PD). Sleep deprivation has been shown to disrupt circadian gene expression and aggravate dopaminergic neurodegeneration, while autophagy-lysosomal dysfunction represents one of the core mechanisms driving α -synuclein accumulation in PD. However, whether sleep deprivation accelerates α -synuclein pathology by disturbing circadian regulation and lysosomal homeostasis during the RBD stage remains unclear.

Materials and methods: An RBD mouse model was generated by bilaterally injecting α -synuclein preformed fibrils (PFFs) into the sublateralodorsal tegmental nucleus (SLD) of 8-week-old mice. Successful modeling was confirmed at 12-week-old by polysomnographic recordings, which verified RBD phenotypes. At 20 weeks, the mice were subjected to a 7-day sleep deprivation protocol. To investigate the molecular consequences of sleep deprivation in RBD mouse, we first performed RNA sequencing of the substantia nigra, which revealed enrichment of circadian rhythm and autophagy-lysosomal pathways. These findings were further validated by multi-timepoint quantitative real-time PCR experiments (RT-qPCR) assessing circadian gene dynamics. In parallel, α -synuclein pathology, lysosomal function, and PD-like behavioral impairments were evaluated using Western blotting, immunostaining, and motor function tests.

Results: Sleep-deprived RBD mice exhibited exacerbated α -synuclein aggregation, increased loss of tyrosine hydroxylase (TH) positive neurons in the substantia nigra, and earlier onset of PD-like motor impairments. Multi-timepoint RT-qPCR revealed suppressed Per2 expression and dampened circadian rhythmicity, accompanied by marked lysosomal dysfunction as confirmed via Western blotting. Concurrently, we demonstrated that Per1/2 knockout mice also exhibited significant lysosomal impairment and a reduction in TH-positive dopaminergic neurons in the substantia nigra, implicating the involvement of core circadian genes in lysosomal homeostasis. To specifically determine the role of Per2, we performed AAV-mediated knockdown of Per2 in the substantia nigra of RBD mice, which reproduced the lysosomal dysfunction and α -synuclein accumulation observed following sleep deprivation. Conversely, Per2 overexpression in the substantia nigra mitigated these pathological changes and delayed disease progression.

Conclusions: These findings identify Per2-mediated lysosomal dysfunction as a critical mechanism by which sleep deprivation promotes the transition from RBD to α -synucleinopathy, providing novel insight into the circadian regulation of prodromal PD progression.

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Striatal dopamine transmission in recurrent dream enactment behaviors with subthreshold REM sleep without atonia: A case-control PET Study

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Introduction: Idiopathic REM sleep behavior disorder (iRBD) is the strongest prodromal marker for Parkinson's disease (PD), which is characterized by dopaminergic neuron loss in substantia nigra. Meanwhile, iRBD is manifested as dream-enactment behaviors (DEB) and REM sleep without atonia (RSWA). Recent evidence found that individuals with DEBs and subthreshold RSWA (isolated DEB) level will similarly predispose to an increased risk of neurodegeneration. This finding suggested that individuals with isolated DEB might indicate early neurodegeneration. However, it is unknown whether dopamine dysfunction could be detected at this stage. Thus, this study aims to investigate the potential dopaminergic dysfunction in individuals with isolated DEB.

Materials and methods: Sixteen subjects with isolated DEB and fifteen age and gender-matched controls without DEB underwent clinical assessment, video-polysomnography, and striatal PET scans using F18-FDG and F18-DOPA tracers. Likelihood ratio (LR) of prodromal PD was calculated as a proxy measure of individual's risk of prodromal PD based on Movement Disorder Society research criteria (2019). Dopaminergic functions were assessed using the standardized uptake value (SUVmean) ratio of striatal regions to cerebellum, the putamen-to-caudate SUVmean ratio, and 18F-DOPA influx constant Ki (K value).

Results: The age and gender were comparable between groups (subjects with isolated DEB vs. controls: mean age = 58.6 vs. 59.0 years, $P = 0.8$, male gender proportion: 81.3% vs. 66.7%, $P = 0.4$). Isolated DEB group had a significantly higher LR of prodromal PD (RBD item excluded, median: 0.16 vs 0.01, $P < 0.001$) compared to controls. As for the PET parameters, no significant differences were observed in any striatal parameters between groups, including the putamen-to-cerebellar SUVmean ratios (subjects with isolated DEB vs. controls: 18F-DOPA: 2.69 ± 0.17 vs. 2.70 ± 0.22 , $P = 0.88$; 18F-FDG: 1.36 ± 0.10 vs. 1.33 ± 0.09 , $P = 0.32$), caudate-to-cerebellar SUVmean ratios (18F-DOPA: 2.13 ± 0.19 vs. 2.12 ± 0.19 , $P = 0.89$; 18F-FDG: 1.13 ± 0.10 vs. 1.08 ± 0.11 , $P = 0.16$), putamen-to-caudate SUVmean ratios (18F-DOPA: 1.26 ± 0.06 vs. 1.28 ± 0.06 , $P = 0.48$; 18F-FDG: 1.22 ± 0.08 vs. 1.23 ± 0.09 , $P = 0.69$), and K values (10^{-3}) (L_putamen: 8.68 ± 0.67 vs. 8.87 ± 0.81 , $P = 0.49$; R_putamen: 8.93 ± 0.80 vs. 8.93 ± 0.95 , $P = 0.66$; L_caude: 6.99 ± 0.65 vs. 6.95 ± 0.83 , $P = 0.88$; R_caude: 7.07 ± 0.83 vs. 7.11 ± 0.73 , $P = 0.89$). Within the isolated DEB group, correlation analyses showed that mean 18F-FDG uptake ratio in caudate was negatively associated with total chin electromyography percentage of RSWA after adjustment for confounders, albeit with marginal significance ($r = -0.53$, $P = 0.06$).

Conclusions: Despite an elevated risk of prodromal PD in individuals with isolated DEB, dopaminergic function measured by PET imaging appeared to remain intact, suggesting dopaminergic dysfunction may not be detectable at this early phase. This potential time window of seemingly preserved dopaminergic function provides an opportunity for early neuroprotection. Further longitudinal studies with larger sample size are warranted to elucidate the relationship between dopaminergic dysfunctions and clinical manifestations at the early stage of prodromal PD.

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[¹⁸F]FDG-PET as staging biomarker in the prodromal to overt neuronal alpha-synucleinopathy continuum

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Introduction: Rapid eye movement (REM) sleep behaviour disorder (RBD) is a parasomnia characterized by dream-like behaviours that emerge during REM sleep, resulting from the loss of physiological muscle atonia. Isolated/idiopathic RBD (iRBD) represent a prodromal stage of alpha-synucleinopathy, with the vast majority of individuals eventually developing parkinsonism and/or dementia over time. Whereas [^{18}F]FDG-PET is currently considered an established biomarker of neurodegeneration in alpha-synucleinopathies, its role as a staging biomarker remains unexplored.

Materials and methods: We enrolled 41 controls (age 70 ± 8.6 , 36.5% males); 86 iRBD (age 71 ± 7 , 75.5% males), representing the prodromal alpha-synucleinopathy stage, and 85 patients with either Parkinson's disease (PD, $n=40$, age 72 ± 7.4 , 57.5% males) or Dementia with Lewy Bodies (DLB, $n=45$, age 76 ± 5.8 , 64.4% males), representing the overt alpha-synucleinopathy stage (age 74 ± 6.8 , 61% males). All subjects underwent baseline [^{18}F]FDG-PET and comprehensive clinical examination. Prodromal patients were followed over time (months 23 ± 21) to assess possible phenoconversion, based on the emergence of parkinsonism and/or dementia. Phenoconverted patients (cRBD, $n=30$; age 73 ± 6.8 , 76.6% males), were further divided according to the phenoconversion outcome into cRBD-PD ($n=14$, age 72 ± 8.3 , 64.2% males) or cRBD-DLB ($n=16$, age 74 ± 5 , 87.5% males). Patients that did not phenoconvert at the last available follow-up (months 30 ± 25) were labelled non-converters RBD (ncRBD, $n=56$; age 70 ± 6.9 , 75% males).

We computed spatial covariance analysis on the [^{18}F]FDG-PET data of overt PD (deriving the OvertPD-Related Pattern -RP), and overt DLB (deriving the OvertDLB-RP) patients separately, as well as overt stages combined (i.e. PD and DLB), deriving the Overt Alpha-synucleinopathy-RP. These [^{18}F]FDG-PET disease-related patterns were applied to our study groups, as follows. First, assuming our groups represent progressive neurodegeneration stages, we evaluated whether baseline Overt Alpha-synucleinopathy-RP could stage the alpha-synucleinopathy continuum at two levels of granularity: I) controls, prodromal and overt stage (3-levels); II) controls, ncRBD, cRBD, and overt stage (4-levels). Then, we investigated mainly-motor (controls, ncRBD, cRBD-PD, and overt PD) and mainly-cognitive (controls, ncRBD, cRBD-DLB, and overt DLB) clinical trajectories by applying the overPD-RP and the overDLB-RP respectively.

Results: Visually, the Overt Alpha-synucleinopathy-RP showed relative hypometabolism in occipital cortices and posterior cingulate cortices, precuneus and lateral prefrontal areas, with relative hypermetabolism in hippocampal and parahippocampal regions, brainstem, cerebellum and anterior cingulate cortex. A progressive and statistically significant increase of this pattern's expression was found across the clinical spectrum (both 3-levels and the 4-levels model, $p < 0.0001$).

Expression of the OvertPD-RP and the OvertDLB-RP also significantly increased across stages in the mainly-motor and mainly-cognitive trajectories, respectively ($p < 0.0001$).

Random Forest analyses across the 3-levels and 4-levels models, as well as clinical trajectories models, showed moderate-to-good Negative Predictive Values (NPVs) for all study groups (70-89%), with highest reliability in preventing misclassification within healthy controls and overt alpha-synucleinopathy groups. NPVs for the prodromal group were comparatively lower, reflecting greater classification uncertainty in this transitional stage, but remained within an acceptable range for multiclass prediction.

Conclusions: This study encompassing alpha-synucleinopathy-continuum suggests a potential role of [^{18}F]FDG-PET imaging as a biomarker for staging neurodegeneration across the continuum from prodromal to overt alpha-synucleinopathy.

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Toward Scalable Detection of REM Sleep Behavior Disorder: A Lightweight Machine Learning Approach Using Overnight Heart Rate Variability

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Introduction: Early diagnosis of neurodegenerative diseases (NDs) such as Parkinson's Disease (PD), Alzheimer's Disease (AD), Multiple System Atrophy (MSA), and Dementia with Lewy Bodies (DLB) is crucial, as it might enable timely interventions that can significantly improve patient outcomes. REM

Sleep Behavior Disorder (RBD) is a parasomnia that entails the loss of physiological muscle atonia during REM sleep, and has emerged as a reliable prodromal marker for several of these conditions. The diagnostic gold-standard for RBD is video-polysomnography (PSG), a comprehensive but invasive, resource-intensive, and costly procedure. Given the growing prevalence of NDs in aging populations, there is an urgent need for scalable, non-invasive, and cost-effective screening tools. Heart rate variability (HRV), derived solely from RR interval time series, reflects autonomic nervous system functioning and has shown promising in distinguishing individuals with neurodegenerative conditions from healthy controls. This study investigates the feasibility of employing Machine Learning (ML) models to classify healthy versus RBD subjects based solely on HRV features.

Materials and methods: We utilized four PSG datasets (three public and one private) comprising recordings from healthy individuals, subjects with RBD, and individuals with obstructive sleep apnea syndrome (OSAS), this latter included to evaluate model robustness against confounding factors. HRV features were extracted using two parallel approaches: first including all detected R-peaks in the recording (All); and then excluding R-peaks corresponding to wake epochs, as identified by hypnograms (Sleep). Multiple experimental configurations were tested by combining four feature selection algorithms with six different ML classifiers. Model performance was evaluated on various dataset combinations to assess generalizability and robustness.

Results: Model performance was assessed using the F1 score, as it balances precision and recall and guarantees robustness despite class imbalance. The best model achieved a 92.31% F1 score using the (All) approach on a single-dataset configuration, indicative of optimal performance. With increasing dataset complexity, performance slightly declined, reaching a F1 score of 86.93% (5.38 percentage point decrease relative to the best-case performance). Nevertheless, the obtained performance remained moderately high, thus reflecting the robustness of the proposed approach. Interestingly, approach (All), that included the whole recording, consistently outperformed (Sleep), with an average improvement of 1.43 percentage points. Including OSAS subjects in the analysis, used as a confounding-factor population, impaired classification performance. Indeed, the transition from a healthy/RBD to a non-RBD/RBD classification witnessed a moderate decrease on the average F1 score, reflecting the diagnostic challenges posed by comorbid sleep disorders.

Conclusions: This study demonstrates the potential of HRV-based ML models for non-invasive RBD screening. Given that HRV data can be collected using simple wearable devices, such as smartwatches, this outcome supports the implementation of large-scale, low-cost screening programs targeting at-risk populations (particularly individuals over 60 years of age). These findings pave the way for accessible early detection tools, thereby supporting timely therapeutic intervention in the prodromal phases of neurodegenerative diseases.

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Updated Data on the Prodromal Synucleinopathy Rating Scale Among Patients with REM Sleep Behavior Disorder in the North American Prodromal Synucleinopathy (NAPS) Consortium

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Introduction: Clinical trials in REM sleep behavior disorder (RBD) are anticipated in the near future, in which interventions to delay the onset or prevent the development of Parkinson's disease, dementia

with Lewy bodies and multiple system atrophy will be tested. The Prodromal Synucleinopathy Rating Scale (PSRS) was developed by the NAPS Consortium investigators to capture the breadth and evolution of clinical burden in those with RBD.

Materials and methods: Ratings on the PSRS range from no symptoms/signs (score of 0) to more severe symptoms/signs (max score of 2-4 depending on the domain) based on clinical judgement for the cognitive (COG), neuropsychiatric (NP), motor-axial (MAX), motor-appendicular (MAP), autonomic (AUT), sleep (SLP), and sensory (SEN) domains. For the cross-sectional analyses, PSRS ratings were analyzed on participants (pts) at the baseline visit conducted 8/22-12/24. Spearman correlations were generated between the ratings for each domain, and the total sum score (SUM), with several measures that reflect similar constructs. For the longitudinal analyses, Wilcoxon signed-rank test compared the difference in PSRS SUM and its domains between visits 1 (V1) and 2 (V2) collected 8/22-12/24.

Results: In cross-sectional analyses, data from 365 pts (80% male, mean age 66 ± 10 yrs) were analyzed. The following correlations were determined: COG and Montreal Cognitive Assessment score ($r = -0.40$) and Clinical Dementia Rating Sum of Boxes score ($r = 0.78$, $p < 0.0001$ for each); NP and modified Neuropsychiatric Inventory ($r = 0.40$, $p < 0.0001$); MAX and MAP and the MDS-UPDRS Motor score ($r = 0.78$, 0.67 , respectively, $p < 0.0001$ for each); AUT and Scales for Outcomes in Parkinson's Disease-Autonomic Dysfunction ($r = 0.37$, $p < 0.0001$); SLP and Epworth Sleepiness Scale ($r = 0.19$, $p = 0.0004$); and SEN and Brief Smell Identification Test ($r = -0.64$, $p < 0.0001$) and FM100 color vision, ($r = 0.11$, $p = 0.04$). The PSRS SUM was correlated with Functional Assessment Scale ($r = 0.48$), Schwab and England Activities of Daily Living ($r = -0.60$), and Clinician Global Impression Severity ($r = 0.72$, $p < 0.0001$ for each). In longitudinal analyses, data from 205 pts (81% male, mean age 66 ± 9 yrs) were analyzed. The median (IQR) duration between V1 and V2 was 12 (11-12) months. From V1 to V2, the score increased for COG ($p < 0.0001$), NP ($p < 0.0001$), MAX ($p < 0.0001$), MAP ($p < 0.0001$), AUT ($p < 0.0001$) and SLP ($p = 0.0123$) but not for SEN. Comparing V1 to V2, the frequency of an increased/stable/decreased score for each domain were COG: 36%/52%/12%, NP: 38%/46%/16%, MAX: 37%/54%/9%, MAP: 40%/47%/13%, AUT: 44%/37%/19%, SLP: 18%/55%/27%, and SEN: 19%/64%/17%. The SUM increased (mean 7.5 ± 4.4 to 9.0 ± 4.7 , $p < 0.0001$) and the frequency of an increased/stable/decreased SUM score were 61%/12%/27%.

Conclusions: In this large cohort of individuals with RBD, moderate to strong correlations exist between the PSRS domain and SUM score ratings and many other measures of clinical burden. Additionally, mildly increasing but variable clinical burden can be demonstrated on the PSRS over one year. Although additional longitudinal work is needed in larger and more diverse samples, the current results demonstrate preliminary validity for the PSRS as a useful outcome of synucleinopathy clinical burden for future disease-modifying therapies in those with RBD.

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Validation of a tissue deformation signature to predict dementia in isolated REM sleep disorder

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Introduction: Isolated REM sleep behavior disorder (iRBD) is a prodromal stage of synucleinopathies, with over 90% of individuals eventually developing either dementia with Lewy bodies (DLB) or Parkinson's disease (PD). Current brain biomarkers do not accurately predict which individuals with iRBD will develop one or the other of these conditions. This study aims to identify a brain tissue deformation signature, detectable via MRI, that could predict the clinical evolution of individuals with iRBD.

Materials and methods: T1-weighted brain MRI scans from 48 individuals with video-polysomnography-confirmed iRBD from the Montreal iRBD cohort were analyzed using a deformation-based morphometry approach to generate individual brain tissue deformation maps. All 48 participants underwent detailed clinical assessments covering 27 clinical variables spanning motor, non-motor, cognitive, autonomic, neuropsychiatric, and sleep domains. Using a partial least squares regression approach, we identified an anatomo-clinical signature that maximized covariance between brain and clinical changes. This brain map signature was then applied to a database assembled by our lab, comprising 1,404 MRI scans from individuals with iRBD or a related synucleinopathy, to extract a per-subject expression score. These signature expression scores were harmonized and used in logistic and Cox regressions to test whether the score predicted the development of DLB in iRBD, as opposed to other progression trajectories. Signature expressions were also compared across iRBD, DLB, PD groups to assess whether higher expression was associated with DLB. Finally, signature expression was also associated with other markers of disease conversion, including increased free water content and glymphatic system impairment.

Results: Partial least squares regression revealed a significant latent variable explaining 28% of the covariance between tissue deformation and clinical variables in iRBD ($p = 0.006$). Cox regression showed that only the deformation score was significantly associated with the risk of developing DLB rather than PD (HR = 2.14, $p = 0.0016$), suggesting that a higher score roughly doubles the risk of DLB. ANOVA across groups also showed a significant group effect on signature expression ($F(2, 700) = 36.8$, $p < 0.0001$), with DLB patients having significantly higher scores than PD patients (diff = -32.2, $p < 0.0001$) and iRBD individuals (diff = -23.0, $p < 0.0001$). Individuals with iRBD also had higher scores than PD patients (diff = 9.2, $p < 0.0001$). Age- and sex-adjusted partial correlations revealed significant associations between signature expression and other biomarkers, including increased free water in the nucleus basalis of Meynert ($r = 0.15$, $p = 0.02$), and reduced glymphatic function ($r = -0.22$, $p < 0.001$).

Conclusions: This study highlights an anatomical signature based on tissue deformation measurable via MRI, capable of predicting DLB development in individuals with iRBD. This biomarker, easily derived from a standard T1-weighted sequence, could support patient stratification in clinical trials, optimize patient care, and enable the integration of risk-reduction strategies.

Restless Legs Syndrome (RLS)

Actigraphy-Derived Sleep Patterns Distinguish Restless Legs Syndrome from Insomnia and Sleep Apnea

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Introduction: Restless Legs Syndrome (RLS) is a neurological disorder characterized by an uncontrollable urge to move while resting and relief by movement. Symptoms are pronounced in the evening and first half of the night, often abating late in the sleep period. Actigraphy provides an objective measure which can be employed for multiple nights to assess sleep. We hypothesized that those with RLS have a delayed sleep pattern, with more time awake early in the night and greater sleep toward morning, and that this pattern would be distinct from those with either insomnia or obstructive sleep apnea (OSA).

Materials and methods: Actigraphic recordings of sleep were obtained from the Multi-Ethnic Study of Atherosclerosis (MESA), an ongoing cohort study, initiated in 1999, with enrollment of 6,814 participants between 2000-2002. 2,237 MESA participants wore an Actiwatch Spectrum wrist sleep

actigraphy device (Philips Respironics) 24-hours per day over 8 days to determine sleep duration and quality.

Actigraphic recordings were scored in epoch-by-epoch increments for 2,159 participants by a technician at the Boston Sleep Reading Center. After excluding 88 night-shift workers and 11 with missing data, 2,060 participants remained: 98 with physician-diagnosed RLS, 1,962 without RLS. Groups with RLS and self-reported physician diagnosis of insomnia and OSA were identified. To control for confounders of age, sex, insomnia and OSA, we employed 1:3 propensity score matching, yielding groups with near-identical insomnia prevalence (RLS=22.4%, non-RLS=20.7%) and OSA prevalence (RLS=25.5%, non-RLS=26.9%). The RLS group was 66.3% female with a mean age of 69.6 years, and the non-RLS group was 65.0% female with a mean age of 69.8 years.

We used unpaired t-tests to compare the average sleep time in the first four hours (9PM-1AM) and last four hours (5AM-9AM) of the sleep period between groups.

Results: Participants with RLS slept significantly less in the first four hours of the night compared to those without RLS (144.9 vs. 155.9 minutes, $p=0.02$). Conversely, those with RLS slept significantly more in the last four hours of the night (140.4 vs. 129.3 minutes, $p=0.03$).

While participants with insomnia slept less in the first four hours of the night (144.8 vs. 153.7 minutes, $p=0.03$), they did not sleep significantly more in the last four hours (133.1 vs. 129.5 minutes, $p=NS$). Participants with OSA did not sleep significantly less in the first four hours of the night (151.2 vs. 151.7, $p=NS$), though they did sleep significantly more in the last four hours (133.4 vs. 126.3, $p=0.05$).

Conclusions: This novel analysis identified a distinct pattern of actigraphy-derived sleep in RLS, characterized by delayed sleep onset and increased early morning sleep. This pattern was not shared by those with insomnia or OSA. Actigraphy-based sleep assessment could contribute as an objective diagnostic tool for RLS and may facilitate earlier identification of the disorder and improved patient outcomes.

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Association between clinical severity and secondary restless legs syndrome in rheumatoid arthritis - a pilot study

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Introduction: Restless legs syndrome (RLS) is a common comorbidity in patients with rheumatological diseases. Prevalence data indicate that RLS occurs more than three times as frequently in individuals with rheumatoid arthritis (RA) compared to the general population. This pilot study explores the clinical and biochemical characteristics of RLS in a cohort of RA patients.

Materials and methods: We enrolled 32 female patients with RA from a single clinic. Patients with conditions (other than RA) or medications known to cause secondary RLS were excluded. Patients completed the Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index (PSQI) and Restless Legs Syndrome Severity Scale. RA disease activity was assessed using the Disease Activity Score 28 – CRP (DAS28-CRP). Complete blood count (CBC), basic biochemical parameters for inflammation, and serum iron levels were also measured. Statistical analysis employed independent samples Mann-Whitney test and Spearman's rho bivariate correlation in SPSS v.26.0.

Results: Based on clinical interviews and sleep-focused histories, 12 patients (37.5%) met the International Classification of Sleep Disorders (ICSD) criteria for RLS (RLS+ group), while 20 did not (RLS- group). The RLS+ group reported significantly longer sleep onset latency on PSQI item 2 (48.75 min vs. 27.75 min, $p < 0.01$), though total sleep duration did not differ significantly (6.17 h vs. 6.5 h). There were no significant differences in age (61.3 vs. 59.9 years) or body mass index (26.4 vs. 24.9). The neutrophil-to-lymphocyte ratio (2.1 vs. 2.32), C-reactive protein (2.8 mg/dL vs. 4.8 mg/dL), rheumatoid factor (11.45 vs. 10.4), and erythrocyte sedimentation rate (34.10 mm/hr vs. 34.45 mm/hr) were not significantly different between groups. However, the RLS+ group had significantly higher disease activity (DAS28-CRP: 4.88 vs. 3.79; $p < 0.01$) and lower serum iron levels (13.56 $\mu\text{mol/L}$ vs.

18.73 $\mu\text{mol/L}$; $p = 0.026$). Moderate negative correlations were observed between serum iron levels and both sleep latency ($r = -0.461$, $p < 0.01$) and DAS28-CRP ($r = -0.411$, $p < 0.01$).

Conclusions: RA patients with comorbid RLS experience longer sleep onset latency and lower serum iron levels compared to those without RLS. While traditional inflammatory markers such as CRP, ESR, and NLR do not differ significantly between groups, disease activity assessed by DAS28-CRP is notably higher in RLS+ patients. These findings suggest a potential interplay between iron metabolism, disease activity, and the pathophysiology of RLS in RA.

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Calcitonin gene-related peptide monoclonal antibodies improve symptoms of restless legs syndrome in patients with migraine

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Introduction: The effects of calcitonin gene-related peptide monoclonal antibodies (CGRP mAb) on restless legs syndrome (RLS) are unclear.

Materials and methods: We retrospectively investigated 15 patients with migraine and concomitant RLS (age, 49.1 ± 5.8 years) who were administered CGRP monoclonal antibodies. The number of migraine days per month (MMD) was obtained from headache diaries. Headache disability was assessed using the Migraine Disability Assessment (MIDAS). The severity of RLS was assessed using the International RLS Group Rating Scale (IRLS). Central sensitization was assessed using the Central Sensitization Inventory (CSI).

Results: After 1, 2, and 3 months, the percentage of patients with a 50% or greater improvement in MMD was 53.3%, 66.6%, and 60.0%, respectively. From baseline to 3 months, there was a significant decrease in the MIDAS score (25.1 ± 23.2 vs. 19.7 ± 22.8 , $p=0.005$) and CSI score (36.3 ± 12.9 vs. 29.1 ± 12.3 , $p=0.001$). The IRLS score significantly decreased from baseline to 1 month (-8.8 ± 2.1 points) and 3 months (-11.6 ± 2.3 points) significantly after CGRP monoclonal antibody treatment.

Conclusions: In our study, CGRP monoclonal antibody treatment significantly reduced RLS symptoms, central sensitization, and headache-related disability in patients with comorbid migraine and RLS.

Chronic Health Risk in Restless Legs Syndrome and its Association with Exercise

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Introduction: Restless legs syndrome (RLS) disrupts sleep and is associated with increased risk of cardiovascular disease, hypertension, stroke, depression and anxiety, and overall poorer health. Exercise represents one of the most promising non-pharmacological approaches for managing RLS and is a potent modifier of health and disease outcomes. However, there is limited knowledge regarding the influence of exercise on the risk of comorbid conditions commonly associated with RLS.

Materials and methods: Patients ($N=23,937$) seen at the Stanford Sleep Disorders Clinic completed the Alliance Sleep Questionnaire (ASQ) as a standard of care. The ASQ is a comprehensive questionnaire designed to collect standardized subjective sleep and sleep disorder data, including current sleep symptoms, sleep habits and schedule, medical history, and social/behavioral habits (e.g., exercise).

Results: Univariate logistic regression controlling for age, sex, BMI, race, ethnicity, and other sleep problems (e.g., sleep-related breathing, insomnia, daytime sleepiness) identified people with RLS had higher risk of hypertension, cardiovascular problems, atrial fibrillation, cardiac surgeries, GI problems, GERD, IBS, gallstones, liver disease, cholecystectomy, neurological problems, peripheral neuropathy, iron deficiency, anemia, urinary/kidney problems, chronic kidney disease, chronic pain/fatigue, frequent headaches/migraines, fibromyalgia, anxiety, and depression than people without RLS. Multivariate forward stepwise regression identified people with RLS ($n=1,559$ [7.3%]) had significantly higher risk of cardiovascular problems, GI problems, cholecystectomy, urinary/kidney problems, neurological problems, fibromyalgia, chronic pain/fatigue, peripheral neuropathy, and psychiatric diagnoses than

people without RLS (n=19,926). RLS had higher BMI and insomnia symptoms, were more likely to be Hispanic and male, and were significantly less likely to exercise than people without RLS. Multivariate regression demonstrated that people with RLS who exercise (n=1,009 [74.2%]) had lower risk of chronic heart failure, neurological problems, peripheral neuropathy, and depression; had lower BMI, better functional outcomes of sleep, and were more likely to be more educated, younger, and male than people with RLS who do not exercise (n=351).

Univariate logistic regression controlling for age, BMI, RLS severity, and other sleep problems demonstrated women with RLS (n=854[54.1%]) had higher risk of GI problems, IBS, gallstones, and cholecystectomy; iron deficiency, pain/fatigue problems, frequent headaches/migraines, fibromyalgia, chronic fatigue syndrome, anxiety, and depression than men with RLS (n=723). Multivariate regression demonstrated that women with RLS had higher risk of frequent headaches/migraines, fibromyalgia, chronic pain/fatigue problems, metabolic problems, cholecystectomy, and anxiety and were less likely to engage in regular exercise than men with RLS. Multivariate regression demonstrated that women with RLS who exercise (507[70%]) had lower risk of depression and peripheral neuropathy, were less likely to have a pacemaker, and had a lower BMI and higher education level than women with RLS who do not exercise. Men with RLS who exercise (n=495 [79%]) had lower risk of autoimmune disease, type 2 diabetes, and chronic heart failure, lower BMI, better functional outcomes of sleep, and higher daytime sleepiness than men with RLS who do not exercise (n=129).

Conclusions: Exercise is associated with less risk of some chronic health conditions in adults with RLS with differential effects in men and women. Future research should evaluate causality among these relationships to understand the effect of exercise.

Clinical Characteristics, Polysomnography, and Iron Metabolism in Restless Legs Syndrome Patients with Obstructive Sleep Apnea: A Comparative and Cluster Analysis Study

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Introduction: Restless Legs Syndrome (RLS) often coexists with obstructive sleep apnea (OSA), worsening symptoms through complex mechanisms. This study investigates the prevalence, clinical features, and phenotypic subtypes of RLS-OSA to improve diagnosis and treatment.

Materials and methods: A multicenter observational study enrolled 1,134 patients with RLS from 23 Chinese sleep labs from January 2020 to December 2024. RLS was diagnosed using the 2014 RLSSG criteria; OSA was confirmed via polysomnography (AHI ≥ 5 with symptoms). Patients were classified into RLS-OSA and RLS-only groups. Clinical characteristics, PSG parameters, and iron metabolism markers were analyzed. To identify distinct subgroups among patients with comorbid RLS and OSA, a K-means clustering analysis was conducted using R. Categorical variables were one-hot encoded and combined with standardized numerical variables (mean = 0, standard deviation = 1) to ensure equal weighting. The optimal number of clusters was determined using the Elbow Method and Silhouette Score. The K-means algorithm was then applied with the identified number of clusters to minimize within-cluster variance. Post-clustering differences in demographic, PSG, and laboratory test variables were evaluated using the t-test or the Mann-Whitney U test for continuous variables and the Chi-square tests or Fisher's exact test for categorical variables.

Results: OSA was present in 69.2% (n=785) of patients with RLS. The RLS-OSA group exhibited higher age, BMI, age at onset, and male proportion, with reduced insomnia (all $p < 0.01$). PSG revealed shorter total sleep time, lower sleep efficiency, increased wake time after sleep onset, and altered sleep stages (less N3, more N1; all $p < 0.01$). Hemoglobin and ferritin levels were elevated ($p < 0.001$). Two RLS-OSA phenotypes emerged: Cluster 1 ("Mild Early-Onset") with younger age, earlier onset, better sleep quality, and relatively normal iron status, and Cluster 2 ("Severe Late-Onset") with older age, later onset, poorer sleep quality, and iron dysregulation (all $p < 0.05$).

Conclusions: OSA is common in RLS, with distinct clinical and sleep-related differences. Two distinct phenotypes of RLS-OSA were identified, highlighting its heterogeneity. These findings underscore the need for tailored diagnostic and therapeutic approaches to improve symptom management and patient outcomes.

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Clinical feature and alpha-synuclein level of restless legs syndrome with leucine-rich repeat kinase 2 encoding gene mutation

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Introduction: Restless leg syndrome (RLS) has been reported associated with Parkinson's Disease (PD). However, it remained largely unknown of the mechanism underlying this association between RLS and PD.

Materials and methods: 199 idiopathic RLS and 114 PD were diagnosed and recruited by neurologists from Ruijin Hospital affiliated to Shanghai Jiao Tong University. And 273 health controls were recruited from community. Eight LRRK2 pathogenic variants were sequenced. Clinical data was collected including symptoms, comorbidities, family history, and iron level. ELISA was used to measure plasma level of α -synuclein.

Results: The G2385R variant was found significantly higher in PD group after Bonferroni correction ($p=0.018$). Taking all LRRK2 mutations as one risk covariant, further logistic regression analysis showed a marginal association of LRRK2 with RLS ($OR=1.847$, $95\%CI:1.022-3.337$, $p=0.042$) after adjusting age and gender. In terms of clinical feature, it was found that RLS-LRRK2 carriers usually reported a positive family history of neurological or psychiatric disorders (48.3% vs 27.6%) ($p=0.026$) and a higher foot involvement of sensory symptoms (33.3% vs 14.0%) ($p=0.042$). Plasma α -synuclein level in RLS ($p=0.021$) and PD ($p=0.018$) was both significantly increased compared to non-manifesting carriers.

Conclusions: Our study showed that LRRK2 mutation was associated with Chinese PD patients but only showed a possible trend of association with RLS. Positive neurological or psychiatric family history and foot discomfort in RLS were important features of indication of LRRK2 mutation in RLS. Plasma α -syn was increased in LRRK2-RLS as well as LRRK2-PD, indicating a possible association of RLS with PD in LRRK2 carriers.

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Clinical influence of restless legs syndrome in migraine patients: a 12-year single-center longitudinal study

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Introduction: A number of studies have shown a significant association between migraine and restless legs syndrome (RLS). However, few studies have investigated RLS in patients with migraine over the long term.

Materials and methods: We conducted a single-center, 12-year longitudinal study of migraine patients to assess the presence of RLS at baseline and after 7 and 12 years, and to evaluate its association with clinical factors. Headache-related disability was assessed using the Migraine Disability Assessment Scale (MIDAS). Sleep quality, daytime sleepiness and depressive symptoms were assessed using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS) and the Beck Depression Inventory-II (BDI-II), respectively.

Results: Of the 262 patients included at baseline, 101 were available after 7 years and 74 after 12 years; RLS prevalence was 13.7%, 20.8%, and 24.3% at baseline, after 7 and 12 years, respectively; this rate increased significantly from baseline to 12 years. RLS severity scores were not significantly different between the three time points. Analysis of covariance adjusted for age and sex showed that MIDAS, BDI-II, PSQI and ESS scores were significantly higher in migraine patients with RLS than in those without RLS at all time points. MIDAS, BDI-II, PSQI and ESS scores were significantly higher in the persistent RLS group, defined as being positive for RLS at the last evaluation in addition to the first and/or second evaluation, than in the RLS-naïve group, defined as having no RLS at any of the three time points.

Conclusions: This 12-year longitudinal study demonstrated a significant impact of RLS on the burden of migraine.

Comparison of Restless Leg Syndrome Characteristics and Treatment Responses Between Male and Female Patients

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Introduction: Restless legs syndrome (RLS), also known as Willis-Ekbom disease, affects sleep quality and overall quality of life worldwide. Understanding the demographic and clinical characteristics of RLS, particularly potential gender differences, is essential for effective diagnosis and management.

Objectives: To examine the demographic and clinical features of RLS, including iron status, polysomnographic parameters, treatment practices, and responses, with a comparison between male and female patients.

Materials and methods: We retrospectively analyzed inpatient and outpatient records, identifying RLS cases using ICD-10 codes. Patients aged 18 years and older diagnosed with RLS based on the 2014 IRLSSG criteria and with at least 12 months of follow-up were included.

Results: A total of 29 patients were included, with a female-to-male ratio of 1.42. The mean age was 64.61 ± 17.58 years for females and 62.57 ± 18.91 years for males ($p=0.767$). Body mass index, comorbidities, and the presence of sleep disorders such as obstructive sleep apnea and insomnia did not differ significantly between genders. Although males showed a trend toward a higher apnea-hypopnea index compared to females ($37.8 [3.25, 17.3]$ vs. $10.1 [10.9, 45]$ events/hour, $p=0.075$), females had significantly lower total sleep time and sleep efficiency (328.75 ± 61.42 vs. 425.75 ± 41.73 minutes, $p=0.040$; $74.17 \pm 9.71\%$ vs. $92.1 \pm 3.86\%$, $p=0.014$, respectively). Combined therapy was prescribed more frequently as the initial treatment in females compared to males (62.5% vs. 20% , $p=0.034$). However, treatment response and final medication dosages were similar across genders. Compared to males, females had significantly lower hemoglobin, serum iron, and transferrin saturation (12.65 ± 1.41 vs. 14.12 ± 1.73 g/dL, $p=0.018$; 71 ± 23.03 vs. 98.44 ± 30.38 mcg/dL, $p=0.029$; $24.43 \pm 8.29\%$ vs. $37.35 \pm 15.67\%$, $p=0.032$, respectively). However, the severity of iron deficiency warranting treatment and ferritin levels did not differ significantly between genders.

Conclusions: Sex-related differences in RLS were observed in sleep parameters, iron status, and initial treatment approaches. Female patients exhibited more pronounced clinical impact, as evidenced by reduced total sleep time and sleep efficiency, possibly contributing to the higher use of combination therapy. Despite lower iron status in females, the deficiency was generally not severe enough to require treatment. These findings underscore the importance of gender-specific considerations in the evaluation and management of RLS.

Complete Resolution of Restless Legs Syndrome Symptoms After CPAP Treatment in a Patient with Moderate Obstructive Sleep Apnea: A Case Report

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Introduction: Restless Legs Syndrome (RLS), or Willis-Ekbom Disease, is a sensorimotor disorder characterized by an uncontrollable urge to move the legs, particularly during rest or inactivity. While comorbid with various sleep disorders, its relationship with Obstructive Sleep Apnea (OSA) remains underexplored. We present a case in which a patient with long-standing RLS symptoms experienced complete remission following Continuous Positive Airway Pressure (CPAP) therapy for moderate OSA.

Materials and methods: This is a single-patient case report based on a retrospective review of electronic medical records from a multidisciplinary sleep medicine outpatient clinic. Clinical history, standardized questionnaires (International Restless Legs Syndrome Study Group Rating Scale and Epworth Sleepiness Scale), polysomnographic data, and CPAP device adherence reports were reviewed and analyzed across multiple follow-up visits between 2023 and 2024.

Results: A 59-year-old male with a history of chronic insomnia reported nightly symptoms consistent with Restless Legs Syndrome (RLS) for over 20 years—described as deep burning pain and an urge to

move the lower limbs during nocturnal awakenings and prolonged sitting. Two polysomnographies (2015 and 2024) confirmed moderate Obstructive Sleep Apnea (OSA), with apnea-hypopnea indices of 24.1/h and 26.4/h, and oxygen saturation below 90% for 5.3% of total sleep time, reaching a minimum of 74%. Relevant comorbidities included bruxism, obesity (BMI: 30.9), systemic hypertension, and gastroesophageal reflux disease, with regular use of metoprolol and olmesartan. He discontinued long-term zolpidem use in late 2023 due to concerns about cognitive side effects. No antidepressants, neuroleptics, antihistamines, or other medications known to worsen RLS were in use.

Baseline laboratory workup showed normal renal, hepatic, thyroid, and hematologic function. Vitamin D (34.1 ng/mL) and B12 (397 pg/mL) levels were within normal limits. Iron metabolism markers were also normal or elevated: serum iron 91 µg/dL, transferrin saturation index (TSI) 30%, and ferritin 404.1 ng/mL—ruling out iron deficiency as a contributing factor to RLS symptoms.

RLS severity was assessed using the International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale, with an initial score of 18 in February 2024 (moderate severity). CPAP therapy was initiated in March 2024. From March to May, usage data from the AirSense 10 AutoSet device showed ≥4 hours of use on 35 out of 41 nights (85% adherence), with a mean daily usage of 5 hours and 5 minutes. By April 2024, the IRLSSG score dropped to 0, indicating full remission of RLS symptoms. The patient reported complete resolution of leg discomfort and urge to move, particularly during evening rest and upon nocturnal awakenings, that used to occur daily for over two decades. Additional subjective improvements were reported in sleep quality, fatigue, mood, and cognition. Epworth Sleepiness Scale score improved from 11 to 4. No pharmacological treatment for RLS was initiated.

Conclusions: This case highlights a potential link between untreated OSA and secondary RLS symptoms. CPAP therapy not only improved respiratory parameters but also resulted in complete resolution of longstanding RLS symptoms. These findings support the consideration of sleep-disordered breathing as a reversible cause of RLS in select patients and underscore the importance of integrated management in sleep medicine.

Efficacy and safety of tonic motor activation (TOMAC) for restless legs syndrome as adjunctive treatment and monotherapy: preliminary results of an individual participant data systematic review and meta-analysis

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Introduction: Tonic motor activation (TOMAC) is a wearable therapeutic device that transmits bilateral high-frequency electrical stimulation to the peroneal nerve to treat symptoms of restless legs syndrome (RLS) and improve sleep. A recently published meta-analysis of TOMAC used aggregate data. In this meta-analysis, we conducted the first individual participant data meta-analysis of TOMAC, which enabled evaluation of TOMAC as adjunctive treatment and monotherapy.

Materials and methods: The protocol and analysis plan were prespecified and registered on PROSPERO (CRD420251005571). The systematic literature search was conducted with Covidence using Web of Science, Scopus, and PubMed from inception to March 31, 2025, to identify randomized clinical trials (RCTs) that evaluated TOMAC (high-frequency peroneal nerve stimulation) for treatment of RLS. Two independent reviewers performed literature search with discrepancies adjudicated by a third reviewer. Study authors provided individual participant data (IPD) for each of the RCTs, which was used for all meta-analysis. The primary endpoint for reducing RLS symptoms was change from baseline (CFB) in IRLS (International RLS Study Group Rating Scale) total score, and the primary endpoint for improving sleep was CFB in MOS-II score (Medical Outcomes Study Sleep Scale). Treatment arm (TOMAC vs. sham control) was the independent variable and primary analyses adjusted for baseline value of the relevant endpoint. Patients who received TOMAC were categorized as adjunctive if taking prescription medication for RLS and as monotherapy if not. Heterogeneity across studies was assessed with Tau statistic based on restricted maximum-likelihood method and conducting a Wald chi-square test and calculating the I² statistic. Pooled analyses were conducted except in the case of substantial heterogeneity, when a random study effect was used. For additional

subgroup analysis, baseline RLS severity (based on IRLS total score) was treated as a categorical variable and age of RLS onset was treated as a continuous variable.

Results: We identified 3 RCTs with a total of 252 RLS patients: 183 with adjunctive RLS medication (92 TOMAC, 91 sham); and 69 with no adjunctive RLS medication ("monotherapy"; 35 TOMAC, 34 sham). Relative to sham, TOMAC treatment significantly reduced IRLS score both as monotherapy (mean difference [MD]: -3.80, 95% confidence interval [CI]: -6.39 to -1.21, $p=0.0047$) and as adjunctive therapy (MD: -3.39, 95% CI: -5.09 to -1.70, $p=0.0001$). Compared to sham, TOMAC treatment also significantly reduced MOS-II score both as monotherapy (MD: -9.65 points, 95% CI: -17.92 to -1.38, $p=0.0236$) and as adjunctive therapy (MD: -8.23 points (95% CI: -12.88 to -3.59, $p=0.0006$). There was no evidence of heterogeneity between study results for any endpoints ($I^2=0$ and Cochran's Q-statistic chi-square P value > 0.50 for all). Additional subgroup analysis across all patients found no difference in IRLS MD based on baseline RLS severity (interaction $p=0.7889$) or age of RLS onset (interaction $p=0.7959$). There were no serious or severe device-related adverse events in any participant.

Conclusions: TOMAC is safe and efficacious at reducing RLS symptoms and improving sleep both as monotherapy and as an adjunctive therapy to prescriptive medication.

Acknowledgments: We thank the authors of the original publications for providing individual participant data.

Evaluating the Efficacy and Safety of Tonic Motor Activation in Restless Legs Syndrome: A Systematic Review with Meta-Analysis

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Introduction: Restless Legs Syndrome (RLS) is a neurological condition marked by an overwhelming urge to move the legs, often disrupting sleep and significantly affecting the health and quality of life of approximately 3% of adults. Current treatments primarily include iron supplementation, dopaminergic agonists and opioids. However, these options are frequently associated with substantial side effects, such as impulse control disorders and dependency. Tonic Motor Activation (TOMAC) has emerged as a promising non-pharmacological intervention, utilizing non-invasive peroneal nerve stimulation to alleviate RLS symptoms while minimizing adverse effects. Growing evidence supports the efficacy and safety of TOMAC, particularly in individuals who have not achieved sufficient relief with conventional therapies. This systematic review aims to assess the efficacy of TOMAC in managing RLS symptoms.

Materials and methods: The PRISMA protocol was used to guide the conduct of this systematic review and meta-analysis. The inclusion criteria encompassed studies involving participants aged 18 years or older with a confirmed diagnosis of RLS, as defined by the International Restless Legs Syndrome Study Group (IRLS) criteria. The intervention of interest was TOMAC for the treatment of RLS. Only randomized clinical trials were considered eligible for inclusion. Statistical analyses were performed using RevMan 5.1.7, and heterogeneity among studies was assessed using the I^2 statistic.

Results: Four Randomized Clinical Trials were located from searching seven databases and 3,193 studies, encompassing 152 participants in the TOMAC group and 163 in the control group, with follow-up durations ranging from 2 to 24 weeks. The mean age ranged from 55.7 to 57.6 years, and 60% of the participants were female. There was a significant reduction in the IRLS rating scale scores among patients treated with TOMAC compared to the control group (MD: -4.11 [-5.49, -2.73]; CI: 95%; $I^2=47\%$, $p<0.0001$). Subgroup analyses revealed a greater mean change in IRLS scores for medication-naïve patients (MD: -4.56 [-5.45, -3.68]; CI: 95%; $I^2=0\%$, $p<0.0001$) and for medication-refractory patients (MD: -3.88 [-4.63, -3.14]; CI: 95%; $I^2=0\%$, $p<0.0001$). In a separate analysis, the Clinical Global Impression-Improvement (CGI-I) responder rate demonstrated an odds ratio (OR) of 7.76 (95% CI: [4.33, 13.90], $I^2=55\%$, $p<0.0001$), favoring TOMAC. Similarly, the Patient Global Impression-Improvement (PGI-I) analysis for medication-refractory patients revealed an OR of 1.10 (95% CI: [0.63, 1.92], $I^2=0\%$, $p=0.7283$). Adverse events reported across all studies were rare, mild, and self-resolving, underscoring the safety of TOMAC.

Conclusions: According to the data from the present meta-analysis, TOMAC is an effective treatment for Restless Legs Syndrome (RLS). Significant reductions in symptoms were observed, as evidenced by improvements in the IRLS rating scale, as well as in CGI-I and PGI-I scores. Subgroup analyses further

demonstrated the efficacy of TOMAC in both medication-naïve and medication-refractory patients. Moreover, the intervention was shown to be safe, with only rare, mild, and self-limiting adverse effects reported. These results highlight TOMAC's potential as a valuable non-pharmacological therapy for RLS, while emphasizing the need for additional robust clinical trials to strengthen and validate these outcomes.

Acknowledgments:

I would like thank **Doctor Salles**. Her guidance was invaluable. I am also deeply thankful to Mr. Tekchandani. His contributions were fundamental.

Genetic Architecture of Restless Legs Syndrome in the Chinese Population and Its Transethnic Correlation with Europeans

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Introduction: Restless legs syndrome (RLS) is a common neurological sensorimotor disorder with a strong genetic component. However, most genetic studies to date have focused on European populations. Here, we conducted a genome-wide association study (GWAS) in a large Chinese cohort and performed cross-ethnic genetic correlation analysis to investigate the shared and distinct genetic architecture of RLS.

Materials and methods: We enrolled 1,493 RLS patients (including 1,226 with primary RLS) and 6,662 ancestry-matched controls from multiple centers across China. GWAS was conducted after stringent quality control and imputation using the 1000 Genomes East Asian reference panel. Transethnic LD score regression (LDSC) was applied to estimate SNP-based heritability and genetic correlation between Chinese and European RLS cohorts. We further conducted functional annotation of lead SNPs and prioritized candidate genes based on chromatin interactions and biological relevance.

Results: A total of **8 genome-wide significant loci** were identified, including **5 novel loci** and **10 RLS susceptibility genes**. Functional interpretation revealed that these loci are significantly enriched in previously published European RLS GWAS results, involved in neural development pathways, overlapped with parapyramidal nucleus-specific gene sets, and overrepresented in BTB/POZ regulatory domains. The SNP-based heritability of RLS in the Chinese population was estimated to be 0.39 ± 0.11 , supporting a substantial heritable component. Cross-ethnic genetic effect correlation ($\rho_{ge} = 0.511$, $P = 0.015$) and genetic impact correlation ($\rho_{gi} = 0.56 \pm 0.19$, $P = 0.002$) were both statistically significant, indicating a moderate degree of shared genetic architecture but also the presence of **population-specific signals**. The most significant associations in the Chinese cohort mapped to **BTBD9** and **GLO1**, both of which are located on chromosome 6 and have been strongly implicated in RLS pathogenesis. Although the **MEIS1** locus did not reach genome-wide significance in our Chinese data, chromatin interaction analysis revealed a physical link between a suggestive SNP (rs10865361) and the MEIS1 promoter, indicating potential long-range regulatory relevance. In addition, 8 of 42 FUMA-annotated genes showed significant enrichment ($P_{adj} = 1.34 \times 10^{-6}$), further supporting their biological involvement.

Conclusions: Our study reveals that RLS in the Chinese population has a higher SNP-based heritability compared to Europeans and shares moderately correlated genetic structure. The identification of BTBD9 and GLO1 as top loci reinforces their central role in RLS etiology, while chromatin interaction findings at MEIS1 suggest long-range regulatory mechanisms. These findings highlight both shared and distinct genetic features across populations and emphasize the value of transethnic GWAS combined with functional annotation in uncovering the biology of complex neurological disorders.

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Identification and Prediction of Phenotypic Subtypes of Restless Legs Syndrome

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Introduction: Patients with restless legs syndrome (RLS) presents prominent heterogeneity. For instance, age correlates significantly with symptom severity in early-onset RLS, whereas ferritin levels are associated with severity in late-onset cases. This study aimed to identify phenotypic subgroups of RLS based on a wide range of features and to develop a predictive model for subgroup classification.

Materials and methods: We screened 537 patients diagnosed with RLS who visited Seoul National University Hospital between 2014 and 2024. Patients with secondary RLS were excluded. Demographic, clinical characteristics, laboratory findings, comorbidities, and sleep-related questionnaires were collected. K-means clustering was applied to identify phenotypic subgroups, and statistical tests were used to compare characteristics across clusters. A decision tree-based algorithm was employed to predict phenotypic subgroups.

Results: A total of 360 patients (63.6% females) were included in the analysis. Onset age was 47.7 ± 17.1 years. Cluster analysis revealed three distinct phenotypes. Cluster 1: Late-onset patients with a stable or fluctuating disease course. Cluster 2: Patients with the most severe RLS symptoms and frequent augmentation, showing a fluctuating or refractory disease course. Cluster 3: Early-onset patients with prominent daytime sleepiness, showing an intermittent or stable disease course. A prediction model using a random forest algorithm based on initial characteristics achieved a macro AUC of 0.895 in classifying patients into phenotypic subgroups.

Conclusions: Three distinct phenotypes of RLS were identified through unsupervised cluster analysis. Tailored management strategies should be considered based on individual phenotypic characteristics. Future studies are warranted to validate these subgroups in independent cohorts and to explore their implications for personalized treatment strategies.

Influence of cerebral ischemic stroke on characteristics and laterality of periodic limb movements during sleep (PLMS)

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Introduction: Periodic limb movements during sleep (PLMS) are repetitive leg jerks occurring in series with an interval between 10 and 90 seconds. The neuronal network and the pathogenesis of PLMS are still unknown. Some evidence suggests that PLMS are the motor expression of a disinhibition of spinal circuits due to a reduced supraspinal control. Single case reports and case series describe the presence of PLMS contralateral to brain lesions at the level of the brainstem, basal ganglia and cortex. The idea behind the present analysis was to use ischemic stroke as a lesion model to investigate the impact of presumed cortical disinhibition on the occurrence, pattern and laterality of PLMS.

Materials and methods: Here we present a secondary analysis of data from the prospective multicenter study (Sleep- Disordered Breathing in Transient Ischemia Attack [TIA]/ Ischemic Stroke and Continuous Positive Airway Pressure [CPAP] Treatment Efficacy; SAS-CARE; NCT01097967). Participants underwent a clinical examination, cerebral MRI, nocturnal polysomnography (PSG) during the acute (1–8 days after stroke) phase and/or 3 months after stroke. We selected 25 patients who showed a clear mono-lateral ischemic stroke in a single vascular either cortical or subcortical territory and had good-quality PSG recordings in the acute and chronic phase. Leg movements (LM) were scored according to the WASM criteria (2016) and respiratory related leg movements excluded from the analysis. Other than reporting descriptive statistics, we constructed regression models to investigate confounding factors impacting the asymmetry of the motor-phenomenon.

Results: The 25 included patients (7 women, 18 men) had a mean age of 62 (8.4) years, median BMI of 26.3 [24.4|29.4] and mostly showed cortical ischemic lesions in the territory of the middle cerebral artery (MCA, n=21 (84%)). Median NIHSS at admission was 4 [1.5|5.5]. Overall PLMS burden was very low (1.24[0.79|3.79]/h) with asymmetry in 18/25 patients and strictly unilateral PLMs in 8 cases (4 ipsilateral and 4 contralateral to the stroke side). PLMS showed low overall periodicity (periodicity index (PI) 0.34 [0.18|0.58]) and no difference in PI between relative sides. The same distribution of LM, PLM and PI was seen in the chronic state with however a slight tendency towards higher values in the chronic vs. the acute state. Regression analysis revealed a significant impact of age ($\beta=0.23$, $p=0.01$), vessel other than MCA ($\beta=-7.30$, $p=0.0001$), stroke volume ($\beta=0.198$, $p=0.03$) and total PLMSI ($\beta=0.85$, $p=0.013$) on PLMSI delta (contralateral minus ipsilateral).

Conclusions: In the current analysis we did not find a clear difference between general and periodic leg movement activity in the limbs ipsilateral or contralateral to ischemic cortical or subcortical stroke, neither in the acute nor the chronic phase. However, having an MCA stroke, larger stroke volume, more PLMS activity and being older seemed to increase asymmetry with bias towards the side contralateral to the stroke. Further analyses therefore need to focus on patients with clear pyramidal tract involvement to more adequately address the question of whether spinal disinhibition due to a lesion of the pyramidal tract can lead to asymmetric motor activity during sleep.

Neurological approaches to restless legs syndrome: a systematic review of non-pharmacological interventions

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Introduction: Restless Legs Syndrome (RLS) is a neurological disorder affecting approximately 3% of adults, significantly impairing health and quality of life. The standard treatment for RLS is pharmacological, but it often leads to significant side effects. Non-pharmacological neurological interventions, such as neuromodulation, neurostimulation, and neuroactivation, are emerging as promising alternatives. This systematic review aims to evaluate the efficacy of these interventions in treating RLS.

Materials and methods: This review was guided by the PRISMA protocol. The search utilized the terms 'Restless Legs Syndrome,' 'Neuromodulation,' 'Neurostimulation,' and 'Neuroactivation.' Inclusion criteria included studies evaluating the efficacy of neurological interventions in treating RLS.

Results: A total of 3489 studies were identified, of which 21 were included. The total sample comprised 1008 participants, with a mean age ranging from 45.7 to 63.0 years. Chahine et al. (2011) observed that Deep Brain Stimulation (DBS) reduced IRLSSG scores from 23.0 to 13.8 ($p=0.037$). Klepitskaya et al. (2018) reported improvements in IRLSSG scores from 24 to 12. Evidente et al. (2021) found a reduction from 15.8 to 8.5 ($p=0.007$) with DBS. Lei et al. (2022) and Yuan et al. (2022) reported improvements in RLS scores from 22 to 10 and from 23 to 11, respectively. Zeng et al. (2020) showed that Transcutaneous Spinal Cord Stimulation reduced IRLS scores from 27.2 to 15.0 ($p<0.05$) and improved sleep, with a reduction in PSQI from 14.9 to 10.3 ($p<0.05$). Lin et al. (2015) reported that Repetitive Transcranial Magnetic Stimulation (rTMS) reduced IRLSS scores from 23.86 to 11.21 ($p<0.05$). Altunrende et al. (2014) found a reduction from 29.6 to 12.7 ($p<0.001$) with rTMS. Feng et al. (2024) observed reductions from 25.3 to 13.4, and Liu et al. (2015) from 26.1 to 14.2. Abedi et al. (2021) showed that Transcutaneous Electrical Nerve Stimulation (TENS) reduced IRLS scores from 23.36 to 12.5 ($p<0.05$). Augustina et al. (2020) reported a reduction in IRLS scores from 32.27 to 11.87 ($p<0.0001$) in pregnant women. Şanlı et al. (2024) found improvements in IRLS scores from 28 to 18 and PSQI from 12 to 7 with the combined use of pramipexole and TENS. Bogan et al. (2023) reported a reduction in IRLS scores from 31.9 to 24.6 ($p<0.01$) with Tonic Motor Activation (TOMAC). Roy et al. (2023) found a reduction of 11.3 points in IRLS ($p=0.0001$) after 24 weeks. Buchfuhrer et al. (2021) reported improvements in IRLS scores from 30 to 18 ($p<0.001$). Hartley et al. (2022) observed a reduction in IRLS scores from 31.9 to 24.6 ($p=0.0003$) with Vagus Nerve Stimulation (tvNS), and confirmed these results in 2023, showing a reduction from 30.7 to 22.1 ($p<0.01$) after 24 weeks.

Conclusions: Non-pharmacological neurological interventions show significant promise as alternatives for treating RLS. These findings support the need for further randomized controlled trials to confirm and expand upon these results.

Acknowledgments: I would like thank Doctor Salles. Her guidance was invaluable. I am also deeply thankful to Mr. Tekchandani. His contributions were fundamental.

PAP Adherence in RLS Patients with OSA

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Introduction: Obstructive sleep apnea (OSA) commonly coexists with restless leg syndrome (RLS). Emerging evidence suggests that positive airway pressure (PAP) treatment for coexisting OSA may also reduce RLS symptom. However, often contributes to secondary insomnia, causing difficulties with sleep initiation and maintenance, which may compromise PAP adherence. The combined impact of RLS and OSA on PAP adherence is underexplored. Our study aimed to evaluate PAP therapy adherence and identify key determinants of adherence in patients with coexisting RLS and OSA.

Materials and methods: This retrospective cohort study analyzed clinical data from patients diagnosed with RLS who reported snoring and underwent overnight polysomnography (PSG), between Jan 2022 and July 2024, at the Division of Sleep Medicine in the Peking University People's Hospital. The study assessed clinical characteristics, PAP adherence, and factors influencing adherence. Adherent patient was defined as device use for ≥ 4 hours per night on $\geq 70\%$ of nights. Patients with coexisting RLS and OSA were followed up 1year after PAP initiation via semi-structured telephone interviews and questionnaires. Objective PAP data were obtained from device memory cards mailed by patients.

Results: A total of 114 patients were diagnosed with RLS. Of these, 84 (73.68%) had coexisting OSA. Among these, 70 patients initiated PAP therapy and continued treatment at hospital. Of these, 37 acquired a PAP, device. and 25 provided objective PAP usage data. PAP adherence declined progressively over time with adherent patients of 76% at 1week, 36% at 1month, 20% at 3 months, 16% at 6 months, and 12% at one year. Influencing factors included subjective symptom improvement, device tolerance, and socioeconomic burden.

Conclusions: PAP adherence is low and declines over time in patients with coexisting RLS and OSA. Targeted interventions addressing symptom relief, device tolerability and socioeconomic factors may improve adherence and outcomes in this population.

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Role of cytokines in RLS: insights into IL6 and iron in the etiology of RLS

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Introduction: Introduction:

Restless Legs Syndrome (RLS) is a sensorimotor disorder that affects 5% to 15% of the world population and 6.40% of the Brazilian population, affecting sleep and daily activities. The etiology of RLS is unclear, but several studies point to iron deficiency. On the other hand, studies point to IL-6 deficiency. We analyzed 35 amateur athletes with and without RLS. Iron levels were measured: IL-6 before the marathon (42 km), which we call baseline, after the race and 72 hours after the race.

Key words: iron, IL6, hepcidine, RLS, Restless Legs Syndrome

Objectives

This work attempts to trace iron and IL6 mechanism in RLS.

Materials and methods: Materials and Methods:

The group consisted of 35 drug-free amateur runners (M = 41.57 years, SD = 6.24) who completed the race within 5 hours. The researchers (SBRF and DJLF) applied a questionnaire using The International RLS Study Group (IRLSG) diagnostic criteria. RLS severity was assessed using the "IRLSG severity questionnaire". How long she/he has RLS, how long they had been running, and whether they had RLS before they started running. Blood was collected at baseline, post-marathon, and 72 hours later.

Results: Results:

12.96% of athletes met the criteria for SPI. Iron levels were: RLS group: basal: 97.12; post: 109.63; 72h: 86.71. Non-SPI group: basal: 94.68; post: 105; 72h: 82.14. IL-6 levels: SPI group basal: 16.46; post: 43.93; 72h: 52.95. Non-SPI group: basal: 28.24; post: 109.76; 72h: 0.15.

Conclusions: The results of changes in the secretion pattern of IL-6 in runners with RLS may be essential for understanding RLS, as they may be associated with changes in metabolism and inflammatory mechanisms, in addition to being essential for sleep.

Cytokines, specifically IL-6, induce hepcidin, and hepcidin regulates iron. After a strenuous effort, such as a marathon, IL-6 kicks in to restore balance in the body. Our data show that IL-6 continues to increase after strenuous efforts, such as a marathon, in the RLS group. There is no significant difference in iron levels between the RLS group and the non-RSL group. Could the mechanism of RLS be between IL-6 and iron? Further studies are needed to confirm trends.

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Severe, refractory restless legs syndrome responding to hyperbaric oxygen therapy: a case report

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Introduction: We present the case of a 73-year-old woman with severe, refractory restless legs syndrome (RLS). She experienced progressively worsening symptoms over more than 20 years, resulting in significantly impaired sleep and daytime dysfunction. This is on a background of mild obstructive sleep apnoea and sleep-maintenance insomnia. Her symptoms of RLS remained debilitating despite multiple pharmacological and non-pharmacological interventions trialled including iron replacement therapy, gabapentinoids, opioids, antidepressants, and cognitive behavioural therapy. At the time of hyperbaric oxygen therapy (HBOT) initiation, she was taking buprenorphine patch 5 mcg/h weekly, amitriptyline 25 mg nocte, agomelatine 25 mg daily, gabapentin 600 mg daily, and zopiclone 7.5 mg nocte.

Materials and methods: Emerging research suggests that peripheral tissue hypoxia may play a role in RLS pathophysiology. A study demonstrated a strong association between reduced leg oxygenation and symptom severity in untreated patients with RLS. Based on this, HBOT was trialled as a novel therapeutic approach. In February 2025, the patient commenced a HBOT protocol consisting of 30 sessions, each lasting 50 minutes and uptitrated to 1.9 atmospheres absolute, delivered 3–4 times per week. No concurrent changes were made to her medication regimen during the HBOT course.

Results: The patient reported symptomatic improvement within two weeks of initiating HBOT. Upon completion of the initial 30-session protocol, she reported marked improvements in subjective sleep quality, mood, and both the frequency and severity of RLS symptoms. Her International Restless Legs Scale score decreased from 21 (severe) to 2 (mild). The treatment was well tolerated, with no reported adverse effects. Given the durability of symptom control between sessions, the patient has continued on HBOT indefinitely with a plan to de-escalate the frequency of sessions. In parallel, the patient began a supervised taper of gabapentin, reducing the dose by 100 mg every three weeks. She is currently stable on gabapentin 400 mg daily, without recurrence of significant symptoms.

Conclusions: This case highlights the potential for HBOT to serve as a novel adjunctive therapy for patients with refractory RLS, particularly when conventional treatment options have been exhausted. If further validated, HBOT may offer a promising avenue for improving quality of life in this challenging patient population.

Acknowledgments: We acknowledge the patient who has provided consent for the abstract.

Tonic motor activation therapy in patients with painful versus painless restless legs: An interim 180-day results from the THRIVE study

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Introduction: Painful and painless restless legs syndrome (RLS) phenotypes have been characterized in several studies. Compared to painless RLS, painful RLS is a more severe clinical form. However, there is scarcity of data evaluating treatments for painful and painless RLS. Bilateral high-frequency peroneal nerve stimulation or tonic motor activation (TOMAC) is a new non-invasive and non-pharmacological treatment cleared for patients with medication-refractory RLS based on its efficacy and safety profile in several recent clinical trials. The current study compared TOMAC effectiveness in patients with painful and painless RLS using real-world interim results from the THRIVE study.

Materials and methods: The THRIVE study, an ongoing multi-center, prospective, post-market, observational study was used to extract interim 180-day data for analysis. The THRIVE study evaluates long-term effectiveness and safety of the NTX100 TOMAC system (Nidra; Noctrix Health, Inc.) in adults with RLS. Painful RLS was classified based on participants answering 'Yes' to both of the following baseline consecutive questions: "Do you have unpleasant or uncomfortable feelings associated with the urge to move your legs?" and "Are these unpleasant or uncomfortable feelings painful?" Baseline assessments were conducted prior to the initiation of TOMAC treatment, with interim outcomes evaluated at Day 180 relative to baseline. Data collected at baseline included age, sex, family history of RLS, age of RLS onset, current RLS medications, augmentation severity rating scale, International RLS Severity Scale (IRLS) score, diagnosis of neuropathy, and the titrated stimulation intensity of TOMAC. The primary endpoint was the change in IRLS score at 180 days. Secondary endpoints at 180 days included the Clinical Global Impression-Improvement (CGI-I) score and the CGI-I responder rate (defined as the proportion of patients with a CGI-I response of "Very Much Improved" or "Much Improved"). Changes in RLS medications at 180 days were also assessed.

Results: A total of 73 adult patients with medication-refractory, moderate-to-severe RLS—36 with painful RLS and 37 with painless RLS—completed 180-day follow-up. These individuals constituted the intent-to-treat population, with data imputed for those who withdrew from the study. At baseline, patients with painful RLS had significantly more severe symptoms compared to those with painless RLS, as indicated by higher mean IRLS scores (27.7 ± 5.6 vs. 23.9 ± 5.4 ; $P = 0.005$), and were more often treated with dopaminergic agents (66.7% vs. 43.2%; $P = 0.044$). Other baseline characteristics were comparable between the two groups. After 180 days, there was no significant difference in the mean change in IRLS scores between painful and painless RLS patients (-8.7 ± 6.6 vs. -7.8 ± 7.7 ; $P = 0.589$). Similarly, mean CGI-I scores (2.5 ± 1.2 vs. 2.4 ± 1.3 ; $P = 0.817$), CGI-I responder rates (66.7% vs. 51.4%; $P = 0.184$), and changes in RLS medications were not significantly different between groups.

Conclusions: Patients with painful RLS exhibited more severe symptoms and higher dopaminergic use at baseline, consistent with painful RLS being a more severe phenotype. However, after 180 days of TOMAC therapy, both painful and painless RLS groups demonstrated similar improvements, suggesting that TOMAC is similarly effective across both RLS phenotypes.

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RevRound 2

Identification of circulating inflammatory proteins as mediators of sleep apnea on aging and validation of inflammation-drug targets using prioritization profiling

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Introduction: Background Sleep apnea (SA) may accelerate aging via inflammation, but its mechanisms and therapeutic targets remain poorly understood. We aimed to explore the causal links between SA, inflammatory proteins, and aging, and prioritize drug targets for SA and healthy aging. We searched PubMed using the search terms "sleep apnea", "inflammation", "aging", "mediation" on March 20, 2024 and identified 14 studies on the associations of SA and aging, showing that SA was associated with several aging indicators (Table S1). However, these studies might be limited by residual confounding

and potential reverse causality, and evidence from randomization clinical trial (RCT) is scarce. Only one RCT reported that adherence to continuous positive airway pressure (CPAP) for 12 months in SA patients slowed epigenetic aging, yet this study examined a single aging marker and involved a short follow-up period.

Materials and methods: Methods We examined the association of SA with aging using data from the Guangzhou biobank cohort study (GBCS) and assessed causality with summary-level statistics from genetic studies involving over 350,000 European participants. We first identified inflammatory proteins mediating the association between SA and aging indicators (leukocyte telomere length (LTL), bioage acceleration (BA) and phenoage acceleration (PA)) using mediation Mendelian randomization (MR), colocalization analysis, and pathway enrichment analysis. Second, we systematically assessed the causal role of these inflammatory proteins on SA and aging outcomes using phenome-wide MR and colocalization analysis, and prioritized drug targets by integrating genetic findings with clinical trial evidence.

Results: Results Of 30,055 participants from the Guangzhou Biobank Cohort Study, with a median follow-up of 11.2 years, 17,487 were assessed for SA, 9,872 for BA, and 2,350 for relative telomere length (RTL). SA was associated with increased PA ($\beta=0.94$, 95% confidence interval (CI) 0.60, 1.28) and higher risk of mortality (Hazard ratio (HR)=1.18, 95%CI 1.07, 1.31), but not with RTL. MR supported the causal association between SA and PA ($\beta=0.82$, 95%CI 0.29, 1.34) and identified HGF and IL-8 as mediators, explaining 17.4% and 15.0% of the variance, respectively. Enrichment analyses showed shared pathways related to cell chemotaxis and cytokine signaling. Drug prioritization profiling in 381 protein-disease pairs identified five inflammatory proteins as promising drug targets for aging, including FGF-5, CCL19, MIP-1 alpha, SLAMF1, and CCL13.

Conclusions: Conclusions This is the first study comprehensively assessing the causal roles of 106 inflammatory proteins as potential mediators of SA on aging and prioritizing inflammation-related drug targets for addressing SA and aging. Phenome-wide Mendelian randomization (MR) analyses support a causal effect of SA on aging acceleration, with HGF and IL-8 mediating a substantial proportion of the effect. Moreover, we identified six promising drug targets for aging deceleration, including two candidates for drug-repurposing (CCL19 and MIP-1 alpha) and three novel protein-aging pairs (FGF-5, SLAMF1 and CCL13) that warrant further investigation.

Acknowledgments: The authors thank the investigators from the GBCS (Guangzhou biobank cohort study) and all the original GWAS used in the present study.

RevRound 3

Effect of Sleep Disordered Breathing on Pregnancy Outcomes in Women Undergoing In Vitro Fertilization: A Systematic Review and Meta-Analysis

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Introduction: Studies suggest that OSA impairs female fertility in patients with polycystic ovary syndrome, suggesting an adverse effect on in vitro fertilization cycle stimulation characteristics and clinical outcomes. Frequent snoring has been found to have an association with a decreased number of available oocytes and an increased risk of pregnancy loss following IVF. Further research is required to understand the potential influence of obstructive sleep apnea (OSA) on infertility and pregnancy outcomes.

Materials and methods: Details of the review are included in the PROSPERO registration CRD420251035788

<https://www.crd.york.ac.uk/PROSPERO/recorddashboard>

Results: Research in progress

Conclusions: There is a potential role for the management of obstructive sleep apnea to improve outcomes in patients undergoing IVF

Sleep Breathing Disorders

A buccal mucosal reflectance oximeter accurately measures arterial oxyhemoglobin saturation and pulse rate

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Introduction: Pulse oximeter devices (SpO₂) suitable for multi-night monitoring of arterial oxyhemoglobin saturation (SaO₂) are not readily available despite a need to monitor SaO₂ decreases in patients with sleep apnea and pulmonary diseases during sleep. The objective of the current study was to assess the SpO₂ and pulse rate accuracy of a buccal mucosal oximeter embedded into a custom-fitted overlay of the upper teeth by comparison to a gold standard (CO-oximeter SaO₂ and 3-lead electrocardiogram [ECG] heart rate).

Materials and methods: Twelve healthy participants (four females) aged 30.7±6.7 (22-39) years underwent a progressive stepwise desaturation protocol consisting of six 7-minute stages of decreasing levels of end-tidal oxygen (P_{ET}O₂; 90.1, 63.8, 53.0, 46.4, 41.6, and 37.9 Torr) to achieve a range of SaO₂ from approximately 97-70% during semi-recumbent, non-motion conditions. P_{ET}O₂ and P_{ET}CO₂ were controlled by a dynamic end-tidal forcing function system. Arterial blood was drawn and analyzed using a Radiometer ABL800 CO-oximeter in the last three minutes of each stage. SpO₂ and pulse rate values from the buccal mucosal oximeter were compared with CO-oximeter values of SaO₂ and ECG heart rate, respectively.

Results: SaO₂ values were evenly distributed over the range of 97-67%. Analysis of 325 CO-oximeter SaO₂/buccal mucosal oximeter SpO₂ data pairs yielded: r = 0.95; bias = 0.72; and accuracy root-mean-square (A_{RMS}) = 2.94%. Analysis of 346 ECG heart rate/buccal mucosal oximeter pulse rate data pairs yielded: r = 0.99, bias = 0.30; and A_{RMS} = 2.08 bpm.

Conclusions: The buccal mucosal oximeter accurately measured SpO₂ and pulse rate, as shown by good agreement with a gold standard, over a wide range of arterial hypoxemia. Such clinically acceptable accuracy indicates that this novel reflectance oximeter may prove useful in the management of patients with sleep-induced hypoxemia by providing multi-night monitoring of SaO₂. Additionally, the intraoral placement of the oximeter might overcome some limitations of other pulse oximeters, as the buccal mucosa is highly vascularized, temperature regulated, protected from ambient light, and appears to lack melanin.

Acceptability and results of home sleep apnoea testing in older adults with mild cognitive impairment and dementia and cognitively unimpaired older adults: Towards a multi-centre study of sleep apnoea prevalence in memory clinics

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Introduction: Good sleep is key to brain health. Yet, sleep is rarely objectively assessed in cognitive disorders clinics. Sleep apnoea (SA) is a common sleep-breathing disorder with significant impacts on cardiovascular health and cognition, effectively treated using established (e.g., continuous positive airway pressure, CPAP) and emerging techniques (e.g., implant devices, weight loss medications). SA is associated with increased dementia risk and may be a modifiable dementia risk factor. To build towards interventional studies, we examined the prevalence of sleep apnoea and barriers and facilitators to sleep apnoea assessment in a cohort of older people with and without dementia.

Materials and methods: 40 participants (10 with mild cognitive impairment, 10 with dementia and 20 age-matched controls) were enrolled in a longitudinal cohort study of sleep and cognition. All participants were asked to complete questionnaires on SA risk (STOP-BANG) and daytime sleepiness

(Epworth Sleepiness Scale, ESS). Participants without an existing diagnosis of SA were asked to complete two consecutive nights of overnight pulse oximetry (Nonin 3150 WristOx2). Oxygen desaturation index (ODI) was calculated based on number of desaturation episodes ($\geq 3\%$ for > 10 seconds) per hour.

Results: Most participants asked ($N=33/37$, 83%) provided at least one night of analysable overnight pulse oximetry data of > 4 hours. Three participants had an existing diagnosis of SA and were receiving CPAP treatment prior to study enrolment. One participant was unable to tolerate the device due to uncomfortable sensations on the finger and three participants declined SA testing. Referrals to the sleep clinic for likely SA were indicated for 21 participants: 10 had mild ODI ($\geq 5 < 15$), 3 had moderate ODI ($> 15 \leq 30$), 3 had severe ODI (≥ 30), and 5 had normal ODI (< 5) but high pulse rise index. 17/21 (81%) participants agreed to referrals. Barriers to SA testing among older adults included concerns around receiving additional diagnoses, potentially stopping driving, not wanting to use CPAP, and the distance required to travel for appointments. An $ODI \geq 5$ was not associated with excessive daytime sleepiness indicated by $ESS \geq 10$ [$p = 0.722$, sensitivity = 33%, specificity = 73%] but was marginally associated with STOP-BANG scores ≥ 3 [$p = 0.047$, sensitivity = 89%, specificity = 47%].

Conclusions: SA may be a reversible contributor to cardiovascular morbidity, poor sleep quality, and cognitive disorders including dementia. However, SA is often undiagnosed in older adults. Existing screening questionnaires may be suboptimal to accurately screen for SA in this population. To establish prevalence of SA in a memory clinic population and which symptoms most strongly predict SA prevalence, the Sleep Apnoea and Memory (SAM) study will invite all patients attending several sleep clinics across England to undergo SA screening using the WatchPAT home sleep apnoea test and complete detailed SA symptom screening.

Acknowledgments: We would like to thank our participants, their relatives, and our lived experience experts. We would also like to thank the North Bristol NHS Trust Respiratory Physiology department and our funders (BRACE, Bristol & Weston Hospitals Charity, David Telling Charitable Trust, Alzheimer's Research UK, and philanthropic donors S Scobie and A Graham).

Acceptance, Compliance and Efficacy of Mandibular Advancement Splint Therapy in Atrial Fibrillation Patients

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Introduction: Clinical guidelines recommend that the management of atrial fibrillation (AF) should include assessment and treatment for obstructive sleep apnoea (OSA) (1-3). However, acceptance and compliance with CPAP therapy is often low (4). Alternative therapy is needed.

This is a pilot study of Mandibular Advancement Splint (MAS) treatment of OSA in AF patients in Australia and Singapore. Primary outcomes were patient acceptance, compliance, and MAS efficacy. Secondary outcomes included AF burden, MAS patient-centred evaluation, side effects, quality of life, and change in ambulatory blood pressure. In addition, the feasibility of tools for the assessment of AF recurrence was assessed.

Materials and methods: Patients with AF and OSA were treated with MAS over 6 months. Polysomnography (PSG) was performed at baseline and 6 months. Patient acceptance was defined as the proportion of patients who continued using the MAS after an initial one-week lead-in period. Compliance was defined as ≥ 4 hours of MAS usage on $\geq 70\%$ of nights, based on the inbuilt compliance recorder (DentiTrac, Braebon). MAS efficacy was assessed via change in Apnea Hypopnea Index between baseline and six months. Feasibility of tools for the assessment of AF recurrence was evaluated by numerous methods for AF detection.

Results: A total of 33 patients (16 in Australia, 17 in Singapore) were recruited, and all participants have completed the study. Interim data from 12 patients (all in Australia, 75% male, mean age 65.5 ± 10.2 years, and BMI 29.6 ± 4.8 kg/m²) have been analysed. Ten out of 12 patients continued using the MAS after one week, giving an acceptance rate of 83.3%. The pre-determined compliance threshold at 3 and 6 months was met by 80% of the study participants. Of the 10 patients who continued to use the MAS

at 6 months, 60% met the liberal criteria for MAS response, and 40% met the strict criteria for MAS response. A daily at-home ECG device (AliveCor Kardia) showed the best performance in detecting AF recurrence (in 58% of patients).

Conclusions: Interim results from this pilot study suggest that treatment of OSA using MAS therapy in AF patients is feasible. A high level of acceptance, compliance and efficacy was observed. Analysis of the remaining data is underway, including a comparison of Australian and Singaporean groups.

Accuracy of a buccal mucosal reflectance oximeter in measuring and reporting oxygen desaturation index in individuals with obstructive sleep apnea: A pilot study

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Introduction: Pulse oximeter devices (SpO₂) suitable for multi-night monitoring of arterial oxyhemoglobin saturation (SaO₂) are not readily available despite a need to monitor SaO₂ decreases in patients with sleep apnea during sleep. ProSomnus Sleep Technologies (Pleasanton, CA) previously developed a buccal mucosal pulse oximeter embedded into a custom-fitted overlay of the upper teeth. The oximeter has previously been validated against the gold standard, i.e., arterial samples analyzed using CO-oximetry, in a controlled desaturation study in healthy, awake volunteers.

The objective of the current pilot study was to assess the accuracy of the oxygen desaturation index (ODI) of the buccal mucosal oximeter in individuals with obstructive sleep apnea (OSA) during sleep by comparing the ODI from the buccal mucosal oximeter to that from a reference oximeter (WristOx 3150, Nonin Medical Inc., Plymouth, MN).

Materials and methods: Eight volunteers previously diagnosed with moderate or severe obstructive sleep apnea wore the buccal mucosal and reference oximeters overnight in the home for two nights of sleep. Volunteers wore only the upper dental overlay of the buccal mucosal oximeter for the first night (untreated). A lower arch of a mandibular advancement device was added for the second night of sleep to provide mandibular protrusion in the range of 30-70% (treated). Data from the buccal mucosal oximeter were compared to the data from the reference oximeter.

Results: Sixteen nights of data were collected from the eight participants. Linear regression showed good concordance between the buccal mucosal oximeter and reference oximeter ($r = 0.94$; $p < .000001$). Bland-Altman analysis showed a bias of 1.9 and upper and lower 95% limits of agreement of 11.0 and -7.2, respectively. With the upper dental overlay only (untreated), the mean ODI was 26.3 ± 12.9 for the buccal mucosal oximeter and 28.1 ± 13.2 for the reference oximeter ($p = 0.2656$), indicating no significant difference between the two ODIs. When the upper dental overlay was used in conjunction with the lower arch of a mandibular advancement device, the mean ODI was 13.4 ± 8.7 for the buccal mucosal oximeter and 15.4 ± 10.6 for the reference oximeter ($p = 0.4609$), indicating no significant difference between the two ODIs. The difference between the untreated and treated position was significant for both the Nonin oximeter and buccal mucosal oximeter ($p < 0.05$ for both).

Conclusions: The results of this pilot study indicate that a reflectance oximeter embedded in a dental overlay can report an accurate oxygen desaturation index in individuals with obstructive sleep apnea both when used on its own and when used in conjunction with a mandibular advancement device, demonstrating that this technology has the potential to objectively quantify the efficacy of mandibular advancement device therapy. Further research is needed to validate these results in a larger population against a gold standard.

Acknowledgments: The authors thank Dr. Trevor Day (Mount Royal University, Calgary, Alberta, Canada) for loaning Nonin WristOx devices for the project.

A comparative study of a finger-worn One Sleep Test (NightOwl)[™] with in-lab polysomnography for the diagnosis of obstructive sleep apnea

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Introduction: Overnight in-lab technician attended polysomnography (PSG) is the gold standard method for the diagnosis of obstructive sleep apnea (OSA). However, long waiting period results in the delay in diagnosis and therapy leading to significant morbidity. For the diagnosis of sleep apnea, newer portable device One Sleep Test™ (OST) is available which is based upon peripheral arterial tonometry rather than conventional flow sensor-based technology. This device has not been well studied in Indian subjects. Aim of the study was to assess the correlation of apnea hypopnea index (AHI) measured using OST and in-lab polysomnography and to estimate the sensitivity and specificity of OST for the diagnosis of obstructive sleep apnea.

Materials and methods: We prospectively evaluated the diagnostic performance of a finger-worn portable sleep study device, the One Sleep Test™, which is a combination of oximetry, actigraphy and peripheral arterial tonometry. Patients with suspected OSA underwent simultaneous in-lab level 1 diagnostic polysomnography and OST testing. The results from both modalities were compared. The PSG scorer was blinded to the result of the OST study.

Results: Thirty-eight patients (25 males and 13 females) were studied and had a mean (SD) age of 40.89 (12.4) years. The mean (SD) body mass index of study subjects was 29.49 (5.17) kg/m². Thirty-one out of 38 patients were found to have OSA (AHI ≥ 5) while 27 had moderate to severe OSA by polysomnography (AHI ≥ 15). The mean (SD) OST sleep efficiency was 83.18% (9.77), whereas the mean (SD) PSG sleep efficiency was 75.46% (17.06). There was a good correlation ($r=0.85$, $p<0.001$) between the median (IQR) OST AHI of 13 (3-45.75) events/hour and the median (IQR) PSG AHI of 20.3 ± 10.87 events/hr.

For the diagnosis of OSA (AHI ≥ 5), the sensitivity as well as specificity of OST were 87.09% and 85.7% respectively. The sensitivity and specificity of OST for the diagnosis of moderate-severe OSA (AHI ≥ 15) were 66.67% and 100% respectively.

Conclusions: OST is a useful portable diagnostic device for the diagnosis of obstructive sleep apnea.

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A Cross-Sectional Study on Sleep-Related Breathing Disorders and School Performance Among School Children in Mindanao, Philippines

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Introduction: Sleep-Related Breathing Disorders (SRBDs) in children, such as obstructive sleep apnea (OSA), are associated with behavioral, cognitive, and emotional impairments that may hinder academic performance. In low-resource, linguistically diverse regions like Mindanao, the lack of validated screening tools limits early identification and intervention.

Materials and methods: Method: A two-phase design was employed. Phase I involved forward-backward translation and expert validation of the PSQ-SRBD into Bisaya, followed by psychometric testing ($n = 128$) and test-retest reliability ($n = 69$). In Phase II, a cross-sectional study screened 2,320 children (aged 8–14) across Mindanao using parent-reported questionnaires (Bisaya, English, or Filipino versions). Logistic regression identified predictors of SRBD risk and academic outcomes.

Results: Result: The Bisaya PSQ-SRBD demonstrated strong psychometric properties, with high internal consistency (Cronbach's $\alpha = 0.77$) and excellent test-retest reliability (ICC = 0.904), confirming its suitability for use in multicultural, community-based settings. Of the 2,320 schoolchildren screened, 8.7% were identified as high risk for SRBD. Multivariate logistic regression revealed that older age (11–14 years), residence in the Caraga region, lower parental education, presence of comorbid conditions, insufficient sleep duration, and engagement in modular or online learning modalities significantly increased the likelihood of SRBD ($p < .05$). Importantly, SRBD risk was strongly associated with decreased academic performance across all major subjects—Filipino, English, Mathematics, and Science ($p < .001$). Moreover, even after controlling for SRBD status, both household smoking exposure and socioeconomic disadvantage (e.g., low income, low parental education) emerged as robust independent predictors of poor school outcomes. These findings highlight the multifactorial nature of academic underperformance, with SRBD acting as both a direct and indirect contributor.

Originality: This is the first study to validate the PSQ-SRBD in Bisaya and apply it to a large-scale

Conclusions: Conclusion: SRBD significantly impairs school performance, especially among older children, those in socioeconomically disadvantaged regions, and those with poor sleep hygiene. Regional and socioeconomic disparities further intensify academic vulnerability.

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Adenotonsillectomy/Adenoidectomy Can Reduce Central Apnea Events in Children with Sleep-Disordered Breathing: A Single-Center 7 Years Prospective Cohort Study Analysis

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Introduction: To analyze the effects of adenotonsillectomy (T&A) or adenoidectomy (AT) on central sleep apnea (CSA) in children with adenotonsillar hypertrophy or adenoidal hypertrophy.

Materials and methods: In this prospective cohort study, children with central apnea index (CAI) ≥ 1 event/h who underwent T&A or AT due to adenotonsillar hypertrophy or adenoidal hypertrophy from June 2017 to November 2024 were included.

Results: A total of 2047 children underwent T&A/AT and full-night preoperative PSG with CAI ≥ 1 . 258 children successfully underwent PSG follow-up and were evaluated for surgical efficacy. Compared with the baseline data, CAI was significantly reduced after surgery ($P < 0.001$). The postoperative CAI in 132 (51.16%) children was significantly improved ($\geq 50\%$). Children with significant CSA improvement had significant higher preoperative CAI, OAH1, AHI, HI, ODI, N1 stage percentage and arousal index ($P < 0.05$). Moreover, improvement of CSA was positively correlated with children's age and reduction of arousal index while severe obese children exhibited limited CAI reduction.

Conclusions: The incidence of CSA was noticeable in children with adenotonsillar hypertrophy or adenoidal hypertrophy. T&A/AT can effectively improve CSA among these children. Children with higher preoperative CAI and OAH1 were more likely to obtain greater improvement in CSA.

Adherence-Driven Outcomes of Orofacial Myofunctional Therapy Combined with CPAP in Severe Obstructive Sleep Apnea: A Retrospective Cohort Study

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Introduction: Obstructive sleep apnea (OSA), a disorder with significant morbidity, requires effective interventions. This study evaluates the clinical impact of Orofacial Myofunctional Therapy (OMT) combined with CPAP on daytime sleepiness and treatment adherence in severe OSA.

Materials and methods: A retrospective analysis of 197 adults (mean age: 54.4 years; 70% male) with severe OSA (mean AHI: 40.3) assessed ESS scores, medication use, sleep-related quality of life (QoL), and adherence. Statistical analyses included paired t-tests, ANOVA, and chi-square tests.

Results: OMT+CPAP yielded a clinically significant ESS reduction of 8.1 points (pre: 12.69 vs. post: 4.59; $p < 0.001$). High adherence (daily 15–20-minute sessions over ~133 days) correlated with optimal outcomes:

- 92.4% medication reduction ($p < 0.001$),
- 100% QoL improvement,
- 9.1% dropout rate.

Low adherence led to minimal benefits (7.5% medication reduction, 61.2% QoL improvement) and universal dropout (100%). Overall, 84.3% reported improved sleep quality. Statistical significance was confirmed for ESS improvements (paired t-test) and adherence-driven differences (ANOVA, $p < 0.001$). Limitations included data inconsistencies in QoL metrics and a 59.9% overall dropout rate.

Conclusions: OMT+CPAP significantly reduces daytime sleepiness in severe OSA, particularly with high adherence. The strong adherence-outcome relationship underscores the need for patient engagement strategies. While results are promising, data quality issues and attrition highlight the necessity for robust prospective studies.

These findings advocate for integrating OMT into OSA management protocols, emphasizing adherence monitoring through telemedicine. Future research should validate these results in controlled trials with long-term follow-up.

Keywords: Sleep-disordered breathing, myofunctional therapy, adherence, therapy duration, clinical outcomes.

Acknowledgments: NA

Airflow Dynamics Effects of Velum Collapse Patterns in Obstructive Sleep Apnea: A Computational Fluid Dynamics Study

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Introduction: Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. This study aimed to investigate the effects of three velum collapse patterns on airway airflow dynamics in patients with OSA using computational fluid dynamics (CFD) analysis.

Materials and methods: A 3D model of the upper airway—including the velum, oropharynx, tongue, and epiglottis region was developed based on a moderate obstructive sleep apnea patient (AHI: 19.3/hr, ODI: 19.0/hr, Minimum oxygen saturation: 86%). The velum region was simulated with three types of 75% airway narrowing: anteroposterior, lateral, and circumferential. Velocity and pressure distributions of the velum region airway structures were investigated.

Tetrahedral element was selected for meshing on the whole airway models. The mesh size and element number of the finite element models were 1.5 mm and 787,274, respectively. A 1.5-second breathing duration was selected in each phase of inspiration and expiration. The initial velocity and pressure at the airway walls were set to zero, and a no-slip condition was applied.

Results: The high velocity (6.51–13.02m/s) of the moderate model occurred at 0.8 seconds in inspiration and 2.2 seconds in expiration, respectively. The major concentrations were detected at the regions of inferior border of velum and anterior border of nasal concha. Comparing peak velocities in the three velum collapse models, the maximum peak velocity (56.11m/s) was detected in the model of the lateral collapse, and the minimum peak velocity (23.05m/s) was detected in the model of the circular collapse. The large velocity was obviously appeared at the inferior border of velum, but area of the peak velocity was significantly increased in each collapse model. For the moderate model, the maximum positive pressure was 65.44Pa at the anterior border of nasal concha during inspiration, and the maximum negative pressure (-59.02Pa) still located at the anterior and posterior border of nasal concha during expiration. The maximum negative pressures of the velum collapse models from large to small were lateral (-1669.70Pa), anteroposterior (-573.87Pa), and circular (-278.42Pa) collapse.

Moreover, the maximum negative was concentrated at the narrowest section of the velum region for three collapse models. The peak positive pressures were confirmed at the upper half airway during inspiration and the lower half airway during expiration. The collapse pattern was demonstrated to affect the fluid performance of airflow entering airway of the velum region.

Conclusions: The worst case of narrow structure in the velum to cause abnormal fluid behavior was significantly obtained in the model of the lateral collapse when the same cross-sectional area of the velum collapses was set. The type of the lateral collapse in the velum could obviously increase resistance of passing airflow by reflecting intensification in positive and negative pressures and high velocities.

AI-rway A Scalable Smartphone based Airway Screening tool for OSA and SDB for use @ Scale in pediatric and adult populations

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Introduction: Accurate assessment of sinonasal anatomy is foundational to diagnosing nasal obstruction, sleep-disordered breathing, and related dentofacial growth issues. However, the use of CBCT imaging for large-scale screening is limited by cost, radiation exposure, and accessibility—particularly in pediatric populations. To overcome these limitations, we have developed an AI-powered mobile platform that estimates sinonasal anatomy and airway function using only a smartphone's camera and microphone.

Materials and methods: The app combines two key biometric inputs: (1) 3D facial scans captured from standard smartphone cameras, and (2) voice recordings taken in both supine and upright positions. The facial scan module extracts craniofacial landmarks predictive of internal nasal dimensions, enabling a virtual reconstruction of airway structures. The voice module quantifies nasal airflow by analyzing speech resonance patterns to produce a real-time "Voice Nasal Flow Index" (VNFI), sensitive to posture-induced congestion and obstruction.

The integrated platform generates three core scores—upper airway susceptibility (linked to allergen entrapment), lower airway resistance (related to structural narrowing), and the VNFI—each contributing to an overall "Airway Health Score." This summary index provides a simple, actionable indicator for users and providers, with a built-in referral system to direct patients to care as needed.

Designed for scale, the Airway App is optimized for both pediatric and adult use, supporting screening programs in schools, dental practices, and sleep clinics. Its non-invasive, radiation-free design makes it particularly suited for early identification of airway dysfunctions that may influence craniofacial development, orthodontic planning, and sleep quality.

Results: Validation studies comparing the algorithms anatomic estimates to clinical CT scans across both adult and pediatric cohorts showed a mean accuracy of 95% for key nasal airway parameters, including nasal cavity width, palatal height, and septal deviation. The voice-based biomarkers further distinguished normal vs. obstructed airflow with high sensitivity, enabling functional profiling in real-world environments.

Conclusions: In conclusion, the smartphone based Airway screening App offers a breakthrough in accessible airway diagnostics—combining CT-equivalent anatomical estimation with posture-sensitive voice biomarkers. It enables precision screening at population scale, positioning it as a powerful front-line tool in dentofacial and respiratory health.

Alcohol Exacerbated Nocturnal Enuresis Associated with Obstructive Sleep Apnea: A Case Report

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Introduction: Adult-onset or persistent nocturnal enuresis is an uncommon and often distressing symptom that can be multifactorial in origin. While urologic, neurologic, or psychiatric causes are more commonly considered, sleep-disordered breathing has emerged as an underrecognized contributor. Obstructive sleep apnea (OSA), particularly when compounded by alcohol-induced airway relaxation and hypoxemia, can lead to enuresis due to increased intrathoracic pressure, sleep fragmentation, and autonomic dysfunction. This report describes a patient whose long-standing but intermittent enuresis became exacerbated by alcohol and resolved with CPAP treatment for severe OSA.

Materials and methods: A 27-year-old male presented with a long-standing history of intermittent nocturnal enuresis. He reported that episodes occurred 2–3 nights per week, exclusively after alcohol consumption. The patient had experienced bedwetting since early childhood but had long periods of dryness during adolescence and early adulthood. There was no history of daytime incontinence or urinary urgency. His past medical history was unremarkable. His mother recalled a difficult birth but no early-life diagnoses were established.

The patient had previously trialed imipramine (Tofranil) and oxcarbazepine (Trileptal) with no improvement. Notably, his mother reported loud snoring, witnessed apneas, and frequent arousals during sleep. A diagnostic polysomnography with continuous EEG monitoring was ordered.

Polysomnography Results:

Total sleep time: 376 minutes

AHI: 61 events/hour (severe OSA)

Obstructive apneas: 37, Hypopneas: 344

Minimum SpO₂: 76%, with SpO₂ <90%: 33 minutes

REM latency: 166 minutes

Sleep efficiency: 77%

No parasomnias, motor or cardiac anomalies were noted. Full EEG performed concurrently showed no paroxysmal activity, interictal discharges, or epileptiform abnormalities, ruling out an ictal cause for the enuresis.

CPAP titration was subsequently performed, and the optimal pressure was determined to be 6 cmH₂O, which effectively eliminated apneas and improved oxygenation. After initiating nightly CPAP, the patient experienced complete resolution of enuresis—even on nights when alcohol was consumed.

Results: This case illustrates how enuresis in adults, particularly when episodic and alcohol-triggered, may reflect underlying sleep-disordered breathing. Alcohol acts as a respiratory depressant, reducing pharyngeal tone and increasing the likelihood and severity of apneas. In this patient, despite a misleading history of primary enuresis, the clear temporal association with drinking, the oxygen desaturation severity, and the complete response to CPAP point strongly to OSA as the primary cause.

The presence of enuresis only during apneic nights suggests a mechanistic relationship, potentially involving increased intravesical pressure during arousals, impaired arousal responses, or nocturnal polyuria mediated by atrial natriuretic peptide due to negative intrathoracic pressure.

This case also highlights the limitations of relying solely on symptoms or AHI to determine the need for therapy. While his AHI was in fact severe (61), it is the oxygen desaturation burden and clinical presentation that made treatment urgent. The EEG ruled out a seizure-related mechanism, further narrowing the differential.

Conclusions: In adults presenting with nocturnal enuresis, particularly when associated with alcohol use and snoring, OSA should be considered. CPAP therapy can result in complete symptom resolution. A full sleep study with EEG may help exclude ictal phenomena and clarify the diagnosis. Clinicians should maintain a high index of suspicion and investigate appropriately.

Alterations in Psychomotor Vigilance and Influencing Factors in Mild Obstructive Sleep Apnea

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Introduction: To investigate the characteristics of cognitive impairment in patients with mild obstructive sleep apnea (OSA) and its influencing factors, providing evidence for early intervention and cognitive health improvement.

Materials and methods: We enrolled patients who underwent polysomnography (PSG) at our sleep center for snoring between November 2022 and August 2024, with an apnea-hypopnea index (AHI) <15. Patients with mild OSA (AHI 5-15 events/hour, n=167) were assigned to the case group, while those with simple snoring (AHI <5 events/hour, n=109) served as controls. Cognitive function was assessed using the Psychomotor Vigilance Test (PVT). PSG recorded sleep parameters, oxygen saturation, and AHI. Additional data including daytime sleepiness (Epworth Sleepiness Scale, ESS), sleep quality (Pittsburgh Sleep Quality Index, PSQI), and subjective snoring impact (Visual Analog Scale, VAS) were collected. Statistical analyses compared cognitive function between groups and examined correlations with various factors.

Results: Compared with controls, mild OSA patients showed significantly prolonged PVT reaction time (504.62 ± 122.96 ms vs 463.95 ± 62.54 ms, $P=0.005$) and increased lapse counts (25.22 ± 20.42 vs 19.29 ± 10.82 , $P=0.001$). The mild OSA group had higher PSQI total scores (7.63 ± 1.96 vs 7.13 ± 1.77 , $P=0.028$), with significant differences particularly in sleep quality ($p=0.04$) and sleep latency ($p=0.006$). Mild OSA patients reported greater subjective snoring severity ($p=0.005$), especially regarding work impact ($P=0.043$), though no significant differences were found in life or family impact. Multivariate analysis identified age and sleep quality as significant predictors of PVT impairment.

Conclusions: Mild OSA patients demonstrate impaired PVT performance compared to simple snorers, with age and sleep quality being key contributing factors. Early identification and intervention targeting these factors may help prevent and mitigate cognitive dysfunction in mild OSA patients.

A Machine Learning Model for Predicting Obstructive Sleep Apnea Using Anthropometric and Bioimpedance Data

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Introduction: Obstructive sleep apnea (OSA) is a prevalent and serious sleep disorder associated with various complications. Polysomnography (PSG) remains the gold standard for diagnosis but is limited by cost, accessibility, and time. This study investigates an alternative method for identifying patients with severe OSA (Apnea-Hypopnea Index [AHI] ≥ 30) using bioelectrical impedance analysis (BIA) and basic outpatient anthropometric data.

Materials and methods: Data were retrospectively collected from patients who underwent both BIA and full-night PSG at Taipei Medical University–Shuang Ho Hospital Sleep Center (N = 6574). Anthropometric features (e.g., age, sex, body mass index, neck and waist circumference) and BIA-derived metrics (e.g., total body water, extracellular/intracellular water ratio, muscle percentage, and basal metabolic rate) were included.

Various machine learning models—including logistic regression (LR), k-nearest neighbors (kNN), Naïve Bayes (NB), support vector machines (SVM), random forest (RF), and XGBoost—were trained to classify OSA severity. Model performance was evaluated via stratified cross-validation and testing set analysis.

Results: Patients with severe OSA (N=3686) had higher values in age and showed elevated BMI, neck and waist circumference, visceral fat level (all $p < 0.01$), compared to non-severe OSA patients (N=2888).

BIA metrics such as reduced total body water, lower muscle percentage, and increased extracellular/intracellular water ratio were significantly associated with severe OSA.

Regarding model performance, Naïve Bayes, Logistic Regression, and XGBoost achieved the best performance. Naïve Bayes showed the highest accuracy (69.20%) and F1-score (67.6%), while Logistic Regression provided the best AUC (77.35%).

Conclusions: This study demonstrates that body composition and anthropometric features obtained from BIA can serve as effective predictors for severe OSA (AHI ≥ 30). The proposed machine learning framework, particularly models such as Naïve Bayes, Logistic Regression, and XGBoost, achieved

clinically acceptable performance in identifying high-risk patients using only outpatient-accessible data. This approach offers a scalable, low-cost, and non-invasive alternative to PSG-based diagnosis.

A Multi-Task Deep Learning Model for Sleep Staging and Apnea Detection Using Single-Channel EEG

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Introduction: Obstructive sleep apnea (OSA) leads to sleep fragmentation and intermittent hypoxia due to recurrent episodes of apnea and hypopnea during sleep. These disruptions impair sleep architecture, resulting in excessive daytime sleepiness, morning headaches, and cognitive dysfunction, ultimately diminishing quality of life. Electroencephalogram (EEG) analysis provides critical insight into both macro- and microstructural changes in sleep, offering a window into the cerebral impact of disordered breathing.

Materials and methods: We utilized the Korea Image-based Sleep Study (KISS) dataset, comprising polysomnography (PSG) data from four hospitals in South Korea (N = 7,745). After excluding records with total sleep time (TST) less than 3 hours (N = 642) and those without EEG data (N = 9), 7,094 PSG recordings were analyzed. The C3-A2 EEG channel was resampled to 128 Hz and normalized using z-scores. EEG signals were decomposed into five canonical frequency bands—Delta (0.5–4 Hz), Theta (4–8 Hz), Alpha (8–12 Hz), Sigma (12–15 Hz), and Beta (15–35 Hz)—to facilitate frequency-specific feature learning. We developed a multi-task deep learning model based on a modified Temporal Convolutional Network (modernTCN) architecture, which concurrently performs binary classification of apnea/hypopnea events (≥ 10 seconds within 30-second windows) and sleep stage classification.

Results: On data from hospital A, the model achieved a macro F1-score of 73.0% and an accuracy of 75.2% for respiratory event detection, demonstrating state-of-the-art performance for single-channel EEG-based approaches. For sleep stage classification, it yielded a macro F1-score of 76.5% and an accuracy of 77.9%. The predicted apnea-hypopnea index (AHI) showed strong correlation with the reference AHI (Pearson $r = 0.86$, $p < 0.001$), with a mean absolute error (MAE) of 17.34. The model also generalized well to external datasets: MAE = 13.97 ($r = 0.83$, $p < 0.001$) on the Hospital B dataset, 16.24 ($r = 0.79$, $p < 0.001$) on Hospital C, and 17.18 ($r = 0.78$, $p < 0.001$) on Hospital D. An ablation study further showed that multi-task learning provided consistent benefits over single-task training, and that using sub-band EEG inputs yielded the most balanced and stable performance across both tasks.

Conclusions: Our findings suggest that a single-channel EEG, when analyzed with a multi-task deep learning model, enables reliable detection of respiratory events and accurate sleep staging. This approach provides a practical and scalable solution for automated sleep scoring, potentially alleviating clinician workload and broadening clinical applicability.

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Analysis of Brain Gray Matter Microstructure Alterations in Obstructive Sleep Apnea Patients Based on NODDI

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Introduction: This study aims to explore the changes in brain gray matter microstructure in OSA patients using NODDI technology, analyze the influencing factors and their correlation with cognitive impairment, and investigate the neural mechanisms of cognitive dysfunction in OSA.

Materials and methods: A total of 42 patients in the control group ($AHI < 5/h$), 87 in the mild-moderate OSA group ($5/h \leq AHI < 30/h$), and 77 in the severe OSA group ($AHI \geq 30/h$) were enrolled. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and computerized cognitive tests. Brain MRI data were collected, and tools such as the MRtrix3 toolbox, AMICO, FreeSurfer's recon-all and segmentHA_T1.sh, and fslmaths and fslstats commands were used to extract NDI and ODI values from the cortex, subcortical nuclei, and hippocampal subfields. Differences in NDI and ODI across the three groups were analyzed, and partial correlation analysis was used to examine the relationship between gray matter parameters and cognitive scores. A mediation model was established to analyze the mediating effect of gray matter structure on the relationship between nocturnal intermittent hypoxia, sleep fragmentation, and cognitive impairment.

Results: Patients in the severe OSA group were older, had a higher body mass index (BMI), more years of education, and higher Epworth Sleepiness Scale (ESS) scores. There were significant differences in polysomnography (PSG) parameters among the three groups. Cognitive assessment revealed significant group differences in MoCA total scores, MoCA subscales (visuospatial/executive function, delayed recall), and other cognitive tests (PRM immediate recognition accuracy, PRM immediate recognition reaction time, PRM delayed recognition reaction time, SRM immediate recognition accuracy, SWM double errors, SWM average completion time). Multiple brain regions showed group differences in NDI and ODI, with OSA generally patients exhibiting elevated NDI and ODI in areas such as the bilateral frontal, parietal, temporal, occipital, and insular lobes, globus pallidus, hippocampus, cerebellar cortex, cingulate isthmus, posterior anterior cingulate, left putamen, left thalamus, and right nucleus accumbens. Intergroup differences in NDI were found in the bilateral parasubiculum, molecular_layer_HP-head, HATA, left presubiculum-head, subiculum-head, CA1-head, right GC-ML-DG-head, fimbria hippocampi, and hippocampal tail. Intergroup differences in ODI were observed in the bilateral subiculum-body, left parasubiculum, and molecular_layer_HP-body. Partial correlation analysis (adjusted for age and years of education) showed that MoCA total scores were negatively correlated with NDI in the right supramarginal gyrus, MoCA delayed recall was negatively correlated with NDI in the right hippocampus, right supramarginal gyrus, left hippocampus, right hippocampal tail, left subiculum-head, and left molecular_layer_HP-head. MoCA visuospatial/executive function was negatively correlated with ODI in the right nucleus accumbens, and SRM immediate recognition accuracy was negatively correlated with NDI in the left cingulate isthmus. Mediation analysis revealed that microstructural parameters mediated the relationship between PSG parameters and cognitive test scores.

Conclusions: OSA is associated with altered brain gray matter microstructure, which is one of the neural mechanisms underlying OSA-related cognitive impairment.

Analysis of Polysomnography in Patients with Sleep Disorders Accompanied by Tinnitus

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Introduction: Tinnitus is a symptom characterized by the perception of sound generated within the body, specifically by the spontaneous depolarization of auditory nerve fibers, without any external auditory stimulus. Although the exact etiology of tinnitus remains unknown, there is a strong electrophysiological hypothesis suggesting that functional changes in the limbic system's amygdala and the cerebral cortex, as well as the subcortical structures, lead to tinnitus through autonomic nervous system dysfunction. Sleep disorders are also known to be influenced by and to influence the complex interactions among the ascending reticular system, central arousal system, cognitive system, and emotional regulating system in the central nervous system. Therefore, based on these theoretical foundations, the authors aimed to analyze the relationship between tinnitus and sleep by examining the association between tinnitus and polysomnography results using the Tinnitus Handicap Inventory (THI). This study intends to elucidate the correlation between tinnitus and sleep disorders.

Materials and methods: A retrospective analysis was conducted on patients who visited the clinic from August 2021 to May 2023 and underwent both polysomnography (PSG) and the Korean version of the Tinnitus Handicap Inventory (THI). The clinical characteristics, polysomnography results, and scores from psychiatric symptom questionnaires were compared between the group with tinnitus and the group without tinnitus. Additionally, the polysomnography results and questionnaire scores were compared based on the THI scores.

Results: There were statistically significant differences in the PLM (Periodic Limb Movement) index, sleep latency, and lowest SpO₂ between the group with tinnitus and the group without tinnitus (Table 1). The tinnitus group exhibited lower PLM index, higher sleep latency, and higher lowest SpO₂ compared to the group without tinnitus. When analyzing the polysomnography results based on THI scores, a significant negative correlation was found between THI and REM latency. There were no significant differences in the average scores of questionnaires (ESS, SSS, PSQI, PSS, PHA-15, BAI, CES-D) between the group with tinnitus and the group without tinnitus. Multiple regression analysis also did not reveal any significant correlations between THI scores and questionnaire scores.

Conclusions: Tinnitus, sleep disorders, and depression are associated with autonomic nervous system overactivity through the limbic system. Studies that examine the relationship between tinnitus, sleep disorders, depression, anxiety, and stress using polysomnography and questionnaires can provide a better understanding of sleep patterns, autonomic nervous system function, and electrophysiological models. Furthermore, such research can contribute to the development of specific treatment approaches aimed at improving the quality of life for these patients.

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Analysis of risk factors for white matter hyperintensities in OSA patients

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Introduction: White matter hyperintensity (WMH) poses significant public health challenges due to its high prevalence and close association with progressive cognitive decline, depression, stroke, and mortality. Obstructive sleep apnea (OSA) is recognized as an independent risk factor for cerebral small vessel disease (CSVD) and WMH pathogenesis. Systematically identifying risk factors for WMH in OSA patients is crucial for understanding disease progression, pinpointing high-risk individuals, and developing early interventions. This study therefore aims to investigate key risk factors for WMH onset/progression in OSA patients, analyze their association with cognitive dysfunction, and provide a scientific basis for risk stratification and targeted interventions.

Materials and methods: This study adopted a cross-sectional design. The subjects were recruited from the Department of Sleep Medicine at the People's Hospital of Guangxi Zhuang Autonomous Region between 2021 and 2023. Patients who met the inclusion criteria underwent polysomnography (PSG). Cognitive function was assessed using the Mini-Mental State Examination (MMSE), and brain magnetic resonance imaging (MRI) data were collected. The severity of WMH was evaluated using the Fazekas visual rating scale. Based on the presence or absence of WMH, OSA patients (with an apnea-hypopnea index [AHI] ≥ 5 events/h) were divided into two groups: OSA patients with WMH and OSA patients without WMH (control group). Differences in the aforementioned indicators between the two groups were analyzed and compared. Multivariate logistic regression analysis was conducted to identify factors associated with WMH in OSA patients. Additionally, a receiver operating characteristic (ROC) curve was constructed to evaluate the predictive performance of the model.

Results: A total of 552 OSA patients were included in the study, including 266 patients (50.0%) in the WMH group and 286 patients (50.0%) in the non-WMH group. The overall median age was 53.0 years (IQR: 46.0-58.0), and 74.3% were males. Compared with the non-WMH group, the WMH group had significantly higher BMI ($P<0.05$) and a higher proportion of insomnia ($P<0.05$). The serum levels of total protein, albumin and prealbumin were significantly lower ($P<0.05$). The patients had longer total sleep time, more hypopnea events, and shorter average duration of obstructive apnea ($P<0.05$). The orientation, memory and total score of MMSE scale were lower in the experimental group than in the control group ($P<0.05$). Multivariate logistic regression showed that: COMISA (OR=2.662, 95%CI: 1.411-5.021), BMI (OR=1.146, 95%CI: 1.056-1.243), numbers of total apnea in stage REM (OR=1.028, 95%CI: 1.003-1.055) were independent risk factors for WMH. The decrease of MMSE score (OR=0.923, 95%CI: 0.868-0.982) was positively correlated with the risk, and total serum protein (OR=0.93, 95%CI: 0.88-0.983) was an independent protective factor.

Conclusions: We propose multimodal interventions targeting COMISA, BMI and numbers of total apnea in stage REM risk factor modulation and total serum protein protection enhancement, combined with dynamic sleep monitoring, to enable early risk stratification and precise prevention of OSA-related WMH, offering new pathways to delay neurodegeneration.

An Analysis of Snoring Characteristics and Their Impact on Obstructive Sleep Apnea

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Introduction: Snoring, a common clinical features associated with OSA, has garnered notable interest due to its potential diagnostic and predictive value. About 59% of women and 78% of men snore, making it a widespread condition. The objective of the study is to investigate the impact of snoring characteristics such as snoring intensity and snoring time on the severity of obstructive sleep apnea (OSA), exploring the dynamics and potential associations between these variables and other polysomnographic parameters.

Materials and methods: Retrospective data analysis on patients who had polysomnography (PSG) between June 2019 and February 2020. The apnea-hypopnea index (AHI) was used as a measure of OSA severity. Snoring recordings were achieved by a non-contact directional microphone placed at the head of the bed, 20 cm from the vertex of the patients. Statistical analyses were performed using version 29 of the Statistical Package for the Social Sciences (SPSS) software. Pearson correlation coefficient, Mann-Whitney U test and Jonckheere Trend's test were used for analysis.

Results: A total of 248 patients underwent a PSG in the study period. Mean age was 41.9 ± 19.5 and mean body mass index was 25.4 ± 4.7 . The polysomnographic parameters progressively increase as the patient's age increases ($P < 0.001$). Number of snoring episode and Epworth Sleepiness Scale (ESS) were higher in male patients and reached statistical significance ($P < 0.05$). In terms of snoring intensity, there is not much variation between male and female patients. Older patients have a progressively longer snoring time, higher snoring rate and a greater number of snoring episodes ($P < 0.001$). The mean for snoring time, snoring rate, the number of snoring episodes, snoring intensity and ESS showed a gradual increase with increasing severity of AHI ($P < 0.001$). Polysomnographic parameters which included AHI, RDI, supine AHI, and REM and NREM index showed a positive correlation with snoring intensity ($r = 0.341$, $r = 0.354$, $r = 0.385$, $r = 0.322$, $r = 0.137$ respectively. $P < 0.001$). Number of snoring episodes also showed a positive correlation with AHI, RDI, supine AHI, and REM and NREM index and ($r = 0.391$, $r = 0.360$, $r = 0.309$, $r = 0.375$, $r = 0.355$, respectively. $P < 0.001$). There was no significant correlation between the PSG parameters and snoring time, snoring rate and longest snoring episode.

Conclusions: This study improves our understanding on the relationship between snoring characteristics and OSA severity. It highlights the intricate interactions between snoring and polysomnographic parameters as well as the substantial correlation between certain snoring qualities and the severity of OSA. Importantly, it suggests that snoring could indicate undiagnosed OSA, advocating for snoring to be used not only as a means of screening for OSA but as part of the diagnostic tool for OSA and as an adjunct to assess treatment outcome.

Acknowledgments: -

A National Survey on Current Knowledge, Diagnostic Approaches, and Management Practices of Sleep-Related Breathing Disorders Among General Medicine Practitioners and Respiratory medicine practitioners in India (Interim results)

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Introduction: In India, where the burden of non-communicable diseases is rapidly rising, the impact of OSA is particularly concerning. Despite its growing prevalence, OSA remains widely underdiagnosed. General physicians and respiratory physicians often serve as the first point of contact for patients,

especially in rural and resource-limited areas, placing them in a pivotal position to identify and manage sleep disorders. Among non-specialists, knowledge about OSA and other sleep related breathing disorders (SRBDs) tends to be poor, even though attitudes toward the disorder are generally positive; unfortunately, this does not translate into optimal clinical practice. In the context of India, where specialized sleep medicine services are limited and unevenly distributed, enabling general physicians to take a more active role in the assessment and management of sleep disorders could help address significant healthcare disparities.

Materials and methods:

Study Design: Cross-sectional online survey using semistructured Google Forms

Study Population: General physicians and respiratory physicians across India

Survey Tool: Semi structured questionnaire

Content validation was performed by two independent sleep researchers. Following this the questionnaire was piloted amongst 15 physicians, feedback and troubleshooting was performed. Subsequently the survey was shared via emails and social media with general medicine and respiratory medicine practitioners across India. The survey included trainees and practitioners.

Results: Of the 273 responses, the mean age of respondents was 35 years (35.0+/-9.7 years). 63% of the respondents were male. 52.7% of the respondents were from a respiratory medicine background. 86.4% worked in the urban sector. Approximately 60% of respondents worked in academic institutions, of which 54% were in teaching roles.

While more than 90% of the respondents screened patients with snoring and elevated BMI, only 35-60% of respondents screened patients with cardiovascular or cerebrovascular diseases. More than 70% had access to polysomnography, however only about 25% were confident in interpreting the reports. Approximately 70-74% reported that lack of awareness of the disease amongst the community followed by accessibility and cost issues hamper the diagnosis of sleep related breathing disorders. 60-70% of the respondents advise Positive airway pressure (PAP) therapy and lifestyle changes as first line in the management. Only 7% of physicians use dental devices in primary management.

While more than 80% physicians advise PAP therapy, only 24% each are confident or very confident to make this advise. 60-65% respondents followed up their patients at weekly and fortnightly intervals. However, approximately 50% respondents monitor adherence only with symptom resolution. In those who do advise PAP therapy, more than 40% are not confident with troubleshooting.

80-90% of the respondents were aware that untreated SRBDs can lead to vascular diseases and cognitive decline. However as noted earlier, only 35-60 % screened these patients at the outset.

Conclusions: While many Indian doctors are aware of SRBDs, there is lack of clear understanding regarding whom to screen, how to treat, how to manage and how to follow up. There is a felt need to conduct training sessions, develop guidelines and referral systems. Cost of evaluation and management may be circumvented with improved harnessing of telemedicine and Artificial Intelligence.

Acknowledgments: The respondents and my students

A new 3D-printed invisible mandibular advancement device for patients with obstructive sleep apnea: A cohort study

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Introduction: Mandibular advancement device (MAD) is recognized as an effective treatment option for patients with mild-to-moderate obstructive sleep apnea (OSA). However, traditional MADs are bulky and associated with low patient compliance. To address this, we developed a novel 3D-printed invisible MAD (iMAD). This study aims to evaluate the effects of iMAD on sleep quality and to investigate its working mechanism.

Materials and methods: This cohort study included 27 mild-to-moderate OSA patients. Clinical efficiency was assessed using polysomnography (PSG) recording and the working mechanism was evaluated using cone beam computed tomography (CBCT) at two time points: at baseline and after 3 months of iMAD use. PSG parameters included the respiratory event index (REI), apnea hypopnea index (AHI) and the lowest blood oxygen saturation. CBCT images are used to compare the change of upper airway, especially the minimum cross-sectional area (CSA).

Results: After 3 months of iMAD use, both REI and AHI were significantly decreased ($P < 0.001$), while the lowest blood oxygen saturation significantly increased ($P < 0.05$). Additionally, CBCT images showed that there was a significant increase in the CSA_{min} of the upper airway with iMAD ($p < 0.001$).

Conclusions: The new iMAD improves the upper airway dimension, demonstrating promising clinical efficacy for OSA treatment.

A Novel Intuitive Model of Endotyping in OSA; A Graphical Visualisation of Ventilation Curve and Arousal Surrounding Respiratory Events

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Introduction: Obstructive sleep apnea (OSA) diagnosis relies on the apnea-hypopnea index (AHI) but overlooks underlying mechanisms. Endotyping identifies key physiological traits – passive ventilation (V_{passive}), active ventilation (V_{active}), arousal threshold (AT), and loop gain (LG) to personalize treatment. This study proposes a visualization method using routine diagnostic clinical polysomnography to map all respiratory event endotypes, aiding targeted, patient-specific OSA therapy.

Materials and methods: Following the Terrils method, the ventilatory drive (VD) was estimated using the ventilation (V_{en}) signal fed into a chemoreflex feedback control model. By linear interpolation of the VD and V_{en} curves over 20 breath cycles surrounding the events, LG1 (LG at one-cycle-per-minute frequency) was calculated in the frequency domain.

To ensure an accurate representation of VD, enhanced event/arousal detection criteria were employed, including the automatic scoring of non-cortical arousals for apneas/hypopneas with ventilatory recovery ($\geq$ eupneic) but no scorable arousal.

Two methods were implemented to assess overall endotype parameters (V_{passive} , V_{active} , AT, LG). In Method 1, the endotype parameters are estimated for each respiratory event throughout the night, and mean values are plotted on a schematic representation based on the average V_{en} and VD curves surrounding respiratory events using linear interpolation. In Method 2, the average V_{en} and VD curves are calculated through a synchronization process that aligns with the end of the events. From these average curves, endotype parameters are then extracted and plotted.

LG1, due to its frequency nature, cannot be visualized in the previously reported phenotype plots. In our study, LG is represented using Wellman's approach to facilitate visualization, allowing all four endotypes to be visible in our graphical models.

Results: The study comprised 12 females and 8 males aged 22 to 72 with moderate obesity (median BMI 27.5 kg/m²) and a median AHI of 37.5/h.

According to Method 1, patients exhibited relatively high collapsibility (45.6 [36.8-56.0] %eupnea), good muscle compensation (22.7 [2.9-36.7] %eupnea), moderate AT (144.4 [131.0-153.5] %eupnea), and relatively low LG (0.58 [0.54-0.74]). The physiological traits derived from Method 2 differed for V_{passive} (higher V_{passive}) and LG (lower LG) compared to Method 1. The correlation coefficients between the two methods are $\rho = 0.2, 0.9, 0.6$, and 0.4 for V_{passive} , V_{active} , AT, and LG, respectively.

Method 1 is based on the average results obtained event by event throughout the night, while Method 2 averages the actual V_{en} and VD curves around the events. Method 2 is more realistic than Method 1 because it allows for observing fluctuations in the V_{en} and VD curves during respiratory events.

Moreover, Method 1 tends to show a higher LG1 than Method 2. This discrepancy can be attributed to the fact that Method 1 relies on instantaneous curves around respiratory events, while Method 2 aligns the curves at the end of these respiratory events.

Conclusions: For the first time, we have developed a novel model of endotyping that incorporates a graphical representation of ventilation and ventilatory drive related to the events, enhancing

visualization and estimation of all four endotypes and facilitating the transition of endotyping from the laboratory to clinical settings.

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A novel method to quantify the role of arousal threshold in obstructive sleep apnea pathogenesis

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Introduction: Obstructive sleep apnea (OSA) is a multifactorial disease. Determining whether a low arousal threshold plays a dominant role in OSA pathogenesis is critical for selecting appropriate treatment strategies. However, there is few accurate method to assess it. This study hypothesizes that in patients with a low arousal threshold, arousal predominantly terminates OSA events, manifested as arousal preceding the activation of upper airway muscle. Therefore, this study analyzed the temporal sequence between submental electromyography (EMG) and electroencephalogram (EEG) changes during OSA event termination and its association with arousal threshold.

Materials and methods: 516 men and women aged 18-85 years were studied. For each OSA event, transfer entropy was applied to determine the temporal sequence between EMG changes and EEG changes. The proportion of OSA events in which EMG preceded EEG was calculated relative to the total number of OSA events. This proportion was then analyzed for correlations with body mass index (BMI) and apnea-hypopnea index (AHI). In 98 cases with drug-induced sleep endoscopy, the mean lowest esophageal pressure was measured as the arousal threshold, and the correlation between the proportion and the arousal threshold was evaluated.

Results: The mean [Q1, Q3] proportion of OSA events with EMG changes preceding EEG changes was 0.78 [0.67, 0.89]. It was negatively correlated with BMI (Pearson correlation coefficient $r = -0.11$, $p < 0.05$), AHI ($r = -0.15$, $p < 0.05$), and positively correlated with arousal threshold ($r = 0.52$, $p < 0.05$).

Conclusions: This study confirmed the hypothesis and proposes a non-invasive quantitative arousal threshold method, which can evaluate the contribution of the arousal threshold in OSA pathogenesis and provide a new direction for revealing the mechanism of OSA.

An Updated Network Meta-Analysis of Pharmacological Therapies for Obstructive Sleep Apnea: Effects on AHI Reduction and Lowest Oxygen Saturation Improvement

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Introduction: Obstructive sleep apnea (OSA) affects nearly one billion adults worldwide and is linked to cardiovascular, metabolic, and neurocognitive complications. Continuous positive airway pressure (CPAP) remains the gold-standard therapy, but adherence is often poor and its effects are limited to airway collapsibility. Pharmacological treatments have emerged as promising alternatives, targeting multiple pathophysiological mechanisms. Recent trials not only assess the apnea-hypopnea index (AHI) but also SpO₂ nadir, a key marker of nocturnal hypoxemia and cardiovascular risk. This review synthesizes new evidence, offering an updated and clinically relevant evaluation.

Materials and methods: We systematically searched PubMed, Scopus, EBSCO, and Taylor & Francis for studies published between January 2019 and June 2025. Eligible articles were randomized controlled trials in humans, available in full text, written in Bahasa Indonesia and English, and reporting pharmacological interventions for obstructive sleep apnea (OSA) with outcomes including AHI and SpO₂ nadir. Non-pharmacological interventions and incomplete data were excluded. Data extraction followed the PICO framework and PRISMA flowchart. Meta-analyses were performed in R with 95% confidence intervals, and study quality was assessed using Cochrane RoB 2.0.

Results: Nineteen randomized controlled trials (RCTs) involving 446 patients (17 crossover, 2 parallel) were included in this network meta-analysis. The network geometry was predominantly placebo-controlled with minimal heterogeneity observed for both AHI ($\tau^2 = 27.057$, $I^2 = 0.8\%$) and nadir SpO₂ (τ^2

= 0.000, I^2 = 0.0%). For AHI, two regimens demonstrated significant superiority over placebo: atomoxetine 80 mg plus trazodone 50 mg (MD -18.60 events/h; 95% CI -32.99 to -4.21) and atomoxetine 80 mg plus trazodone 100 mg (MD -10.80; 95% CI -21.17 to -0.43). Both achieved the highest SUCRA probabilities (0.917 and 0.753). Other agents, including atomoxetine monotherapy and atomoxetine-oxybutynin, showed non-significant numerical improvements, while sedatives such as morphine, dexmedetomidine, and propofol tended toward AHI worsening with the lowest SUCRA values. For nadir SpO₂, significant improvements were observed with atomoxetine 80 mg plus trazodone 50 mg (MD +5.00; 95% CI 2.99–9.00), atomoxetine 80 mg plus trazodone 100 mg (MD +2.00; 95% CI 1.43–2.57), and atomoxetine 80 mg plus lemborexant 10 mg (MD +2.00; 95% CI 0.99–3.01). In contrast, morphine (-1.30; 95% CI -2.55 to -0.05) and propofol (-1.80; 95% CI -2.94 to -0.66) significantly reduced nadir SpO₂. SUCRA rankings aligned with these findings, positioning atomoxetine-trazodone combinations as most effective and sedatives as least favorable. Both outcomes suggested no likelihood of major publication bias.

Conclusions:

Pharmacological therapy may provide a promising alternative for patients with OSA who struggle to tolerate CPAP. Among the agents studied, atomoxetine-trazodone combinations offered the most consistent improvements in reducing AHI and improving SpO₂ nadir, reflecting a synergistic effect on airway tone and arousal threshold. While these findings highlight potential therapeutic value, the evidence is still limited underscoring the need for larger head-to-head trials to confirm efficacy, safety, and long-term benefits.

A Pilot Study of Personalized Obstructive Sleep Apnea Therapy in Patients with Acute Coronary Syndrome

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Introduction: Recent randomized controlled trials of obstructive sleep apnoea (OSA) treatment for the secondary prevention of cardiovascular disease have produced neutral results. Key limitations of such studies include poor compliance to CPAP treatment, raising the need to broaden treatment options in clinical trial. Hence, we aimed to assess the feasibility and impact of delivering personalised OSA therapy as a strategy to optimize acceptance, compliance, and treatment efficacy in patients with established cardiovascular disease.

Materials and methods: Eligible participants aged 18 to 75 years old with a recent diagnosis (<12 months from hospital discharge) of acute coronary syndrome (ACS) and OSA (oxygen desaturation index 3%>10 events/h) were recruited and randomized to receive either personalized OSA therapy (PT) or usual medical care (UC) with a follow-up at 6-months. The PT group were given a choice of CPAP and/or mandibular advancement device (MAD) therapy for the treatment of OSA in addition to standard medical care for ACS. Treatment optimization strategies including a 4-week run-in period, augmented support and patient engagement tools were implemented with the goal of optimizing therapy, as well as rapid triage between treatment modalities in participants unable to tolerate a therapy. The UC group received standard medical care for ACS and lifestyle modification advice only. The primary outcome of the study was compliance with personalized treatment for OSA reported as mean hours of usage per night and number of therapy days during the 6-month period. Secondary outcomes include treatment effectiveness and cardiovascular markers between baseline and 6-months follow-up.

Results: To date, 40 participants (15 participants in UC and 25 participants in PT) were recruited. Nine participants in PT failed OSA treatment during the run-in period and were withdrawn from the study. Twelve participants in the PT group selected CPAP for the treatment of OSA had a mean usage time of 6.23±0.89 hours per night and CPAP was used 93.0±5.5% of nights during the 6-month period. Four participants selected MAD for OSA treatment, mean usage was 6.7±0.9 hours per night with 96.9±0.01% of nights on therapy during the 6-month period. Nine participants using CPAP and all 4 participants using MAD met the criteria for optimal compliance of ≥5 hours/night usage for ≥70% of

nights during the 6-month period. Greater significant reduction in apnea-hypopnea index (AHI) was observed in the PT group ($AHI=34.5\pm14.0$ versus 7.3 ± 6.3 events/h, $P<0.0001$) compared to UC group ($AHI=30.8\pm16.8$ versus 25.03 ± 17.8 events/h, $P=0.04$) at 6-month follow-up. Central augmentation pressure (-1.5 ± 1.5 mmHg, $P=0.007$) and central pulse pressure (-1.83 ± 2.33 mmHg, $P=0.02$) during wakefulness was increased at 6-month follow up compared to baseline in the UC group. PT group had comparable central blood pressure between baseline and 6-month follow-up. Mean 24-hour blood pressure was comparable to baseline at 6-month follow-up in both UC and PT groups ($P>0.05$).

Conclusions: These preliminary data suggests that it is feasible to implement personalised and optimised OSA therapy in patients with ACS. The impact on cardiovascular risk markers remains to be determined.

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Apnea-hypopnea duration changes after Sulthiame - a new biomarker for treatment efficacy?

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Introduction: Sulthiame (STM), a carbonic anhydrase inhibitor, reduced obstructive sleep apnea (OSA) severity in a randomized controlled trial (Hedner et al. 2022). Residual apnea-hypopnea (AH) event duration was increased. We performed a post-hoc analysis to identify predictors of the AH event extension after STM and its relation to the clinical effect of STM in OSA.

Materials and methods: OSA patients (71% males, age 60 ± 10 years, body mass index [BMI] 28 ± 3 kg/m², waist circumference 99 ± 10 cm, apnea-hypopnea index [AHI] 56 ± 22 events/h, AH duration 24 ± 5 sec) were randomized to receive placebo ($n=22$), STM 200mg ($n=12$), or STM 400mg ($n=25$) treatment for 4 weeks, respectively). Baseline anthropometrics and polysomnography measures were analysed to predict the mean AH duration change after STM treatment. Nocturnal hypoxic metrics (ABOSA, Karhu et al. 2022) and OSA endotypic characteristics (PUP, Terrill et al. 2015) were determined. (EudraCT Number: 2017-004767-13)

Results: Placebo, STM 200mg, and 400mg improved overnight mean oxygen saturation by 0.4 ± 1.0 , 1.1 ± 1.0 , 1.1 ± 1.0 %, $P=0.108$, 0.003 , and <0.001 , respectively. The corresponding extension of AH duration after intervention was 1.2 ± 2.6 , 3.6 ± 3.3 , 4.8 ± 4.8 sec, $P=0.046$, 0.003 , and <0.001 , respectively. Desaturation severity was reduced by 0.7 ± 39.3 , 12.7 ± 75.4 , and 27.4 ± 37.9 %, $P=0.411$, 0.104 , and 0.005 , respectively. STM drug concentration was not associated with a change in AH duration. Baseline BMI, waist circumference, and $V_{\min}$ (a low value indicates increased upper airway collapsibility) predicted event extension after STM (Spearman correlation, $r=0.391$, 0.435 , and -0.344 , $P=0.017$, 0.007 , and 0.040 , respectively). In the STM group ($n=37$), AH duration changes were correlated with percentage of AHI reduction and improvement of desaturation severity, as well as increases in circulatory delay ($r=-0.381$, -0.573 , and 0.379 , $P=0.021$, <0.001 , and 0.023 , respectively). Compared to subjects with event extension >5 secs, patients with an AH event extension ≤ 5 secs showed stronger AHI reduction (median [IQR]: -30.0 [-45.3 – -21.1] vs. -54.9 [-64.8 – -26.7] %, $P=0.019$) after STM.

Conclusions: STM is associated with a reduction in sleep-disordered breathing, improved nocturnal oxygenation, and a mild prolongation of residual events. The extension of AH event duration with STM should be further explored as a potential biomarker of treatment efficacy in OSA.

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Apnea/hypopnea-related drops in pulse transit time predicts left ventricular dysfunction in obstructive sleep apnea

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Introduction: Pulse transit time (PTT) is widely used to assess vascular compliance and elasticity. This study aimed to determine whether the respiratory event-related PTT response would identify subclinical Left ventricular (LV) remodeling and dysfunction in obstructive sleep apnea (OSA).

Materials and methods: This retrospective study included OSA patients without pre-existing LV damage who underwent polysomnography between January 2014 and May 2017 at the Affiliated Huaian No.1 People's Hospital and The First Affiliated Hospital of Nanjing Medical University. LV measurements were assessed via echocardiography from December 2023 to May 2024. PTT measurements were validated using SOMNOscreen+ polysomnographic monitoring system. PTT drop magnitude refers to the difference between the initial value of the PTT decrease and the nadir triggered by apneas/hypopneas; PTT drop index is the number of drops per hour; PTT drop rate is the rate of decrease in PTT per second during the descending phase, and PTT area is the area above the waveform after respiratory events. Cox proportional hazard models estimated adjusted hazard ratios for incident LV damage, and receiver operating characteristic (ROC) curves assessed the predictive value.

Results: The sample included 517 individuals with a median (interquartile range) age of 53.0 (43.1-62.4) years and an AHI of 50.6 (32.6-65.5) events/hour. During a median follow-up of 8.3 (7.6-9.3) years, 112 patients (21.7%) had left ventricular hypertrophy (LVH), 249 (48.2%) had left ventricular diastolic dysfunction (LVDD), and none had LV systolic dysfunction. Individuals in the fourth quartile of PTT drop rate had a hazard ratio of 2.53 [95% (CI), 1.47-4.35] for LVH and 4.77 [95% CI, 3.15-7.21] for LVDD, respectively, compared to those in the first quartile. The results remained significant after adjusting for AHI and CVD. In contrast, no consistent associations were found with other PTT metrics, including drop magnitude, nadir, index, or area. In ROC curve analysis, PTT drop rate showed higher accuracy in predicting LVDD than compared to traditional polysomnography metrics.

Conclusions: Respiratory event-related PTT drop rate may be useful for predicting which patients with OSA are at increased risk for LV damage.

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Apnea severity is associated with low skin temperature variability

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Introduction: Higher cutaneous blood flow (vasodilation) causes skin temperature to rise. Conversely, vasoconstriction which indicates reduced cutaneous blood flow is associated with a decrease in skin temperature.

Obstructive and central sleep apnea are associated with sympathetic activation, inflammation, atherosclerosis, and hemodynamic changes which can affect cutaneous blood flow.

Reduced skin temperature variability has been associated with future disease risk in healthy individuals and severity deterioration in patients affected by conditions including sepsis and liver disease.

In this study, we tested the hypothesis that skin temperature variability is associated with apnea severity as measured by the apnea/hypopnea index (AHI). The apnea severity is: Mild for $5 \leq \text{AHI} < 15$; Moderate $15 \leq \text{AHI} \leq 30$; Severe $\text{AHI} \geq 30$.

Materials and methods: The data from 18 participants (9M/9F); mean age 44.5 [standard deviation 6.7] years-old, who recorded two nights in a sleep lab were used in this study. The data included polysomnography (PSG) and skin temperature signals. The latter were collected at a distal location (right foot; DST) and a proximal location (near the left collar bone; PST).

The PSG data were annotated by an expert sleep technician to obtain the sleep stages sequence

(hypnogram) and respiratory events from which the AHI was calculated.

For each sleep session, sleep bouts (i.e., sequences of uninterrupted sleep) were detected from the hypnogram. For each sleep bout that was at least ten-minute long, both proximal and distal skin temperature variability were estimated as the median absolute difference from the median of the skin temperature within the sleep bout: Variability = median($T - \text{median}(T)$), where T is the vector containing the bout's temperature values.

The distal and proximal skin temperature variability (DTV and PTV) for each sleep session were calculated as the mean DST and PST variability across all considered sleep bouts in the sleep session.

Results: Out of the 18 participants, six had AHI < 5. Eight, three and one participants were in the mild, moderate, and severe apnea category respectively.

The Pearson correlation between AHI and DTV was -0.44 ($p < 0.01$) which suggests that high AHI significantly correlates with low DTV. However, no significant associations were found between AHI and PTV (Pearson correlation 0.04 ; $p = 0.82$). This suggests that peripheral blood flow may be more notably affected by apnea compared to proximal blood flow.

The potential for DTV to screen for apnea at AHI levels of ≥ 5 , ≥ 15 , and ≥ 30 was evaluated by estimating receiving-operator curves (ROC) for each AHI level. The corresponding values for the area under the ROC were 0.75 , 0.76 , and 0.80 . For AHI = 5 and DTV threshold of 0.16 °C, the sensitivity and specificity were 0.85 and 0.76 respectively.

Conclusions: We found a significant, negative correlation between AHI and distal skin temperature variability. At a distal skin temperature variability threshold of 0.16 °C, sleep sessions with AHI exceeding five can be detected with sensitivity and specificity of 0.85 and 0.76 respectively. These results are promising since home apnea testing devices have mean 0.90 sensitivity and 0.50 specificity for AHI = 5.

Application of Novel Voice Biomarkers to Predict Site of Airway Collapse in Patients with Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a heterogeneous disorder characterized by repetitive upper airway obstruction during sleep, with significant variability in the anatomical site of collapse. These collapse sites, which are the tongue base, the lateral pharyngeal walls, the epiglottis, and the complete concentric collapse of the pharynx, have important clinical implications. Traditional diagnostic tools such as drug-induced sleep endoscopy provide detailed anatomical information but are invasive, costly, and not widely accessible. Even non-invasive methods like snoring acoustics and nasal pressure waveforms require overnight recordings. Given the anatomical and physiological relationship between speech production and upper airway structure, this study explores the use of voice biomarkers analyzed through machine learning to non-invasively predict site-specific airway collapse during wakefulness.

Materials and methods: Twenty adults, diagnosed with OSA and with no history of stroke (10 females, 10 males; BMI: 36.76 ± 6.60 kg/m²; AHI: 43.96 ± 30.84 events/hour) participated in the study. Participants articulated five sustained vowels while being recorded using a 48MP smartphone camera. Audio was extracted at 48 kHz. Additionally, portable level II polysomnography (Nox A1) captured sleep and respiratory signals. Collapse site labels (lateral wall, tongue base, epiglottis, or concentric pharyngeal) were derived from airflow shape analysis.

Spectral, temporal, and time-frequency voice features such as pitch, formants, and jitter were extracted using Librosa and Parselmouth. A machine learning pipeline was constructed using Recursive Feature Elimination (RFE) and Ridge Regression to identify the most predictive features. Bootstrapping was applied to enhance generalizability, and model performance was evaluated using Pearson's correlation (r), Mean Absolute Error (MAE), and Root Mean Squared Error (RMSE).

Results: The ML model demonstrated strong predictive ability for all collapse sites:

- Lateral Wall: $r = 0.93$, MAE = 0.14 , RMSE = 0.17

- Epiglottis: $r = 0.85$, MAE = 0.14, RMSE = 0.19
- Tongue Base: $r = 0.76$, MAE = 0.16, RMSE = 0.20
- Complete Concentric Collapse: $r = 0.80$, MAE = 0.17, RMSE = 0.20

The model's ability to estimate the probability of occurrences of each anatomical collapse site during wakefulness highlights the relevance of speech-derived features for capturing airway physiology. Bootstrapping reduced overfitting and confirmed model robustness despite the modest sample size.

Conclusions: This preliminary study presents a novel, non-invasive method for predicting anatomical sites of airway collapse in OSA using voice biomarkers and machine learning. The approach achieved high correlation with validated airflow-derived collapse classifications and offers a promising, scalable alternative to invasive diagnostics. Future work with larger cohorts is warranted to confirm generalizability and explore integration into personalized OSA management pathways.

A report of hypoglossal nerve stimulation cases in Japan

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Introduction: Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive collapse of the upper airway during sleep, resulting in recurrent arousals. Continuous positive airway pressure (CPAP) is the standard of care for treating OSA. Despite the uniform success of CPAP therapy, patient compliance remains a problem. A relatively novel treatment in OSA for patients unable to use CPAP therapy is upper airway stimulation (UAS) therapy using a fully implanted system. The Inspire UAS system (Inspire Medical Systems, Inc, Maple Grove, MN) is an FDA-approved system offered for the treatment of moderate to severe OSA.

Materials and methods: A few years later, the Japanese Ministry of Health, Labour and Welfare has approved for the UAS system since June 2021. This procedure has been shown to decrease the severity and symptoms of OSA in select patients.

Results: With the cooperation of providers and under the control of Japanese Society of Stomato-pharyngology, cadaver surgery training (CST) of UAS is implemented to ensure that safe and appropriate treatment. Treatment facilities are required to submit an entry sheet by the third case to ensure they are following the academic guidelines. A proctor physician is also dispatched to perform the initial implantation, providing an accurate technical evaluation and feedback. It is also important to note that physicians are required to attend a workshop by the Japanese Society of Sleep Research for the long-term management of treatment.

Conclusions: Afterwards, I will report on the treatment progress and the current situation in Japan.

A retrospective service evaluation into non-compliance in patients with mild obstructive sleep apnoea being treated on continuous positive airway pressure (CPAP)

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Introduction: Obstructive sleep apnoea is a sleep breathing disorder. It is characterised by episodes of repetitive airway closure which can either be a partial or full closure of the airway. With the repetitive collapse and opening of the airway, this leads onto oxygen desaturations, excessive daytime sleepiness, snoring and nocturia. The primary treatment according to NICE guidelines for OSA is CPAP therapy. This generates airflow to provide a stream of pressurized room air to splint open the upper airway during sleep via a mask. There are two main factors which measure adherence. AHI must be 4 h a night for at least 70%–80% of the night's. With the change in guidance for mild patients being offered CPAP, the audit will look at the following: Is low compliance seen in those who have a low Epworth sleepiness score and Body mass Index. Is there is a link between adherence data to pre-dict future adherence? If

noncompliance is high overall, can the service offer an alternative treatment pathway for Mild OSA patients?

Materials and methods: Data was collected retrospectively from a secure database used by the lung function and sleep department. Patients sleep studies were collected from September 2021 to October 2023. A sample size of 385 was estimated in order to generalise the results to a 95% confidence interval for the Welsh population with OSA. All patient identifiable information was removed. Not all patients were suitable due to the inclusion and exclusion criteria.

Results: Multiple linear regression was used. Initial consultation compliance data showed there was no significant relationship between the ODI and Average Hours ($p = 0.499$), mask fit ($p = 0.843$) and $\% > 4$ h ($p = 0.410$). There was no significant relationship between the ODI and Average hours ($p = 0.372$), mask fit ($p = 0.520$) and $\% > 4$ h ($p = 0.65$) data after 3 months of treatment.

Conclusions: There is no correlation between in compliance in mild patients from their initial consultation and at 6 months and there was no significant correlation between ESS and BMI against adherence data. However, this does give room to explore and develop the service with regards to making alternative pathways and referral in non-adhering patients.

Artificial Intelligence Diagnosis of Obstructive Sleep Apnea: Bayesian Meta-Analyses of 80 Studies with 248 Models

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Introduction: Among 1 billion patients worldwide with obstructive sleep apnea (OSA), 90% remain undiagnosed. Their main barrier is the overnight polysomnogram, which requires specialized equipment, skilled technicians and inpatient beds available only in tertiary sleep centers. In recent years, artificial intelligence (AI) has made significant strides, offering promising new avenues for OSA diagnosis.

Materials and methods: We systematically searched PubMed, Embase, Scopus, Web of Science and IEEE Xplore till 20th July 2024. Two blinded reviewers selected English-language articles of studies comparing the diagnostic performance of AI models using 8 inputs (facial recognition, overnight audio, awake speech, electrocardiography, electroencephalography, pulse oximetry, photoplethysmography or multimodal), versus conventional diagnosis [apnea-hypopnea index (AHI) from PSG or home sleep apnea test (HSAT)]. We excluded studies if they only detected apneic events without providing a patient-level diagnosis, or if they did not use a train-test split or k-fold cross-validation for model evaluation. We assessed the risk of bias via QUADAS-2, performed Bayesian bivariate meta-analysis and meta-regression, computed 95% credible intervals, visualized summary receiver operating characteristic curves with 95% prediction regions, assessed publication bias via Copas-like selection modeling, and graded evidence quality via GRADE, following a PROSPERO-registered protocol. Analyses were conducted using R and Stan.

Results: From 6,254 records, we included 80 studies (low-moderate bias) with 248 AI models trained/tested on 35,300/30,420 participants. Across 8 modalities, AI demonstrated good or excellent diagnostic performance compared to conventional diagnosis. The pooled sensitivity (Sn) and specificity

(Sp) of each modality, arranged from the highest to lowest Sn, were: pulse oximetry [Sn: 91.1% (89.4–92.7%), Sp: 86.1% (82.1–89.4%)]; overnight audio [Sn: 90.3% (86.9–93.1%), Sp: 86.7% (83.1–89.7%)]; multimodal inputs [Sn: 89.2% (81.5–94.3%), Sp: 87.1% (82.6–90.8%)]; facial recognition [Sn: 84.9% (77.1–90.7%), Sp: 71.2% (60.7–81.4%)]; awake speech [Sn: 82.9% (80.0–86.4%), Sp: 83.3% (80.7–86.1%)]; electroencephalography [Sn: 81.6% (73.4–88.8%), Sp: 78.2% (64.1–87.0%)]; electrocardiogram heart rate variability [Sn: 79.0% (74.9–82.7%), Sp: 75.0% (67.9–82.3%)]; photoplethysmography [Sn: 70.8% (63.3–77.2%), Sp: 91.7% (86.8–95.1%)]. Bayesian meta-regression demonstrated similar diagnostic performance across AHI cut-offs. Deep learning (convolutional neural networks) was the most accurate classification algorithm for facial recognition (91.1% sensitivity, 79.2% specificity), pulse oximetry (93.7% sensitivity, 89.4% specificity) and photoplethysmography (75.9% sensitivity, 93.5% specificity) models, and performed better than domain expert manual feature extraction for pulse oximetry and electroencephalography models. Overnight audio models were more sensitive when using higher sampling frequencies and non-contact microphones. Smartphone versus professional camera/microphone inputs showed similar performance. Among 30 multimodal AI models, all used pulse oximetry with electroencephalography, electrocardiography, airflow and/or thoracic signals. Performance did not correlate with the number of modalities. Publication bias was shown to be unlikely to alter conclusions. The evidence was of high quality.

Conclusions: AI models trained on overnight audio and pulse oximetry achieved excellent diagnostic accuracy—far superior to STOP-Bang and comparable to common HSATs in clinical practice. Smartphones are a reliable source of images and audio, and AI performance is mainly driven by a small number of essential inputs. Digital medicine should be further explored and externally validated for accessible and equitable OSA diagnosis.

Assessing the correlation between physician seniority and the risk of Obstructive Sleep Apnea (OSA): a cross-sectional study

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Introduction: Obstructive sleep apnea (OSA) is a prevalent sleep disorder that remains relatively underdiagnosed, leading to a substantial number of untreated cases with serious economic and health implications. While extensive research has identified various risk factors for OSA, such as age, obesity, and gender, there is a notable gap in the literature regarding the relationship between OSA and the medical profession, specifically concerning the impact of medical career stage and seniority. This study aims to address this gap by exploring the association between medical professional status and the risk of developing OSA.

Materials and methods: A cross-sectional study was conducted at individual medical center, involving medical students, interns, and residents. Participants were surveyed for demographic and clinical data, the Sleep Hygiene Index (SHI) to assess sleep hygiene, and STOP-BANG questionnaire (SBQ) and Epworth Sleepiness Scale (ESS) to assess the risk for OSA and daytime sleepiness, respectively. Data were statistically analyzed, including logistic regression to identify risk factors.

Results: A significant association was identified between career stage and sleep hygiene, with residents, particularly those post-Step A exam, demonstrating poorer sleep hygiene compared to medical students and interns ($P = 0.017$). While no direct or significant relationship between professional seniority and the risk for OSA was observed based on SBQ and ESS scores, multivariate analysis indicated that poor sleep hygiene was a significant independent risk factor for both daily fatigue and OSA ($P < 0.001$). Furthermore, male gender, Jewish ethnicity, and resident status were independently associated with higher ESS and SBQ scores.

Conclusions: This study established a direct relationship between medical seniority and poor sleep hygiene, emphasizing that, in this study, inadequate sleep hygiene is the most significant and consistent risk factor for daily fatigue and OSA. Additionally, male gender, Jewish ethnicity, and residency status emerged as significant risk factors for OSA development. To the best of our knowledge, this study is the first to explore this topic among physicians and medical students, offering novel insights into the interplay between medical career stages and sleep health. These findings highlight the importance of advancing our understanding of the factors contributing to OSA in healthcare professionals and underscore the potential benefits of early risk identification and targeted preventative interventions.

Assessment of a Vibrotactile Device for Positional Therapy in Healthy Volunteers: A Pilot Study

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Introduction: Sleep-disordered breathing encompasses a continuum of respiratory pathologies occurring during sleep, ranging from simple snoring, which may progress to more severe conditions such as obstructive sleep apnea (OSA). International studies indicate that the prevalence of obstructive sleep apnea (OSA) is increasing annually due to lifestyle changes, the growing prevalence of obesity, and population aging. A particularly common form is positional obstructive sleep apnea (pOSA), in which symptoms occur exclusively in the supine position. In 50–60% of patients, the severity of apnea and snoring is directly influenced by sleep position. Positional therapy (PT), which aims to prevent supine sleep, represents a promising alternative to continuous positive airway pressure (CPAP) therapy, particularly given the low adherence rates associated with the latter. The aim of this study is to evaluate the effectiveness of the new vibrotactile device “SoftSleep” (LLC SOFTSLEEP, Moscow, Russia) for positional therapy in healthy volunteers. The results may serve as a foundation for future clinical trials and the development of personalized treatment strategies for positional obstructive sleep apnea.

Materials and methods: A single-center clinical-experimental study was conducted with 20 adult volunteers to assess the effectiveness of the vibrotactile positional therapy device “SoftSleep” (LLC SOFTSLEEP, Moscow, Russia). The volunteer group included 14 males (70%). The mean age of the participants was 41.8 ± 11.2 years. Each participant underwent two nights of home-based monitoring using the system for automated polysomnography studies “Astrocard-SomnoSTUDIO” (LLC MEDITEK, Moscow, Russia): one night without the device and one with SoftSleep activated. Body position data were collected via “SomnoSTUDIO”, and subjective sleep quality was assessed using a modified Pittsburgh Sleep Quality Index. Key results included an assessment of total sleep time and time spent in a supine position.

Results: The “SoftSleep” vibrotactile device significantly reduced supine sleep time from 56.0% to 7.8% (-48.2 pp) without affecting total sleep duration ($7:42 \pm 1:19$ vs. $7:39 \pm 1:33$) and subjective sleep quality. In 90% of cases, participants rated sleep as “very good” or “fairly good” during device use. Supine avoidance was achieved via vibrotactile feedback without full awakenings, supporting the arousal-based mechanism of positional therapy. It is also significant that only three participants experienced brief vibration-related awakenings that subjectively did not exceed 3 minutes in duration and did not lead to withdrawal from the study. Variability in individual response suggests future studies should explore factors like sleep depth or baseline sleep position. Despite limitations—small sample, lack of polysomnography, and use of healthy volunteers—these results support “SoftSleep” as an effective, well-tolerated, non-invasive option for positional OSA. Further trials in clinical populations with objective sleep staging are warranted.

Conclusions: The results of the present study demonstrated high efficacy and good tolerability of the SoftSleep vibrotactile device designed for positional therapy of sleep breathing disorders and snoring prevention. The use of the device significantly reduced the duration of sleep in the supine position without adversely affecting the total time and quality of sleep.

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Assessment of Sympatho-Vagal Dysfunction in Patients with Obstructive Sleep Apnea and Its Association with Disease Severity

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Introduction: Obstructive Sleep Apnea (OSA) is a common but underdiagnosed sleep disorder associated with increased cardiovascular risk. Autonomic imbalance, characterized by increased

sympathetic tone and reduced parasympathetic activity, has been implicated in this pathophysiology. This study aimed to assess autonomic nervous system (ANS) dysfunction during wakefulness in patients with OSA and evaluate its correlation with disease severity.

Materials and methods: Study Design and Participants:

This cross-sectional observational study enrolled **55 adult patients** with polysomnography-confirmed obstructive sleep apnea (OSA; Apnea-Hypopnea Index [AHI] ≥ 5) and **110 age- and sex-matched healthy controls**. Exclusion criteria comprised diabetes, cardiac diseases, neurological disorders, or any condition affecting autonomic function.

A comprehensive autonomic evaluation included cardiac autonomic reflex tests and 5-minute heart rate variability (HRV) analysis. Time-domain and frequency-domain HRV parameters were log-transformed for statistical analysis. Sympatho-vagal imbalance was assessed using both raw and composite autonomic scores.

Results: Patients with OSA showed significantly reduced parasympathetic activity compared to controls. Key findings included lower RSA (0.25 ± 0.19 vs. 0.32 ± 0.13 , $p = 0.0007$), E:I ratio (1.19 ± 0.34 vs. 1.3 ± 0.18 , $p = 0.04$), and Valsalva ratio (2.03 ± 1.00 vs. 2.45 ± 1.20 , $p = 0.019$). Frequency domain analysis revealed reduced HF power ($p = 0.0002$) and elevated The LF/HF ratio (1.83 ± 1.92 vs. 0.85 ± 0.61 , $p = 0.0002$) indicates sympathetic dominance. Over half of the OSA patients (52.7%) had abnormal composite autonomic scores compared to 22.7% of controls ($p = 0.0002$).

Disease severity correlated significantly with autonomic markers. AHI was negatively associated with log HF_norm ($r = -0.305$, $p = 0.0234$) and positively with log LF/HF ratio ($r = 0.318$, $p = 0.0181$). Arousal and desaturation indices were also strongly associated with increased sympathetic and decreased parasympathetic activity.

Conclusions: Patients with OSA exhibit marked sympatho-vagal imbalance even during wakefulness, primarily driven by parasympathetic withdrawal and relative sympathetic overactivity. The extent of dysfunction correlates with the severity of OSA, arousals, and nocturnal desaturation. These findings underscore the utility of autonomic assessment in OSA and highlight the need for early diagnosis and intervention to mitigate cardiovascular risk.

Association between baseline characteristics and subsequent CPAP adherence in OSA patients

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Introduction: CPAP is regarded as efficient treatment for reducing incidence of future cardiovascular events in OSA patients so long as good adherence is achieved. The purpose of this study is to explore factors associated with CPAP adherence.

Materials and methods: This is a single-center retrospective observational study. Patients with OSA who was diagnosed by PSG and started CPAP in Kansai Electric Power Hospital between October 2013 and April 2022 were included. The outcomes were 1) graduation from CPAP defined as improving in symptoms by weight loss and termination of CPAP decided by attending physicians, 2) discontinuation of CPAP by patients' judgement during the period from October 2013 to April 2024, 3) good CPAP adherence defined as CPAP usage of ≥ 4 hours for $\geq 70\%$ period for more than one month before the last visit. Patients' follow up was conducted once every one to three months according to Japanese National Health Insurance System. Cox proportional hazard analysis to determine factors associated to each outcome was performed using patients' characteristics, diagnostic PSG data, and CPAP usage log at early phase (2-3 months) from starting CPAP.

Results: There were 247 patients who were administered CPAP (age 57.9 ± 12.4 y.o, male 85.8 %, BMI: 27.4 ± 5.0 kg/m², AHI 44.1 ± 21.3). During the follow-up periods (median: 1532, interquartile range: 782-2352 days), 9 patients (3.6 %) graduated from CPAP, 60 patients (24.3 %) discontinued, and 99 patients (40.1 %) achieved good CPAP adherence. Poor improvement in symptoms at early phase from starting CPAP was associated with both graduation from CPAP and discontinuation of CPAP, and higher body weight and higher CPAP adherence at early phase from starting CPAP were associated with good CPAP adherence. None of age, Epworth Sleepiness Scale, AHI or % time in SpO₂ $< 90\%$ was associated with all outcomes.

Conclusions: Baseline information and adherence at the early phase from starting CPAP may be useful to predict subsequent CPAP adherence.

Association Between Co-Morbid Insomnia and Sleep Apnea (COMISA) and Low Back Pain: Findings from the EPISONO Study

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Introduction: The concomitant occurrence of obstructive sleep apnea (OSA) and insomnia is referred to as COMISA. Its prevalence is estimated at 17.64% when considering all cases of OSA and insomnia, and 2.47% when limited to moderate-to-severe cases. COMISA may have a significant public health impact due to its association with various comorbidities. However, its relationship with chronic pain, particularly low back pain (LBP), the most disabling musculoskeletal condition worldwide—remains understudied. The objective of this study was to investigate the association between COMISA and LBP in a population-based sample.

Materials and methods: This cross-sectional study used data from the 4th edition of the EPISONO study, conducted between 2018 and 2019. OSA was diagnosed using full-night laboratory polysomnography, and insomnia symptoms were assessed with the Insomnia Severity Index (ISI). COMISA was defined by the concurrent presence of mild to severe insomnia symptoms and a confirmed diagnosis of OSA. Data were analyzed using binary logistic regression models.

Results: The sample consisted of 548 participants with a mean age of 48.64 years. Individuals with moderate-to-severe OSA and insomnia had a significantly higher likelihood of experiencing LBP (OR = 2.28, 95% CI: [1.047; 4.993], $p = 0.038$). The results showed that COMISA was associated with a twofold increase in the odds of reporting LBP, compared to those with insomnia alone.

Conclusions: COMISA is significantly associated with an increased risk of LBP. These findings highlight the need for clinicians to consider COMISA in the evaluation and management of patients with LBP.

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Association between duration of moderate to severe obstructive sleep apnea and cardio-metabolic comorbidities: A cross-sectional observational study

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Introduction: Obstructive Sleep Apnea (OSA) is associated with an increased risk of cardio-metabolic disorders, while the link between OSA and various comorbidities is well-documented, there is a notable gap in research specifically examining the influence of OSA duration on these health risks. The primary objective was to evaluate the association between OSA duration and cardio-metabolic comorbidities, including hypertension, diabetes mellitus, metabolic syndrome, dyslipidemia, coronary artery disease (CAD), arrhythmia, and heart failure.

Materials and methods: This cross-sectional study, approved by the IEC at AIIMS Rishikesh, India, included 279 newly diagnosed moderate to severe OSA patients through in-lab polysomnography, having ≥ 35 years of age and ≥ 20 BMI. OSA duration was estimated using an algorithm given by Olaithe M et al.¹, based on BMI (WHO classification), AHI, and sex. The prevalence of cardio-metabolic comorbidities was analysed across tertiles of estimated OSA duration. Statistical methods included chi-square tests, logistic regression, and Bonferroni correction (α -adjusted p -value < 0.017).

Results: The overall median age of the study population was 52 years (interquartile range [IQR]: 45–58 years). Of the 279 participants, 137 (49.1%) were male and 142 (50.9%) were female. The median AHI was 42.8 (IQR: 24.72–64.9), with 29% and 71% of participants having moderate and severe OSA,

respectively. The median duration of OSA was 18.70 years (IQR: 9.41–27.88 years), ranging from 0.19 to 63.29 years. The median OSA duration in males (25.82 years, IQR: 12.99–36.32) was significantly higher compared to females (14.92 years, with IQR: 8.23–21.51; $U = 5245$, $p = 0.000$).

For comparative analysis, participants were stratified into tertiles based on OSA duration: the lower tertile included those with <12.86 years ($n=93$), the middle tertile with 12.86–25.08 years ($n=93$), and the upper tertile with >25.08 years ($n=93$).

Systemic hypertension (79.5%, $n=222$) and dyslipidemia (78.5%, $n=219$) were the most common comorbidities, followed by metabolic syndrome (74.5%, $n=208$) and diabetes mellitus (50.8%, $n=142$), while CAD, arrhythmia, and heart failure were less prevalent (6.8%, 5%, and 4.3%, respectively). A significant trend was observed in the prevalence of hypertension across OSA duration tertiles as 68.8%, 83.9% and 86% in the lower, middle, and upper tertiles, respectively ($\chi^2 = 610.054$, $p = 0.007$). However, the prevalence of other comorbidities did not differ significantly across the tertiles.

Conclusions: This study highlights a substantial burden of cardiovascular and metabolic comorbidities among individuals with moderate to severe OSA. Notably, a longer duration of OSA was significantly associated with increased prevalence of systemic hypertension, suggesting a potential dose-response relationship. These findings underscore the importance of early identification and management of OSA to mitigate potential long-term cardiovascular risks. The lack of statistical significance in other cardio-metabolic comorbidities suggests that OSA duration alone may not be a key determinant of cardio-metabolic risk.

Reference:

1. Olaithe M, Hagen EW, Barnet JH, Eastwood PR, Bucks RS. OSA-Onset: An algorithm for predicting the age of OSA onset. *Sleep Med.* 2023;108:100-104. doi:10.1016/j.sleep.2023.05.018

Association between PLMS and LM-related parameters according to AAMS and WASM criteria in patients with OSA

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Introduction: There were no studies compared limb movements (LMs) related parameters using manual re-scoring by the American Academy of Sleep Medicine rules (mAASM) and World Association of Sleep Medicine criteria (mWASM) for respiratory event-related limb movements (RRLM), periodic limb movements during sleep (PLMS), and limb movements, which were compared to auto-scoring by the AASM (aAASM). We aimed to assess how these different scoring methods (aAASM, mAASM, mWASM) influence the relationship between PLMS and LMs related parameters, particularly in relation to the resolution of respiratory events during continuous positive airway pressure (CPAP) titration.

Materials and methods: We retrospectively re-scored diagnostic and CPAP titration polysomnography (PSG) recordings from 16 patients with obstructive sleep apnea (OSA). Association between PLMS and other LM related parameters were examined using the manual re-scoring with AASM and WASM criteria and automated scoring method by the AASM.

Results: As a result of analyzing the diagnostic PSG results of patients with OSA, as the AHI and respiratory disturbance index (RDI) by aAASM increased, the PLMS tended to decrease significantly. In addition, in aAASM and mWASM, the PLMS significantly increased as the LMs, LM with no association, and LM in NREM2 increased. In the case of mAASM, AHI, RDI, LMs, and RRLM did not have a significant relationship with PLMS in the diagnostic PSG, but in the PSG where respiratory events were resolved by CPAP titration, the PLMS showed a significant relationship as the LMs and RRLM increased.

Conclusions: In the case of mAASM, PLMS may tend to appear worse due to the high correlation between other parameters and PLMS after titration. At this time, it is important to better differentiate PLMS. The criteria for periodic limb movement disorder might be adjusted according to the choice of scoring manual

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Association Between Positive Airway Pressure Titration Sleep Data and Adherence to Therapy in Obstructive Sleep Apnea

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Introduction: This study aimed to investigate the impact of objective sleep parameters, specifically sleep efficiency (SE), wake after sleep onset (WASO), and sleep latency (SL), derived from the positive airway pressure (PAP) titration, on short-term adherence to PAP therapy in patients with obstructive sleep apnea (OSA).

Materials and methods: A total of 227 subjects diagnosed with OSA underwent overnight PAP titration and were subsequently categorized into adherence or non-adherence groups. Baseline demographics, clinical data, diagnostic polysomnography, and PAP titration data were collected. Paired sample t-tests compared sleep parameters between polysomnography and PAP titration within each group. Binomial logistic regression analyzed the predictive ability of changes in SE, WASO, and SL on PAP adherence, determining optimal thresholds. Chi-square tests examined the association between categorized improvements in SE and WASO and PAP adherence.

Results: The study population was distributed such that 176 (77.5%) participants were in the adherence group and 51 (22.5%) were in the non-adherence group. SE during PAP titration ($83.3 \pm 12.6\%$) was significantly higher than during baseline polysomnography ($80.9 \pm 12.4\%$, $p = .020$), while WASO was significantly lower (63.9 ± 58.9 min vs. 77.7 ± 67.2 min, $p = .016$). SL showed no significant change in either group. Logistic regression revealed that higher SE (OR = 1.025, $p = .039$) and shorter WASO (OR = 0.994, $p = .027$) were significant predictors of adherence, though their predictive ability was limited (AUC = 0.60 for SE; 0.62 for WASO). Thresholds for improved adherence were $\Delta SE \geq 2.39\%$ and $\Delta WASO < -1.5$ min. Subjects with improved SE ($\chi^2=5.296$, $p=.021$) and WASO ($\chi^2=6.877$, $p=.009$) were significantly more likely to adhere to PAP therapy.

Conclusions: This study reveals that objective improvements in sleep quality, specifically increased SE and reduced WASO, during initial PAP titration are significantly linked to short-term PAP adherence in OSA patients.

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Association between restorative sleep and sleep fragmentation in obstructive sleep apnea

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Introduction: It has been suggested that the feeling unrefreshed upon awaking, referred to as non-restorative sleep (NRS), is associated with various worse health outcomes, including mortality. In obstructive sleep apnea (OSA), although the severity does not always reflect subjective symptoms such as NRS and daytime sleepiness, it robustly reflects mortality risks. It has also been suggested that sleep fragmentation, reduced sleep efficiency, decreased N3 sleep, and increased REM sleep are associated with mortality risks. However, the relationship between sleep abnormalities and NRS remains poorly understood in OSA. In addition, OSA patients often present with periodic limb movements (PLM), which also fragments sleep, but the influence of PLM on NRS has not been independently investigated. This study examined (1) the relationship between NRS and sleep abnormalities in OSA patients without PLM, and (2) the influence of comorbid PLM on this relationship in OSA patients.

Materials and methods: Patients diagnosed with OSA who underwent overnight PSG and completed an assessment of restorative sleep at our sleep disorders center between April 2020 and April 2025 were included. The restorative sleep was assessed at the morning after PSG using a 5-point Likert

scale. Total sleep time (TST), WASO (% total sleep period [SPT]), REM sleep (%TST), N2 sleep (%TST), N3 sleep (%TST), and AHI were also assessed by PSG. Parameters such as time in bed, SPT, sleep efficiency, and N1 sleep (%TST) were excluded to avoid multicollinearity. Patients were classified into four groups: severe OSA-only (SG; AHI ≥ 30 , PLM index <15) and mild to moderate OSA-only (LG; AHI < 30 , PLM index <15), severe OSA with significant PLM (SGWP; AHI ≥ 30 , PLM index ≥ 15) and mild to moderate OSA with significant PLM (LGWP; AHI < 30 , PLM index ≥ 15). Multiple regression analyses were conducted, with restorative sleep as the dependent variable and PSG parameters as independent variables, adjusting for age, BMI, and other potential confounders.

Results: Four hundred and sixty-one patients (SG: 78, LG: 223, SGWP: 56, LGWP: 104) were included in the study. Mean restorative sleep ratings were 3.05 for SG, 3.00 for LG, 3.16 for SGWP, and 2.89 for LGWP. In the OSA-only groups (SG and LG), higher WASO was significantly associated with poorer restorative sleep ($\beta = -0.19$, 95% CI: -0.38, -0.01), the relationship remained significant in the LG group ($\beta = -0.24$, 95% CI: -0.45, -0.04) after adjusting for age, AHI, and TST. However, the relationship did not remain significant in the SG group ($\beta = 0.01$). In contrast to the OSA-only group, longer TST was associated with better restorative sleep in the LGWP group, but the significant relationship disappeared in the SGWP group. The OSA with significant PLM groups had significantly shorter TST and higher WASO compared to the OSA-only groups.

Conclusions: Restorative sleep is strongly associated with sleep fragmentation, suggesting potential utility as an indicator of health risks in OSA. However, this relationship may diminish in severe OSA. Increased restorative sleep could indicate a breakdown in homeostasis, even as TST decreases with worsening sleep fragmentation.

Association between Sarcopenia-Related Genetic Variants and Sleep-Breathing Index in Patients with Obstructive Sleep Apnea: A Cross-Sectional Study

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Introduction: Obstructive sleep apnea (OSA) and sarcopenia share common pathophysiological features, yet their genetic relationship remains unclear. This cross-sectional study aimed to investigate whether sarcopenia-related single nucleotide polymorphisms (SNPs) are associated with OSA severity and its related traits.

Materials and methods: A total of 4,925 individuals with suspected OSA in the Shanghai Sleep Health Study were enrolled. All participants underwent overnight polysomnography, biochemical testing, physical measurements, and genome-wide genotyping. Ten sarcopenia-associated SNPs that passed quality control were selected from published genome-wide association studies. Linear regression and logistic regression were utilized to assess associations between each SNP and sleep and respiratory related indicators. Functional annotations, protein interactions, and pathway enrichment analyses were conducted using Ensembl, STRING, Metascape, and DAVID databases.

Results: Rs2899611 (located in *ALDH1A2*) was significantly associated with higher AHI ($\beta = 1.480$, $p = 0.006$) and ODI ($\beta = 1.303$, $p = 0.025$) in the overall cohort, and conferred increased odds of severe OSA (OR = 1.264, $p = 0.032$) among OSA subjects. Functional enrichment analyses indicated rs2899611 may influence retinol metabolism and enzyme activities involved in cellular respiration and oxidative metabolism. Rs10952289, located adjacent to *AOC1*, was correlated positively with stage 1 sleep (S1) duration and proportion (S1 duration: $\beta = 4.036$, $p = 0.033$; S1/SPT: $\beta = 0.858$, $p = 0.040$; S1/TST: $\beta = 1.098$, $p = 0.020$) and inversely with stage 3 sleep (S3) metrics (S3 duration: $\beta = -3.120$, $p = 0.030$; S3/SPT: $\beta = -0.660$, $p = 0.039$; S3/TST: $\beta = -0.726$, $p = 0.037$). *AOC1* encodes a primary amine oxidase involved in histamine metabolism, suggesting a potential mechanistic link to sleep architecture.

Conclusions: Genetic variants associated with sarcopenia, rs2899611 and rs10952289, were significantly associated with AHI, ODI, and sleep architecture in OSA patients. The SNPs may alter sleep and respiratory traits by modulating the key biological pathways. Integrating sarcopenia-related genetic screening into OSA management may enhance prevention, early detection, and personalize therapy.

Association Between Tonsillectomy and Risk of Type 1 Diabetes Mellitus: A Multi-center Cohort Study

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Introduction: The role of tonsillectomy in modulating systemic immune responses has been debated, but its association with autoimmune disorders like type 1 diabetes mellitus (T1DM) remains unclear. The study aimed to evaluate the risk of T1DM in patients undergoing tonsillectomy compared to non-surgical controls.

Materials and methods: Using the TriNetX collaborative network, we conducted a retrospective cohort study of patients diagnosed with tonsil/adenoid disorders (ICD-10: J03, J35, J36). Surgical (tonsillectomy/adenoidectomy) and non-surgical cohorts were propensity score-matched (1:1) for age, sex, race, BMI, comorbidities, and socioeconomic status. Outcomes were incidental type 1 diabetes, defined by ICD-10 codes. Cox proportional hazards models and survival analysis were analyzed. Subgroup and sensitivity tests were also performed.

Results: Among 2,240,430 eligible subjects, 252,087 underwent surgery and 1,826,933 did not. After matching, each cohort included 242,838 patients. The surgical group showed a higher cumulative incidence of T1DM (1.71% vs. 1.12%; HR = 1.35, 95% CI: 1.21–1.51). Subgroup analysis revealed elevated risks in individuals aged <18 years (HR = 1.32, 95% CI: 1.17–1.49), females (HR = 1.41, 95% CI: 1.17–1.69), ethnic Black or African American (HR = 1.47, 95% CI: 1.11–1.95), and those with obesity (HR = 1.89, 95% CI: 1.19–3.00). Sensitivity analyses confirmed robustness, and negative outcome controls showed no association.

Conclusions: Tonsillectomy is associated with an increased risk of T1DM, particularly in younger populations, female, ethnic Black or African American and individuals with obesity. Further studies are needed to explore underlying immunological mechanisms.

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Association of Obstructive Sleep Apnea with Cancer Risk & Mortality

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Introduction: Obstructive sleep apnea (OSA), characterized by intermittent hypoxia and sleep fragmentation, has been biologically implicated as a potential carcinogen. While animal studies support this link, epidemiological findings in humans remain inconsistent. To clarify these associations, we conducted a comprehensive systematic review and meta-analysis assessing the relationship between OSA and cancer incidence and mortality, incorporating a wide range of cancer types and OSA severity metrics.

Materials and methods: We systematically searched PubMed, Embase, Scopus, and the Cochrane Library from inception through June 2021 (updated to November 2023 for urological cancers). We included observational and randomized studies reporting on the association between OSA—defined by diagnostic codes or sleep-study-derived indices—and cancer outcomes in adults. Two independent reviewers screened studies, extracted data, and assessed bias using the Newcastle-Ottawa Scale. We rated the quality of evidence using the GRADE framework and pooled maximally adjusted hazard ratios (HRs) using inverse variance-weighted random-effects models.

Results: Across 20 eligible studies involving over 9 million participants, OSA was associated with increased incidence of several cancer types. Using sleep-derived metrics (time spent with SpO₂ <90%), moderate (T90 >1.2%) and severe nocturnal hypoxemia (T90 >12%) were linked to 28% (HR=1.28, 95%CI: 1.07–1.54) and 43% (HR=1.43, 95%CI: 1.16–1.76) higher all-cancer incidence, respectively. Severe nocturnal hypoxemia also tripled all-cancer mortality (HR=2.66, 95%CI: 1.21–5.85), independent of confounders including obesity.

Cancer-specific analyses revealed the following associations:

- **Breast Cancer:** In six studies (n=5.2 million), OSA was associated with a 36% increased risk (HR=1.36, 95%CI: 1.03–1.80). Subgroup analyses with ≥ 5 years follow-up yielded HR=1.57 (95%CI: 1.14–2.18).
- **Gastrointestinal (GI) Cancers:** Among seven studies (n=5.1 million), OSA was associated with a 70% increased risk of colorectal cancer (HR=1.70, 95%CI: 1.48–1.96), while associations with pancreatic and liver cancers were not statistically significant.
- **Lung Cancer:** Four studies (n=4.8 million) showed OSA increased lung cancer incidence by 25% (HR=1.25, 95%CI: 1.02–1.53). With ≥ 5 years follow-up, the risk rose to 32% (HR=1.32, 95%CI: 1.27–1.37).
- **Melanoma:** Six studies (n=5.3 million) showed a 71% higher incidence (HR=1.71, 95%CI: 1.08–2.69), though heterogeneity was high.
- **Thyroid Cancer:** In three studies (n=1.6 million), OSA tripled thyroid cancer risk (HR=3.27, 95%CI: 2.80–3.82), with up to 22.5% of global cases potentially attributable to OSA.
- **Urological Cancers:** From 12 studies (n=9.3 million), OSA was associated with increased kidney (HR=1.75, 95%CI: 1.21–2.53) and bladder cancer (HR=1.76, 95%CI: 1.05–2.96) incidence, but not prostate cancer (HR=1.29, 95%CI: 0.82–2.04).

Conclusions: Across diverse cancer types, OSA—particularly when characterized by nocturnal hypoxemia—is associated with elevated cancer incidence and, in some cases, mortality. These findings support the carcinogenic potential of OSA and underscore the need for prospective studies to examine cancer-specific mechanisms, dose-response relationships, and the impact of OSA treatment on cancer outcomes.

ASSOCIATION OF UPPER AIRWAY MORPHOLOGICAL PHENOTYPES WITH OBSTRUCTIVE SLEEP APNEA IN MIDDLE-AGED KOREAN ADULTS

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Introduction: Obstructive sleep apnea (OSA) is a multifactorial disorder characterized by the recurrent collapse of the upper airway during sleep. It is commonly associated with obesity, enlarged pharyngeal soft tissues, and restricted craniofacial skeletal structures. The present study aims to investigate the relationship between (i) craniofacial morphology and (ii) volumetric measurements of the upper airway and surrounding soft tissues, and the prevalence of OSA in middle-aged Korean adults.

Materials and methods: This cross-sectional study was conducted using data from a population-based cohort of Korean adults. A total of 89 participants (mean age: 61.65 ± 6.27 years; 50 males, 39 females) from the Korean Genome and Epidemiology Study in Ansan were included in the analysis. All participants underwent 1.5-Tesla MRI-based volumetric assessment of the upper airway (Magnetom Espree; Siemens Healthcare, Erlangen, Germany) and overnight in-home polysomnography (Embletta X-100; Embla Systems, Broomfield, CO, USA) between 2014 and 2015. Based on their apnea-hypopnea index (AHI), participants were categorized into two groups: no OSA (AHI <10 events/hour) and OSA (AHI ≥ 10 events/hour). Using Amira 5.4.0 image analysis software, a total of 23 volumetric measurements (airway and surrounding soft tissues) and 15 linear and angular cephalometric measurements were obtained from the upper airway MRI scans.

Results: Based on multivariable linear regression analysis adjusted for age, sex, BMI, diabetes, and cardiovascular disease, several MRI-based volumetric and cephalometric features were significantly associated with the OSA group compared to the non-OSA group. Among the volumetric measurements, the OSA group exhibited a narrower anteroposterior dimension of both the retropalatal and retroglossal airways (β [SE] = -1.88 [0.66] ($p=0.01$); and -2.48 [0.95] ($p=0.01$), respectively), as well as a longer overall airway length (β [SE] = 3.69 [1.61], ($p=0.02$)). In terms of cephalometric

characteristics, the OSA group showed a significantly greater maxillo-mandibular discrepancy and increased upper facial height compared to the non-OSA group (all p-values <0.05).

Conclusions: This study identified distinct craniofacial and upper airway morphological features in individuals with OSA, including reduced anteroposterior airway dimensions and increased airway length. These findings emphasize the important role of upper airway phenotypes in the pathophysiology of OSA in middle-aged Korean adults.

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Associations between CPAP use and risk for Major Adverse Cardiac Events in sleep clinic patients? A real-world study

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Introduction: The relationship between continuous positive airway pressure (CPAP) use and risk for long-term major adverse cardiovascular events (MACE) is poorly understood. This study aimed to assess the relationship between CPAP use and MACE among typical patients attending an Australian tertiary centre sleep clinic diagnosed with moderate/severe OSA.

Materials and methods: Design: Observational cohort study - West Australian Sleep Health Study (WASHS).

Participants: Adults (n=2,646) with moderate/severe OSA (AHI ≥15/hour) diagnosed by in-lab polysomnography between 2006–2010.

Follow-up: Median of 7.1 years; endpoint January 2016.

CPAP exposure: CPAP use as continuous variable: Week 1 CPAP (hrs/night) and All CPAP (hrs/night) (mean of all CPAP use over the follow-up period), tertiles of CPAP use: Week 1 and All CPAP (reference: 0 hours).

Outcome: Time to cardiac death or non-fatal hospitalisations due to MACE (a composite of coronary heart disease (CHD), cerebrovascular disease, revascularisation procedures for CHD or cerebrovascular disease, peripheral vascular disease, heart failure, and atrial fibrillation), or end of follow-up/non-cardiac death, based on ICD codes (administrative health databases).

Analysis: Cox proportional hazards models adjusted for: age; sex; body mass index (BMI); socio-economic status; education; prevalent cardiovascular disease; smoking; Epworth sleepiness scale (ESS); self-reported sleep duration; ODI 3%; hypertension; diabetes; cholesterol. Restricted cubic spline analysis was used to explore potential non-linear associations between CPAP use and MACE.

Results: MACE occurred in 18% of participants (n=475).

Each additional hour of Week 1 CPAP use was associated with a 5% reduction in hazard of MACE (HR 0.95, 95% CI: 0.92–0.99; p=0.007). Each additional hour of All CPAP use associated with a 6% reduction in hazard (HR 0.94, 95% CI: 0.91–0.98; p=0.002).

Compared to no use, Week 1 CPAP tertiles showed significantly reduced hazard (T1: 0.01–3.58 hrs/night, HR 0.55, 95% CI: 0.41–0.74, p<0.001; T2: 3.59–6.12 hrs/night, HR 0.62, 95% CI: 0.46–0.82, p=0.001; T3: 6.13–13.86 hrs/night, HR 0.64, 95% CI: 0.48–0.85, p=0.002). Compared to no use, all follow up CPAP use tertiles showed significantly reduced hazard (T1: 0.01–3.60 hrs/night, HR 0.57, 95% CI: 0.42–0.76, p<0.001; T2: 3.61–6.00 hrs/night, HR 0.60, 95% CI 0.45–0.80, p<0.001; T3: 6.02–11.44 hrs/night, HR 0.60, 95% CI 0.45–0.80, p<0.001).

Restricted cubic spline analysis suggested reduced MACE hazard at any level of CPAP use, albeit with lesser risk reduction at intermediate use (>3 to <6hrs/night), compared to low (0-3hrs/night) or high use (≥6 hrs/night).

Conclusions: Increasing CPAP use was associated with lower risk of MACE in sleep clinic patients with moderate/severe OSA. However, benefit appears to occur at very low levels of use and cubic spline analysis suggests more benefit at low and high CPAP use levels, compared with intermediate levels of use. MACE risk reduction from CPAP can be predicted as early as 1 week. These findings highlight the potential importance of supporting CPAP use from treatment outset to reduce risk of long-term MACE.

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Association study of gut microbiota abnormalities and cognitive dysfunction caused by obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA), the most prevalent sleep-related breathing disorder, induces neurocognitive dysfunction through intermittent hypoxia (IH) mediated mechanisms. Although clinical studies have identified gut microbiota dysbiosis and altered microbial metabolite profiles in OSA populations, the causal relationship between OSA progression and microbiota-metabolite axis dysregulation remains unestablished. Furthermore, the pathophysiological mechanisms linking microbiota-metabolite axis disturbances to OSA-mediated cognitive impairments require systematic elucidation.

Materials and methods: This multi-tiered methodology comprised: (1) Leveraging OSA GWAS data from FinnGen and gut microbiota/metabolome datasets from MiBioGen consortiums, we conducted bidirectional two-sample Mendelian randomization to identify OSA-associated microbial features, followed by multivariate MR analysis adjusting for obesity, sex, and smoking to establish causal relationships; (2) Establishing intermittent hypoxia (IH) murine models with cognitive assessment through behavioral paradigms and neural function evaluation via resting-state fMRI; (3) Multi-omics integration (fecal metagenomics, serum metabolomics, and hippocampal transcriptomics) delineated IH-induced gut-brain axis perturbations, with qPCR validation of key regulatory genes and Luminex cytokine profiling; (4) Therapeutic exploration of sodium butyrate supplementation on IH-mediated cognitive deficits and gut-brain circuitry.

Results: 1. Multiple MR Analysis determined that increased serum levels of three gut microbiota derived metabolites (leucine, epimandrosterone sulfate and 3-dehydrocarnitine) were independently associated with increased risk of OSA, and multiple SCFAs producing bacteria represented by Rumenococcaceae showed independent protective effects on OSA risk even after correction of confounding bias. 2. Behavioral experiments found that IH would lead to learning and memory dysfunction in mice. Functional MRI showed that IH mice showed inconsistent intensity of nerve activity in the whole brain and decreased nerve function in cognitive-related brain areas. Multi-omics analysis revealed multi-dimensional pathological changes in the gut-brain axis of IH mice, including reduced abundance of SCFAs producing bacteria, altered metabolic pathway levels, over-activation of hippocampal microglia, accumulation of inflammatory factors and activation of inflammatory pathways. 3. Exogenous SB supplementation significantly improved the learning and memory dysfunction of IH mice, and up-regulated the level of neural activity in brain regions related to cognitive function; Microbiota remodeling, regulation of metabolic environment, inhibition of microglia activation and expression of inflammatory factors may be the potential mechanisms by which SB improves IH cognitive impairment.

Conclusions: Multiple gut microbiota and derived metabolites have independent causal relationship with OSA. Exogenous SCFAs (butyric acid) supplementation can significantly improve IH-related cognitive dysfunction. This study provides evidence for the association between gut microbiota and OSA and related cognitive dysfunction, and SCFAs supplementation based on gut microbiota metabolites can be used as a potential drug therapy for OSA related cognitive dysfunction.

Asthma, Arytenoid Edema, and Conversion Disorder

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Introduction: Recurrent intubations for dyspnea typically imply the presence of severe organic airway pathology requiring mechanical intervention. However, when structural abnormalities are mild or insufficient to account for the clinical severity, functional etiologies such as conversion disorder must be considered. We report a unique case of persistent upper airway symptoms resulting in repeated intubations, driven by the complex interplay of asthma exacerbations, mild arytenoid swelling, and conversion disorder.

Materials and methods: Case report

Results: A 23-year-old woman with a history of allergic asthma presented with recurrent episodes of severe dyspnea, leading to multiple intubations and ICU admissions. Initial desaturation was associated with asthma exacerbation confirmed by positive rhinovirus testing. Subsequent evaluations revealed mild arytenoid mucosal swelling but no significant structural airway obstruction. During acute episodes, head rotation immediately improved symptoms, suggesting dynamic upper airway compromise. Later, drug-induced sleep endoscopy (DISE) was performed for diagnostic purposes, confirming mild arytenoid edema and positional airway improvement. Psychological assessment indicated conversion disorder, characterized by la belle indifférence. Symptom recurrence was triggered by allergen exposure and emotional stress events.

Management included asthma control, acute positional therapy for symptom relief, long-term voice therapy to reduce laryngeal tension, and psychiatric intervention targeting functional symptoms and underlying psychological stressors. Surgical intervention was not pursued.

Conclusions: This case highlights the importance of considering both organic and functional components in patients with persistent dyspnea, especially when structural abnormalities are insufficient to explain clinical severity. Dynamic airway evaluation and psychological assessment were essential for diagnosis and tailored management.

A Study on Differentiating Obstructive and Central Sleep Apnea and Identifying Cheyne-Stokes Breathing Using Non-Invasive Fiber Optic Physiological Monitoring Technology and AI

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Introduction: Currently, the detection of sleep apnea primarily relies on polysomnography (PSG) and photoplethysmography (PPG). However, while PSG is considered the diagnostic gold standard, it requires multiple wires attached to the body, significantly disturbing natural sleep and making it unsuitable for long-term or home monitoring, especially for elderly individuals, children, and patients with dementia or psychiatric disorders. Although PPG is more convenient, its signals are easily affected by vascular contractions, skin pigmentation, and improper sensor placement. Moreover, oxygen desaturation alone cannot distinguish between obstructive sleep apnea (OSA) and central sleep apnea (CSA). In addition, the widely used apnea-hypopnea index (AHI) merely counts the number of events without considering the duration, depth, or morphology of respiratory events, potentially underestimating disease severity and failing to accurately identify complex breathing patterns such as Cheyne-Stokes Breathing (CSB).

Materials and methods: This study developed a system integrating non-invasive fiber optic physiological monitoring technology (nFOPT Biosensor) with artificial intelligence (AI) models. Data were collected from 100 subjects, including signals from fiber optic sensing mats placed under the pillow and chest, thoracic and abdominal belts, and oxygen saturation, resulting in a total of 5,685 annotated apnea events. A hybrid CNN-LSTM AI model was constructed to detect apnea events and

classify OSA and CSA. Furthermore, an expert-annotated dataset containing 8,823 data points, along with CNN-DENSE and BiLSTM AI models, was utilized for the identification of CSB.

Results: The proposed AI model achieved detection accuracies of 90.9% for the chest fiber optic biosensors and 89.7% for the pillow biosensors. For the classification of OSA and CSA, the model achieved an overall accuracy of 90.37%, with a sensitivity of 90.92% for OSA and 83.33% for CSA. Regarding CSB identification, the AI model achieved an accuracy of 97.58% and a precision of 86.36%. These results demonstrate that even in the presence of highly variable breathing patterns like CSB, the nFOPT technology combined with AI maintains stable and excellent performance.

Conclusions: This study confirms that nFOPT Biosensor offers significant advantages, including non-contact monitoring, freedom from electromagnetic interference, and high sensitivity. It enables continuous, non-invasive monitoring of respiratory waveforms and precise analysis of the time-frequency characteristics of breathing events. The technology not only overcomes the limitations of traditional PSG and PPG but also allows for accurate differentiation of sleep apnea subtypes and abnormal breathing patterns. In the future, this technology holds great potential for clinical precision diagnostics, remote health monitoring, and cardiovascular risk prediction, representing a groundbreaking innovation in the field of sleep medicine.

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A Study on Selected Factors and Their Association with the Severity of Obstructive Sleep Apnea in Overweight and Obese Hypertensive Patients at Family Hospital in Vietnam

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Introduction: Obstructive sleep apnea (OSA) is prevalent among overweight and obese individuals with hypertension and is associated with an increased risk of cardiovascular, metabolic, and neurological complications. Identifying factors linked to OSA severity can support early diagnosis and improve management strategies. Therefore, this study aims to examine the relationship between various risk factors and the severity of OSA in hypertensive individuals who are overweight or obese.

Materials and methods: A cross-sectional study was conducted on 52 overweight and obese hypertensive patients at Family Hospital, Da Nang, Vietnam, from August 2024 to April 2025. Clinical data, including age, gender, BMI, neck circumference, and blood pressure, were collected. OSA was diagnosed using the American Academy of Sleep Medicine (AASM) criteria, and classified into mild, moderate, and severe by AHI. Statistical analysis included descriptive statistics, binary, and ordinal logistic regression.

Results: Of the 52 patients, 90.4% had OSA, with the majority being male (73.1%) and having grade 1 obesity (61.5%). The average age was 54.6 years $\pm$ 3.9 (95% CI), average systolic blood pressure was 137.5 $\pm$ 6.7 mmHg, diastolic pressure was 78.1 $\pm$ 4.8mmHg (95% CI), and neck circumference was 41.6 $\pm$ 0.5 cm (95% CI). The majority of patients were diagnosed with severe obstructive sleep apnea (61.7%). The mean Apnea-Hypopnea Index (AHI) was 44.2 $\pm$ 8.2 events/hour (95% CI), with values ranging from 2.2 to 117.9 events/hour. The most common symptoms of OSA in obese patients with hypertension included loud snoring (100%), witnessed apneas during sleep (95.7%), excessive daytime sleepiness (93.6%), and daytime fatigue (87.2%). Many patients also had coexisting coronary artery disease.

Binary logistic regression showed that gender, age $\geq$ 60 years, and obesity were associated with OSA risk. Female gender was a potential protective factor (OR = 0.118; p = 0.069), while age $\geq$ 60 (OR = 6.835; p = 0.164) and obesity (OR = 2.661; p = 0.240) were linked to increased OSA risk, though the results were not statistically significant possibly due to a limited sample size. Ordinal logistic regression showed that BMI was significantly associated with OSA severity (OR = 1.24; 95% CI: 1.01–1.52; p = 0.039).

Conclusions: Gender, age $\geq$ 60, and obesity may influence OSA risk in hypertensive overweight/obese patients, though the results were not statistically significant possibly due to a limited sample size, further studies with larger sample sizes are necessary. BMI was significantly associated with OSA severity.

A Tiny Bone with a Pivotal Impact: Boosting Hypoglossal Nerve Stimulation to Improve Upper Airway Function

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Introduction: Obstructive sleep apnea (OSA) is characterized by repeated upper airway collapse during sleep, leading to significant cardiovascular, metabolic and neurocognitive consequences. Although continuous positive airway pressure (CPAP) is the gold-standard treatment, it is poorly tolerated by approximately 50% of those with OSA. Hypoglossal nerve stimulation (HNS) has emerged as an alternative therapy, targeting the genioglossus (GG) muscle - a primary upper airway dilator in the tongue - to maintain airway patency. However, HNS treatment outcomes vary. One factor that may influence HNS effectiveness is the position of the hyoid bone, a mobile structure sitting at the base of the tongue. In individuals with OSA, the hyoid bone is positioned more inferiorly, potentially limiting GG-mediated airway dilation. While HNS stimulation parameters, such as current amplitude, are often adjusted to improve treatment efficacy, the role of hyoid bone repositioning remains unknown. This study aimed to assess how directional and incremental anterior hyoid bone repositioning, combined with different HNS amplitudes, influences upper airway function.

Materials and methods: An anesthetized New Zealand White rabbit model (n=6) was used to investigate upper airway dynamics. Rabbits were positioned supine with head and neck position controlled. Upper airway airflow (V) was measured using a pneumotachograph connected in series with the trachea, while upper airway pressure (Pua) was recorded via a pressure transducer. The hypoglossal nerve was surgically exposed via a midline neck incision and carefully dissected for bipolar hook electrode placement. Stimulation was delivered using an electric stimulator. The hyoid bone was also exposed, and a custom-made device was used to perform anterior repositioning of the hyoid (0, 2, 4 mm) - a direction previously shown to have the greatest impact on upper airway collapsibility. Data were collected during HNS at two current amplitudes (Stim 1; Stim 2 = 2xStim 1), with and without hyoid repositioning. Stimulation was delivered at a frequency of 40 Hz, with pulse widths ranging from 60–500 μ s and current amplitudes of 50–800 μ A for Stim 1, and 100–1600 μ A for Stim 2. Maximal inspiratory flow (Vlmax), nadir upper airway pressure (Pua_min), and upper airway resistance (Rua) were quantified.

Results: Preliminary results indicate that both anterior hyoid repositioning and HNS alone improved upper airway function. When combined, anterior hyoid repositioning generally augmented the effect of HNS on upper airway outcomes, producing greater increases in Vlmax and reductions in Pua_min and Rua compared with stimulation alone. The greatest improvements across all three outcomes were observed with hyoid repositioning of 4 mm.

Conclusions: Anterior repositioning of the hyoid bone tends to improve upper airway patency by increasing airflow and reducing susceptibility to upper airway collapse. The findings highlight the synergistic potential of combining hyoid bone repositioning with HNS and individualized stimulation parameters to boost upper airway function. This combined approach may offer a promising strategy to optimize HNS outcomes and advanced personalized therapies for the treatment of OSA, ultimately helping to reduce the disorder's serious health consequences.

Auto-PAP Adherence in Obese Pediatric Patients with OSA: A Retrospective Study

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Introduction: Long wait times for CPAP (continuous positive airway pressure) titration studies and poor adherence to CPAP machines continue to be major barriers to effective fixed-pressure CPAP therapy in children and adolescents. During the COVID-19 pandemic, auto-titrating CPAP (auto-PAP) gained popularity in adults due to its ease of initiation—eliminating the need for a titration study—and increased comfort during use. However, data on auto-PAP adherence in the pediatric population remain limited. This study aims to identify characteristics associated with improved auto-PAP

compliance in children and adolescents, with the goal of predicting which patients may be optimal candidates for this therapy.

Materials and methods: Charts and PAP adherence data were retrospectively reviewed for 77 obese children and adolescents initiated on auto-PAP therapy between 2021 and 2024. Patients with autism or genetic syndromes associated with global developmental delays were excluded. Collected variables of interest included demographic data (age and gender), baseline apnea-hypopnea index (AHI), and adherence rates at 7, 30, and 90 days following the initiation of therapy.

Results: There were no significant differences in auto-PAP adherence between males and females or between children and adolescents. At day 7, a non-significant trend was observed, suggesting that patients with severe OSA (AHI > 5) were more likely to be adherent. This trend was no longer observed at days 30 or 90. Notably, a higher BMI z-score was significantly associated with poorer adherence at day 30, but not at days 7 or 90.

Conclusions: Auto-PAP adherence in pediatric patients does not appear to differ significantly by gender or age group. A higher BMI z-score may be associated with decreased adherence at the 30-day mark, highlighting a potential at-risk group. While severe OSA may initially correlate with improved short-term compliance, this trend does not persist in the long term. These findings underscore the need for further research to better understand adherence barriers, particularly among patients with higher BMI, and to identify subgroups most likely to benefit from auto-PAP therapy.

Belun Sleep Platform versus In-lab polysomnography for obstructive sleep apnea diagnosis

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Introduction: The Belun Sleep Platform (BSP) is an innovative network-based technology for home sleep apnea testing, designed using an artificial intelligence system that analyzes patterns of oxygen saturation, heart rate, and accelerometry signals. Few studies have been conducted to validate the device. This article aims to compare the BSP with full-night PSG for OSA diagnosis.

Materials and methods: Participants without significant cardiovascular or neuromuscular comorbidities scheduled for PSG were recruited. Simultaneous in-laboratory full-night PSG was conducted with the BSP. The diagnostic features, including sensitivity, specificity, PPV, NPV, and accuracy, were determined using IBM SPSS, version 27.

Results: A total of 35 individuals (54.3% male) were enrolled, with an average age of 49.9 years. The accuracy, sensitivity, and specificity with an AHI cut-off value of ≥ 15 events/h were 0.68 (0.51 to 0.83), 0.35 (0.14 to 0.61), and 1.0 (0.81 to 1.0), respectively, for both AASM scoring criteria 1A and 1B with AUROC 0.67. The diagnostic property of BSP with distinct AHI cut-off values of ≥ 5 events/h and ≥ 30 events/h revealed a sensitivity of 0.82 (0.63 to 0.93) and 0.33 (0.07 to 0.70), respectively, and a specificity of 0.14 (0.00 to 0.57) and 1.0 (0.86 to 1.0). The combination of BSP-AHI with STOP-Bang ≥ 3 results in an increased sensitivity of 0.38. The BSP-AHI demonstrated a moderate correlation with the PSG-AHI (ICC = 0.737). Likewise, a good correlation was observed between BSP-ODI and PSG-ODI (ICC = 0.882).

Conclusions: The accuracy of the Belun Sleep Platform in predicting AHI and ODI in patients without significant comorbidities was still controversial. Future research with a larger sample size and the enrollment of participants with comorbidities is recommended to ascertain the role of the BSP as an alternative device for the diagnosis of OSA in high-risk OSA patients.

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Benefits of Community-Based Intervention for Mild OSA on Cardiac Remodeling: A Secondary Analysis of a Randomized Trial

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Introduction: Evidence for the efficacy of continuous positive airway pressure (CPAP) therapy in patients with mild obstructive sleep apnea (OSA), particularly in community-based settings, remains limited. This study investigated the effects of CPAP on cardiac remodeling, symptoms, and blood pressure in mild OSA through a secondary analysis of data from a community randomized controlled trial (RCT).

Materials and methods: This study conducted a secondary analysis on a specific subgroup of the population in February 2025, based on the RCT trial published in the journal *SLEEP* in September 2024. A total of 94 participants with mild OSA (apnea-hypopnea index 5–15 events/hour) were randomized to either CPAP therapy (N=44) or routine community management (N=50), with 12-week follow-up. Secondary outcomes focused on left atrial diameter (LAD), Short Form 36 Health Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and blood pressure. Analysis of covariance was used to assess between-group differences in outcomes.

Results: The mean age of participants was 55.6 years, with 40.4% male. Compared to baseline, the intervention group showed a mean reduction of 0.1 mm in LAD, while the control group exhibited a mean increase of 0.6 mm, resulting in a between-group difference of -1.2 mm (95%CI: -2.3 to -0.1, $P=0.036$). At 12 weeks, the CPAP group demonstrated significant improvements over the control group in SF-36 physical function score (adjusted $\beta = 3.5$, 95% CI: 0.9 to 6.0), ISI score (adjusted $\beta = -1.8$, 95%CI -3.5 to -0.1), and PSQI score (adjusted $\beta = -1.1$, 95%CI -2.1 to -0.1). Additionally, the CPAP group showed greater reductions in systolic blood pressure (adjusted $\beta = -7.0$, 95%CI: -11.7 to -2.4), diastolic blood pressure (adjusted $\beta = -4.6$, 95%CI: -7.3 to -2.0), and body mass index (adjusted $\beta = -0.3$, 95%CI: -0.6 to -0.0).

Conclusions: Interventions targeting mild OSA can improve cardiac remodeling, while demonstrating multifaceted benefits including enhanced physiological function, improved sleep quality, blood pressure reduction, and decreased insomnia severity.

Benefits of Early Body Weight Reduction in Participants with Obesity and Moderate-to-severe Obstructive Sleep Apnea: A Post Hoc Analysis of SURMOUNT-OSA

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Introduction: Previous studies demonstrated that weight reduction within the first year of treating obstructive sleep apnea (OSA) significantly reduced Apnea-Hypopnea Index (AHI). However, further investigation is required to understand the relationship between early weight reduction and OSA outcomes, especially with treatments such as positive airway pressure (PAP) therapy. This post hoc analysis of the SURMOUNT-OSA study explored the association between early weight reduction at Week 20 and OSA improvement in participants with moderate-to-severe OSA and obesity.

Materials and methods: This post hoc analysis of the global multi-center, phase 3, 52-week, double-blind, study SURMOUNT-OSA (NCT05412004) randomized participants to receive either tirzepatide or placebo, with trial 1 enrolling those not receiving PAP and trial 2 enrolling those receiving PAP therapy. Participants were retrospectively categorized based on the percentage of weight reduction at Week 20 into four subgroups: <5%, $\geq 5\%$ <10%, $\geq 10\%$ <15%, and $\geq 15\%$. Least Squares Mean (LSM) change in AHI (events/hour) and percent change in AHI from baseline, as well as OSA remission at week 52, were assessed using mixed model repeated measures.

Results: The analysis included 469 participants, 234 from trial 1 and 235 from trial 2. The baseline characteristics were comparable across subgroups. In trial 1 at Week 20, participants with $\geq 5\%$ <10%, $\geq 10\%$ <15%, and $\geq 15\%$ weight reduction showed significant improvement in AHI with mean change (events/h) of -12.4, -18.8, -30.6 ($p<.001$ for all), and percent change from baseline of -20.0, -38.0, -56.1 ($p<.001$ for all), respectively, compared to the <5% weight reduction group (-6.2; -14.9; $p<.05$ for both). By Week 52, participants in <10%, $\geq 10\%$ <15%, and $\geq 15\%$ weight reduction groups, sustained significant improvements in AHI with mean change of -15.8, -28.5, -32.4 ($p<.001$ for all) and percent change from baseline of -32.2, -56.9, -58.3 ($p<.001$ for all), respectively, compared to the <5% weight reduction group (-6.5; $p=.02$; -9.6; $p=.09$).

Similarly, in trial 2, participants with $\geq 5\% < 10\%$, $\geq 10\% < 15\%$, and $\geq 15\%$ weight reduction at Week 20 showed significant improvement in AHI with mean change from baseline (events/h) of -12.0, -17.0, -27.2 ($p < .001$ for all) and percent change from baseline of -22.7, -37.2, -56.4 ($p < .001$ for all), compared to the $< 5\%$ weight reduction group (-9.5; -17.7; $p < .01$ for both). By Week 52, participants in the $\geq 5\% < 10\%$, $\geq 10\% < 15\%$, and $\geq 15\%$ weight reduction groups sustained improvements in AHI (events/h) with mean change of -14.8, -27.5, -35.2 ($p < .001$ for all), and percent change from baseline of -29.5, -58.5, -74.5 ($p < .001$ for all), respectively, compared to the $< 5\%$ weight reduction group (-10.4, $p < .001$; -13.7; $p < .05$).

In both trials, participants with $\geq 10\% < 15\%$ weight reduction at Week 20 exhibited OSA remission rates of 48.7% and 49.8% by week 52, while those with $\geq 15\%$ weight reduction demonstrated higher remission rates of 50.7% and 75.3%. Participants with $\geq 5\% < 10\%$ and $< 5\%$ weight reduction had $< 30\%$ and $< 15\%$ OSA remission rates, respectively.

Conclusions: In this post hoc analysis, early weight reduction of $\geq 10\%$ was associated with greater AHI improvement. These findings support the importance of early and intensive weight reduction strategies for optimizing sustained improvements in participants with OSA and obesity, with or without PAP therapy.

Beyond AHI: Hypoxic Burden As A Superior marker in the Management of Opioid-Associated Central Sleep Apnea with Acetazolamide

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Introduction: Sleep-disordered breathing (SDB) is common in patients with substance use disorders, but the Apnea-Hypopnea Index (AHI) may not fully reflect the physiological burden—particularly due to challenges in scoring central hypopneas. This study evaluates acetazolamide's effects on central apnea and introduces Hypoxic Burden and Hypoxic Area Under the Curve (**HAUC**) as alternative markers.

Materials and methods: Nocturnal SpO₂ and airflow data were collected from 10 patients with substance use disorder and sleep-disordered breathing (SDB), of which approximately 50% of the respiratory events were central apneas and hypopneas, at Masih Daneshvari Hospital. Across baseline, placebo, and acetazolamide phases, signals were processed using MATLAB. Hypoxic Burden counted distinct desaturation events, while HAUC measured cumulative desaturation severity. Both were compared to AHI.

Results: Acetazolamide significantly improved oxygenation in ~80% of patients. While AHI showed minimal changes, Hypoxic Burden and HAUC revealed marked reductions in event frequency and severity ($p < 0.05$), offering more sensitive indicators of treatment response.

Conclusions: Our findings suggest that reconsideration of the sole reliance on AHI may be beneficial. When evaluating therapeutic outcomes in SDB, particularly in substance-dependent Patients. Metrics such as Hypoxic Burden and HAUC provide more physiologically Meaningful insights and may better reflect real clinical improvements compared to AHI.

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Biomarker Discovery in Obstructive Sleep Apnea: A Bibliometric Mapping of Research Frontiers (2000-2023)

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Introduction: Obstructive sleep apnea (OSA) is a harmful, complex and heterogeneous disease with limited diagnostic and therapeutic frameworks. This study analyzed global research output on OSA biomarkers to help advance precision sleep medicine.

Materials and methods: We conducted a keyword search in the Web of Science Core Collection (2000–2023) to identify research and review articles on OSA biomarkers. VOSviewer, CiteSpace, and R were performed to analyze annual publications, citations, contributions, co-authorships, and co-occurrences, identifying the most productive and highly cited countries, authors, institutions, journals, keywords, and references.

Results: The analysis included 1108 publications. Annual publication counts, and citations have consistently increased over the past two decades. The United States of America leads OSA biomarker research in volume and citation impact, with extensive collaboration with China. Dr. Gozal D is the leading author. The University of Chicago is the top institution regarding publications and citations. *Sleep and Breathing*, *Sleep Medicine*, and *Sleep* are the most productive journals. *Sleep* is the most cited, followed by the *American Journal of Respiratory and Critical Care Medicine*, *Chest*, and *Circulation*. Over half of the top journals are high-impact Q1, including *The New England Journal of Medicine*, indicating significant academic interest. Recent research focuses on comorbidities, pathogenic mechanisms, and indicators of phenotype and endotype, which are likely future trends.

Conclusions: We identified research hotspots, trends and leading contributors to OSA biomarkers. These results may benefit further studies to better understand OSA's heterogeneity and improve diagnosis, risk identification, and prognosis prediction.

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Body Weight Change and Nocturnal BP Pattern influence the effect of CPAP treatment on 24-Hour Ambulatory Blood Pressure in OSA Patients

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Introduction: Obstructive sleep apnea (OSA) is associated with elevated blood pressure (BP), and continuous positive airway pressure (CPAP) treatment has shown heterogeneous effects on BP control. To address this variability, a comprehensive evaluation of factors influencing the BP response to CPAP was conducted, with particular emphasis on weight change during treatment and nocturnal BP pattern.

Materials and methods: This study is a post hoc analysis of the Peking University People's Hospital cohort from a randomized, controlled, non-inferiority trial on the effect of telemedicine-based CPAP management on 24-Hour Ambulatory Blood Pressure (ABPM) in Patients with OSA (PKUPH-TM). We included patients for whom 24h ABPM data were available at baseline and 12 weeks after the intervention. Parameters analyzed included weight change, sleep apnea severity, oxygen desaturation burden, nocturnal BP pattern, antihypertensive medication use, and CPAP adherence, to identify predictors of BP reductions following 12 weeks of CPAP therapy.

Results: A total of 256 OSA patients were included in the analysis. Baseline BMI, weight gain, 24-Hour mean arterial pressure (MAP), nocturnal BP pattern, duration of oxygen desaturation below 90%, and CPAP adherence were significantly associated with changes in 24h BP. Among these, logistic regression identified baseline 24h MAP, weight gain, nocturnal BP pattern, and CPAP adherence as independent predictors (all $P < 0.05$). To further clarify the impact of body weight dynamics on BP outcomes, patients were categorized into three groups based on weight change: no weight change ($n = 207$), weight loss ($n = 32$), and weight gain ($n = 17$). The weight loss group exhibited the greatest reduction in 24h BP, while the weight gain group showed the smallest reduction. After adjusting for baseline 24h MAP and CPAP adherence, the difference in daytime mean BP reduction remained significant among the groups (mean reductions: 4.73 mmHg, 6.64 mmHg, and 2.34 mmHg for no weight change, weight loss, and weight gain groups, respectively; adjusted $P = 0.04$). To further assess the impact of nocturnal BP pattern, participants were stratified into dipper and non-dipper groups based on nocturnal BP decline. Compared to dippers ($n = 86$), non-dipper patients ($n = 170$) showed significantly greater reductions in nighttime mean BP (5.51 mmHg vs. 1.54 mmHg in non-dipper and

dipper groups, respectively; estimated difference = 3.96 mmHg; 95% CI: 1.20 to 6.72; adjusted P = 0.004) and nighttime diastolic BP (4.59 mmHg vs. 0.33 mmHg in non-dipper and dipper groups, respectively; estimated difference = 4.25 mmHg; 95% CI: 1.70 to 6.80; adjusted P = 0.001).

Conclusions: Our findings indicate that the effect of CPAP on 24h ABPM in OSA patients is influenced by both weight change and nocturnal BP pattern. Patients who lost weight experienced the greatest benefit in daytime BP reduction, while those with a non-dipping BP pattern demonstrated more pronounced improvements in nighttime BP, particularly in diastolic pressure. These results highlight the importance of individualized BP management strategies in OSA treatment.

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Building a Comprehensive Upper Airway Stimulation Program: Beyond the Implant

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Introduction: The expansion of HGNS therapy has highlighted variations in post-implant care delivery and outcome reporting. With increasing implant volumes across practice settings, there is a need to establish clear guidelines for care pathways and standardized outcome measures. Current literature demonstrates the importance of comprehensive care protocols beyond the technical aspects of implantation.

Materials and methods: "Building a Comprehensive Upper Airway Stimulation Program: Beyond the Implant" addresses practical aspects of establishing successful hypoglossal nerve stimulation programs. While surgical aspects are well-standardized, pre and post-implant care pathways can vary significantly. This panel examines key elements for program success: (1) implementing structured pre-operative psychological evaluation for select patients, (2) developing sustainable post-operative care models balancing the roles of sleep physicians, advanced practice providers, and industry representatives, (3) standardizing outcome measures, and (4) creating clear pathways for long-term patient care. We will discuss practical solutions for both academic and private practice settings, including staffing considerations, workflow optimization, and quality metrics tracking.

Results: The team will discuss current literature, which shows wide variation in how programs handle post-implant care and report outcomes, from fully surgeon-managed to sleep physician-led models. Understanding these different models and their outcomes helps surgeons develop sustainable programs appropriate for their practice environment. The session addresses critical questions about staffing, resource allocation, and quality metrics tracking. There is substantial variability on reported outcomes of HGNS, and average AHI at the ideal therapeutic amplitude was significantly lower in tPSG compared to eHST (8.8 vs. 17.6 events/hour, $p < 0.001$). When comparing Sher15 response rates (post-op AHI ≤ 15 and $\geq 50\%$ reduction), 80% met the criterion via tPSG, but only 46% via eHST.

Conclusions: Successful HGNS programs require careful coordination between multiple providers and services. There is an unmet need to understand staffing requirements, workflow optimization, and quality metrics tracking. Recent literature highlights the complexity of measuring program success and the importance of standardized reporting. This knowledge helps all stakeholders develop sustainable programs that maintain high-quality care.

Can Acute Post-Surgical Changes in PSG Features Inform Subsequent Management of Patients with Moderate-to-Severe Obstructive Sleep Apnea? A Pilot Study

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Introduction: Obstructive sleep apnea (OSA) is a multifactorial sleep-related breathing disorder. Uvulopalatopharyngoplasty (UPPP) is the predominant surgical intervention for moderate-to-severe

OSA. This study aimed to evaluate acute changes in polysomnography (PSG) characteristics following surgery to predict UPPP efficacy and guide long-term post-surgical management.

Materials and methods: Patients eligible for sleep surgery at Guangzhou Medical University between 2023 and 2025 were enrolled. All underwent in-lab PSG during diagnostic and post-operative night 5 after UPPP. Patients were classified into "surgically effective" or "non-effective" groups based on whether their apnea-hypopnea index (AHI) decreased by ≥ 15 events/hour.

Results: A total of 97 patients who underwent UPPP surgery were included in the final analysis. Based on the surgical outcome defined by a reduction in the apnea-hypopnea index (AHI) of ≥ 15 events/hour, 48 patients were classified into the surgical-effective group, while the remaining 49 patients were categorized into the non-effective group.

Effective group

Patients in the surgical-effective group demonstrated significant improvements across multiple polysomnographic parameters:

Respiratory events: AHI decreased by 35.1 ± 17.2 events/h ($p < 0.001$), REM/NREM AHI reduction > 30 events/h ($p < 0.001$)

Oxygenation Parameters: Oxygen saturation levels showed substantial enhancement. The mean SpO_2 during REM sleep increased by 4% ($p < 0.001$), and the lowest SpO_2 value recorded throughout the study rose by 8.9% ($p < 0.001$).

Non-Effective Group

The non-effective group showed no clinically or statistically meaningful improvements:

Respiratory and Oxygenation Measures: The change in AHI was negligible, with a mean ΔAHI of -0.1 events/hour ($p = 0.944$). Similarly, only minimal improvements were noted in oxygenation measures, which did not approach statistical significance.

Sleep architecture parameters

No statistically significant alterations in sleep architecture were observed in either group following surgery.

Conclusions: OSA patients exhibited significant improvements in respiratory disturbances, oxygen desaturation, and arousal/awakening indices post-operatively, but not in sleep architecture. Whether acute alterations in PSG variables after UPPP surgery predict long-term efficacy remains undetermined. Further large-scale studies are warranted to investigate the clinical implications of acute post-surgical PSG patterns.

Can Awake End-tidal CO₂ Predicts Sleep-related Hypoventilation in Children with Neuromuscular Diseases?

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Introduction: Children with neuromuscular diseases (NMD) are at risk for hypoventilation, which often first manifests during sleep. Polysomnography (PSG) is the gold standard for detecting sleep-related hypoventilation (SRH) and determining the need for noninvasive positive pressure ventilation. This study aimed to evaluate whether awake end-tidal carbon dioxide (EtCO₂), a simple and noninvasive outpatient measure, can predict SRH in children with NMD. We hypothesized that patients with SRH may exhibit high-normal awake EtCO₂ values.

Materials and methods: We retrospectively reviewed medical records of children (0–18 years) with congenital NMD who underwent diagnostic PSG at Ramathibodi Hospital. From PSG results, SRH was defined as $> 2\%$ of total sleep time (TST) with $EtCO_2 > 50$ mmHg. Children with NMD were divided into those with SRH and without SRH groups. Demographic and anthropometric data and neuromuscular diagnoses were collected. Awake parameters including baseline oxygen saturation (SpO_2), pulmonary function tests (PFTs), awake EtCO₂, venous partial pressure of carbon dioxide (PCO₂), and serum HCO₃ were extracted. The collected variables were compared between the SRH and non-SRH groups.

Results: A total of 50 diagnostic PSG records were included. The mean age was 12.34 ± 3.50 years; 76% were male and 48% had Duchenne muscular dystrophy. SRH was identified in 8 PSGs (16%). Baseline characteristics did not differ significantly between patients with and without SRH. Awake EtCO₂ values were significantly higher in patients with SRH compared to those without SRH ($42.25 \pm$

3.77 vs 33.52 $\pm$ 3.29 mmHg, $p < 0.001$). Serum bicarbonate (HCO_3) levels were also significantly higher in patients with SRH (26.92 $\pm$ 2.53 vs 22.77 $\pm$ 2.56 mEq/L, $p = 0.002$). Venous PCO_2 trended higher in patients with SRH but did not reach statistical significance. ROC analysis showed high diagnostic accuracy for predicting SRH, with AUCs of 0.966 for awake EtCO_2 and 0.892 for serum HCO_3 . An awake EtCO_2 cutoff of 38.5 mmHg yielded 87.5% sensitivity and 95.2% specificity, while a serum HCO_3 cutoff of 25.2 mEq/L yielded 80% sensitivity and 80.8% specificity. Based on the 16% prevalence of SRH in our cohort, the positive predictive value (PPV) and negative predictive value (NPV) were calculated. For awake $\text{EtCO}_2 > 38.5$ mmHg, the PPV was 77.8% and the NPV was 97.6%. For serum $\text{HCO}_3 > 25.2$ mEq/L, the PPV was 44.4% and the NPV was 95.5%. These findings indicate that both awake EtCO_2 and serum HCO_3 have high NPV, suggesting potential utility in stratifying the lower-risk cases.

Conclusions: Our findings suggest that awake EtCO_2 and serum HCO_3 may serve as simple and noninvasive indicators for early SRH detection. These tools could help guide clinical decisions and facilitate timely PSG referral and intervention, especially when PSG is delayed or unavailable.

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Can oxygen desaturation during gastrointestinal endoscopy under conscious sedation predict obstructive sleep apnea?

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Introduction: This study explored whether oxygen desaturation during gastrointestinal endoscopy under conscious sedation could serve as a predictive marker for obstructive sleep apnea (OSA).

Materials and methods: In this retrospective chart review, adults who underwent both polysomnography (PSG) and gastrointestinal endoscopy under conscious sedation were divided into two groups based on the lowest oxygen saturation: desaturation group ($\leq 90\%$) and non-desaturation group ($> 90\%$). PSG metrics were compared, and associations between procedural desaturation and OSA severity were analyzed using linear-by-linear association and Pearson correlation tests. Multiple linear regression with stepwise selection was used to identify independent predictors of apnea-hypopnea index (AHI).

Results: Among 48 patients, 22 were in the desaturation group and 26 were in the non-desaturation group. The desaturation group exhibited significantly higher AHI, hypopnea index, respiratory disturbance index, oxygen desaturation index, and cumulative time with O_2 saturation below 90%, indicating more severe OSA-related metrics. A significant linear trend ($P = 0.045$) suggested a higher likelihood of severe OSA in the desaturation group. Additionally, the lowest oxygen saturation during endoscopy correlated negatively with key PSG metrics. In multiple linear regression analysis, the lowest oxygen saturation during endoscopy showed a negative association with AHI, with borderline significance (standardized $\beta = -0.25$, $P = 0.058$, variance inflation factor = 1.173).

Conclusions: Oxygen desaturation during gastrointestinal endoscopy under conscious sedation is associated with more severe OSA and may serve as a useful clinical indicator. PSG should be considered in patients experiencing desaturation during endoscopy.

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Cardiovascular Autonomic Function in Patients with Co-morbid Insomnia and Sleep Apnoea

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Introduction: Co-morbid insomnia and sleep apnoea (COMISA) has been associated with increased risk of developing cardiovascular disease. Mechanistic studies of cardiovascular risk in patients with COMISA are lacking. This study aims to compare cardiovascular autonomic function as measured by heart rate variability (HRV) and pulse wave amplitude drop (PWAD) parameters in patients with COMISA, obstructive sleep apnoea (OSA), insomnia, and those without OSA and insomnia.

Materials and methods: Data from the Sydney Sleep Biobank was analysed. Anthropometry, comorbidities, medications, Insomnia Symptoms Questionnaire (ISQ) and overnight polysomnography data were extracted from the database. Patients were categorised into four groups: 1) Insomnia was defined as meeting the criteria of insomnia based on the ISQ; 2) OSA was defined as having an apnoea-hypopnoea index (AHI) of at least five respiratory events per hour of sleep; 3) COMISA was defined as meeting the criteria of both insomnia and OSA; 4) patients who did not meet the criteria of insomnia or OSA. HRV and PWAD parameters were derived from the electrocardiogram and photoplethysmography signals of the overnight polysomnogram. Time and frequency domain measures of HRV were calculated during stage N2 sleep. PWAD measures of the number of PWAD events per hour of sleep (PWAD_{index}), duration (PWAD_{duration}), area under the curve (PWAD_{AUC}) and amplitude (PWAD_{amp}) was calculated during sleep. Polysomnographic, HRV and PWAD measures were compared between patient groups.

Results: Five hundred and eighty-nine patients (mean $\pm$ standard deviation age = 50.0 ± 15.3 years, body mass index [BMI] = 29.7 ± 7.3 kg/m², 62% males) were included for analysis. Forty-two percent of patients had OSA, 19% insomnia, 26% COMISA, and 14% neither insomnia nor OSA. HRV measures of SDNN, pNN50, Total Power, absolute LF power and normalised LF power were significantly different between groups. Specifically, patients with COMISA had significantly lower HRV measures (SDNN, pNN50, Total Power, absolute LF power and normalised LF power) compared to patients with insomnia only. RMSSD, LF:HF ratio, and normalised HF were not different between patient groups. PWAD_{index} and PWAD_{duration} were lower and longer, respectively, in patients with COMISA compared to patients with insomnia only and patients with OSA only. PWAD_{AUC} and PWAD_{amp} were not different between patient groups. Neither HRV or PWAD measures were different between groups after adjusting for age, sex, and BMI.

Conclusions: Elevated cardiovascular risk in patients with COMISA indicated by HRV and PWAD measures are driven by age, sex and BMI which are shared risk factors for cardiovascular disease and OSA. Appropriate management of shared risk factors in patients with COMISA should be considered for managing cardiovascular disease risk. Additional studies are warranted to understand the mechanistic associations of autonomic function in patients with COMISA.

Acknowledgments: The authors thank the Sydney Sleep Biobank investigators for providing access to the data.

CASE REPORT: BILEVEL POSITIVE AIRWAY PRESSURE TREATMENT OF SLEEP APNEA SYNDROME IN A PATIENT WITH CROUZON SYNDROME

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Introduction: Crouzon syndrome (CS) is a hereditary disorder characterized by deformities of the face and skull brought on by syndromic craniosynostosis or the premature fusion of coronal sutures. Pediatric patients with Crouzon syndrome have a high likelihood of developing obstructive sleep apnea (OSAS), primarily due to skeletal hypoplasia and facial dysmorphism. Treatment of OSAS in patients with Crouzon syndrome requires multidisciplinary and sequential treatment planning because Crouzon syndrome often has different phenotypes with varying severity in OSA and facial dysmorphism.

Materials and methods: In this clinical case, we describe the first case of a child with Crouzon syndrome with sleep apnea who was treated with positive pressure ventilation in Vietnam.

Results: A 7-year-old child was diagnosed with Crouzon syndrome and had frequent nocturnal dyspnea and recurrent respiratory infections. The patient underwent craniofacial and otorhinolaryngological (ENT) surgery with tonsillectomy, orthodontics, ENT rehabilitation, posterior arch decompression, cranial vault correction, elevation and positioning. Polysomnography showed severe sleep apnea with an apnea-hypopnea index (AHI) of 41.7/h and a SpO₂ minimum of 63%. After AutoCPAP failed, she

was switched to BiPAP with good treatment tolerance. Subsequent titration showed that this patient's airway pressure was relatively high (IPAP/EPAP: 19/7) with good tolerability and symptom improvement.

Conclusions: This is the first reported case of Crouzon syndrome treated with positive pressure ventilation in Vietnam. Some isolated reports in the world show that tonsillectomy and lymphadenectomy are the first line. Nasal CPAP is used as a treatment modality and it can help improve the quality of life of these children. This clinical case shows the benefit of PAP treatment for sleep apnea in children with Crouzon syndrome. Pressure titration and sleep endoscopy are necessary techniques that we are gradually approaching in the not-too-distant future.

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Catathrenia: A Retrospective Case Analysis of a Single Respiratory Sleep Disorders Centre

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Introduction: Catathrenia is a rare sleep-related condition characterized by expiratory groaning during sleep. It was previously classified as a parasomnia but is now recognized as an isolated symptom and normal variant under sleep-related breathing disorders in the most recent *International Classification of Sleep Disorders (ICSD-3)*. Its true prevalence is unknown, but according to literature, approximately 0.5% of patients referred to sleep centers present with catathrenia. The underlying pathophysiology remains unclear.

Although it has been proven that catathrenia does not cause direct harm to the patient's health, recognizing and correctly diagnosing the condition is very important — it helps reassure patients and their relatives, as catathrenia often leads to social problems due to unusual sounds during sleep that disturb others.

Materials and methods: Aim: To estimate the prevalence of catathrenia among patients referred for sleep-related breathing disorders and to describe the clinical characteristics .

This retrospective case analysis included patients evaluated at the Sleep Laboratory of the Department of Pulmonology, Lithuanian University of Health Sciences, from 2010 to 2024. All patients underwent:

- Clinical evaluation
- Physical examination
- Completion of the Epworth Sleepiness Scale (ESS)
- Full overnight videopolysomnography

Results: Of the 3873 patients who underwent polysomnographic evaluation, 24 individuals (0.62%) were diagnosed with catathrenia. The gender distribution included 17 males and 7 females. The average age of patients was 32.38 ± 12.02 years, and the average Body Mass Index (BMI) was 27.30 ± 5.61 kg/m². The mean Epworth Sleepiness Scale (ESS) score was 7.25 ± 4.26 .

Isolated catathrenia, without any comorbid sleep disorders, was diagnosed in 8 patients. Snoring was observed in 10 patients. Obstructive sleep apnea (OSA) was identified in 6 individuals—3 with positional OSA and 3 with mild OSA.

The most commonly reported complaints were disturbance of bed partners or roommates due to unusual nocturnal sounds and concern from family members.

Conclusions: The prevalence of catathrenia in our case analysis (0.62%) is similar with previous literature data.

One-quarter (25%) of patients with catathrenia were also diagnosed with OSA.

Although no specific treatment has consistently proven effective, recognizing and correctly diagnosing catathrenia is important — not only to differentiate it from other sleep-related breathing disorders, but also to reassure patients and their relatives that it is a benign condition with no direct health risks.

Causal Relationship Between Female Reproductive Factors and Risk of Obstructive Sleep Apnea

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Introduction: The association between Obstructive sleep apnea (OSA) and gender related factors has always been a hot research topic. We aim to investigate the causal association between reproductive factors and OSA in women at different reproductive stages.

Materials and methods: We applied two-sample Mendelian Randomization for analysis. The genome-wide association studies summary datasets were mainly obtained from the UK biobank and FinnGen. Inverse-Variance Weighted approach was used as the primary analysis, while heterogeneity and horizontal pleiotropy were evaluated using the Cochran Q test and the MR-Egger intercept, and sensitivity analysis included a single SNP analysis and a leave-one-out analysis.

Results: After false discovery rate correction ($P_{FDR} < 0.05$), we found that earlier age at menarche (OR = 0.86; 95% CI, 0.82 to 0.91), age at first sexual intercourse (OR = 0.78; 95% CI, 0.65 to 0.93) and age at first live birth (OR = 0.92; 95% CI, 0.87 to 0.97) were associated with increased risk of OSA, while individuals with higher risk of OSA were likely to have earlier age at menarche (beta = -0.21; 95% CI, -0.32 to -0.10), higher age at menopause (beta = 0.30; 95% CI, 0.06 to 0.53), and longer years of ovulation (beta = 0.80; 95% CI, 0.32 to 1.29). However, there were no positive results between sex hormone levels and OSA.

Conclusions: In the prevention and treatment of OSA, we should pay more attention to those with early age at menarche and long years of ovulation, and to those influences other than hormone levels.

Causal relationships between circulating micronutrients and obstructive sleep apnea

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Introduction: Previous observational studies have linked several circulating micronutrients to obstructive sleep apnea. However, this causality was subjected to residual confounding and reverse causation. Hence, this study aims to evaluate the causal impact of genetically predicted serum micronutrients on OSA.

Materials and methods: A two-sample Mendelian randomization (MR) was carried out to evaluate the causal impact of circulating micronutrients on OSA. Genome-wide association studies (GWAS) summary statistics related to six types of minerals (iron, selenium, copper, zinc, magnesium and calcium) and nine types of vitamins (vitamins B6, B12, C, A, D, E, K and β -carotene) were included. More specifically, inverse variance weighting (IVW) was considered the primary result for causality. Weighted median, MR-Egger, and MR-PRESSO were applied to complicate potential violations of MR assumptions. Then, heterogeneity and horizontal pleiotropy were evaluated by Cochran's Q heterogeneity test, Egger-Intercept, and MRPRESSO Global test. After outliers were removed, the analysis above was performed again.

Results: By IVW analysis, the serum calcium is a protective factor against OSA, with the per one SD increment in the genetically-determined serum calcium level causing an 8% disease in the risk of OSA (OR= 0.92, 95%CI [0.86, 0.98], $p=0.011$). This finding was also robust after removing outliers. As for other micronutrients, we observed little evidence supporting the associations between the two, micronutrient and OSA.

Conclusions: Among common circulating micronutrients, calcium could protect from OSA risk.

Central Sleep Apnea Before and After Atrial Fibrillation Ablation: Association with Cardiac Function Improvement

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Introduction: Sleep-disordered breathing (SDB), linked to atrial fibrillation (AF), is recognized as a risk factor for recurrence following AF ablation. Furthermore, given that AF is a risk factor for central sleep apnea (CSA) irrespective of heart failure, the pattern of sSDB may alter before and after ablation, but the specifics are not well defined.

Materials and methods: We examined individuals who underwent both AF ablation and polysomnography between November 2016 and May 2023. We gathered echocardiographic parameters prior to and following AF ablation. We used echocardiography after the ablation for post-ablation polysomnography and before the ablation for pre-ablation polysomnography to assess the link between polysomnography and echocardiographic parameters.

Results: The study comprised 95 patients: 82 males and 13 females, with a mean age of 62.7 ± 8.9 years and a mean body mass index (BMI) of $26.1 \pm 3.8 \text{ kg/m}^2$. Before the ablation, 58 patients had paroxysmal AF and 37 had chronic AF, with an average left ventricular ejection fraction (LVEF) of $57.2 \pm 9.3\%$ and an average left atrial diameter (LAD) of $41.7 \pm 9.3\text{mm}$. In comparing the pre-ablation polysomnography group (25 cases) with the post-ablation polysomnography group (70 cases), there were no significant differences in age, sex, or pre-ablation cardiac function. However, the average number of combined central and mixed respiratory events per hour (CMAHI) was 11.5 for the pre-ablation group and 5.0 for the post-ablation group, with the pre-ablation group showing a significantly higher rate ($p=0.039$). The analysis of heart ultrasound results before and after the procedure showed an increase in LVEF from 57.2% to 59.9% and a decrease in LAD from 41.7mm to 39.9mm. Creating a model to predict CMAHI values showed links to being older ($\beta=0.32$, $p=0.037$) and having a lower LVEF ($\beta=-0.56$, $p<0.001$), but there were no links found with sex, BMI, LAD, or AF during polysomnography.

Conclusions: Central respiratory events were documented more frequently during polysomnography before AF ablation compared to after, suggesting that this may result from changes in rhythm and improvements in cardiac function post-ablation.

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Central Sleep Apnea caused by low dosage of Baclofen : a case report

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Introduction: Baclofen can relax muscle spasticity by inhibiting the transmission of both mono- and polysynaptic reflexes at the spinal cord. It has been increasingly used off-label for the management of spinal cord lesions or neurologic disorders. However, the expansion use has led to an increase in baclofen-associated complications. Here we report a case of CSA induced by low dose baclofen orally.

Materials and methods: A 60-year-old female patient was admitted to the department of Respiratory and Sleep Medicine, Peking University People's Hospital due to CSA on December 10, 2023. She suffered from nocturnal choking and daytime sleepiness for more than 5 years, and her left lower limb cramped intermittently, as well as cramping of the lower back accompanied by numbness. On November 13, 2023, she underwent a nocturnal PSG in a local hospital which showed AHI 65.5 events/h and the main respiratory events were central apnea. The patient was titrated on continuous positive airway pressure (CPAP) treatment (ResMed, S10). With a pressure of 10 cmH₂O, the reports downloaded from the device showed residual AHI 18.8 events/h, of which CAI 14 events/h. After that, we tried BiPAP (9/5cmH₂O), CPAP (6 cmH₂O) with oxygen 2 L/min, CPAP 7 cmH₂O in sequence. However, the residual AHI has not reached the satisfactory level.

We conducted a series of examinations, including head MRI, echocardiography, long-term video electroencephalogram, lung function and other examinations. we ruled out common causes of CSA. One of the drugs she used "baclofen", aroused our suspicions. Obtaining the patient's consent, baclofen was discontinued. Three days after the withdrawal, a second PSG was conducted and showed a significant decrease of CAI to 1.5 events/h. Then the patient was treated with CPAP (7 cmH₂O). Three days after discharge, we followed up the patient and found that she was well tolerated by CPAP

treatment. The downloaded data of the CPAP device showed the AHI dropped to 4.5 events/h, CAI to 1.1 events/h. Therefore, we further confirmed that the CSA in this patient is associated with baclofen.

Results: Baclofen was associated with a higher risk of CSA in patient with preexisting sleep-related breathing disorders. After withdrawal of baclofen, CSA can be significantly improved.

Conclusions: More attention should be paid to the adverse reactions on respiratory control of baclofen even with low dosage. Regular polysomnography before and after prescription of baclofen is helpful to detect the effects of baclofen on sleep and breathing.

Cephalometric differences between REM and NREM OSA patients may help in choosing the right surgical candidate

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Introduction: Obstructive sleep apnea (OSA) is a prevalent disorder characterized by recurrent upper airway collapse, leading to intermittent hypoxemia and disrupted sleep. Factors such as age, gender, body mass index (BMI), and lifestyle contribute to the severity of OSA, while body position and rapid eye movement (REM) state have been shown to influence its occurrence. The purpose of this study was to find the relationship between anatomical features observed on cephalometry and polysomnographic data in OSA patients.

Materials and methods: This retrospective cohort study included 74 OSA patients who were confirmed with polysomnographic evaluation and took lateral, PA cephalometric and panoramic radiographs. Patients were classified into positional and non-positional OSA categories based on their supine and lateral AHI values. REM-dependent and NREM-dependent OSA status was determined based on the REM and NREM AHI values. Demographic, polysomnographic, and cephalometric data were analyzed, and correlations were explored using Pearson's correlation coefficient.

Results: The study found no significant differences in cephalometric and panoramic parameters between positional and non-positional OSA patients. However, REM-dependent OSA patients showed shorter N-ANS length, shorter perpendicular distance between the anterior hyoid bone and mandibular plane, and longer tongue length compared to NREM-dependent OSA patients. Logistic regression analysis revealed that a narrower nasal cavity and maxilla width, relative to the mandibular width, were significant risk factors for non-positional OSA. In addition, the posterior and inferior position of the hyoid bone and longer tongue length were identified as risk factors for REM-dependent OSA.

Conclusions: The study suggests that anatomical factors, such as the width of the nasal cavity and maxilla, as well as the position of the hyoid bone and tongue length, are associated with the severity and type of OSA. These findings may contribute to the development of targeted treatment strategies, including surgical interventions, for improving upper airway space in OSA patients.

Challenges of acute non-invasive ventilation in patients with schizophrenia

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Introduction: Acute hypercapnic respiratory failure (AHRF) is a life-threatening emergency. Non-invasive ventilation (NIV) is the standard of care, but its delivery can be challenging in patients with significant psychiatric comorbidity. We aim to evaluate the acute outcome for patients with schizophrenia presenting with AHRF requiring NIV

Materials and methods: We conducted a retrospective longitudinal observational cohort study of consecutive admissions to a single tertiary centre for AHRF requiring acute NIV from 1st January 2017 to 31st December 2019. Cases were included if they had underlying chronic obstructive pulmonary

disease (COPD) or overlap between COPD and obstructive sleep apnea (Overlap). We excluded patients requiring invasive ventilation or admissions to intensive care units.

Results: Among the 261 admissions, there were 110 recurrent admissions from 37 individual patients, of which 40.5% had schizophrenia. COPD (83.8%) was the predominant underlying chronic respiratory condition. Patients with schizophrenia were significantly younger (63.7 ± 9.8 vs 76.1 ± 8.7 , $p = 0.000$) and less likely to be on domiciliary respiratory support (26.7% vs 59.1 %, $p = 0.052$). Mean initial pH from blood gas was 7.3 in both but patients with schizophrenia were assessed to have lower level of consciousness and to be more challenging for acute NIV therapy. Patients with schizophrenia had shorter duration of hospitalisation (7 vs 9.5 days, $p = 0.004$) and acute NIV therapy (3 vs 5 days, $p = 0.026$). They also had shorter median time to readmission (18 vs 69 days, $p = 0.017$). Multivariate log regression showed chronic schizophrenia was the only independent predictor of recurrent admissions for acute NIV therapy (odds ratio 7.277, $p = 0.008$).

Conclusions: Patients with comorbidity of chronic schizophrenia may pose a unique challenge to acute NIV therapy. Though the duration of acute NIV therapy and hospitalization may be shorter, they have a higher risk of recurrent admissions for AHRF requiring acute NIV.

Change in Peripheral Apnea-Hypopnea Index (pAHI), and Body Weight in Participants with moderate-to-severe OSA with Obesity from SURMOUNT-OSA

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Introduction: Obstructive sleep apnea (OSA) is a breathing disorder associated with cardiovascular comorbidity and mortality. Obesity represents a major modifiable risk factor for OSA. SURMOUNT-OSA is a master protocol guiding 2 placebo-controlled trials investigating the efficacy and safety of tirzepatide in participants with OSA and obesity. Each trial had the primary endpoint of change in apnea-hypopnea index (AHI) measured by laboratory polysomnography (PSG). In this pre-specified analysis of SURMOUNT-OSA, we also report the change in peripheral apnea-hypopnea index (pAHI) measured using WatchPAT, a home sleep study device which uses peripheral arterial tone technology, and the corresponding change in body weight.

Materials and methods: SURMOUNT-OSA master protocol guided two double-blind, randomized, placebo-controlled phase 3 clinical studies including participants with moderate-to-severe OSA and obesity to determine the efficacy and safety of once-weekly (QW) tirzepatide at the maximum tolerated dose (MTD). Study 1 included those unable or unwilling to use PAP therapy and Study 2 included those on PAP therapy at study entry. WatchPAT measurements were collected at Week 0, 4, 12, 20, and 52 for participants in Study 1 ($n = 117$ at baseline, $n = 59$ assigned to tirzepatide and $n = 58$ on placebo). The mixed model repeated measures (MMRM) statistical analysis was conducted based on the data points from modified intent-to-treat (mITT) participants, collected on treatment and not on PAP for Study 1.

Results: The change from baseline in pAHI and percent change from baseline in body weight among participants in Study 1 are reported. A statistically significant change in pAHI versus baseline was observed as early as at week 4 (-2.2 , $p = 0.455$) and week 12 (-6.5 , $p = 0.064$), statistically significant change vs placebo was observed at week 20 (-10.8 , $p < 0.001$) and week 52 (-15.1 , $p < 0.001$) in participants treated with tirzepatide. Even with a smaller sample size ($n = 31$ and $n = 32$ for tirzepatide and placebo at Week 52, respectively), the effect size is comparable to previously reported PSG data collected at baseline, Week 20 and Week 52. Reductions in pAHI with tirzepatide treatment were accompanied by a statistically significant and clinically relevant decreases in body weight at all timepoints measured ($p < 0.001$ versus placebo).

Conclusions: Treatment with tirzepatide reduced pAHI in participants with moderate-to-severe OSA and obesity as early as in Week 4 after treatment initiation, with statistical significance in comparison with placebo from Week 20. Reductions in pAHI were accompanied by a statistically significant decrease in body weight.

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Changes in EEG functional connectivity in patients with obstructive sleep apnea and cardiovascular diseases

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Introduction: Obstructive sleep apnea (OSA) and cardiovascular diseases (CVD) are among the most common comorbid conditions. They share several risk factors, including obesity, smoking, and alcohol consumption, as well as overlapping pathophysiological mechanisms such as sympathetic hyperactivation, hypoxemia, and alterations in intrathoracic pressure and haemodynamics (Zamarrón C. et al. *Pulm Med.* 2013). Beyond their systemic effects, both OSA and CVD contribute to impaired cognitive functioning and disrupted sleep architecture, which further exacerbates patients' quality of life and disease progression (Lal C. et al. *Chest.* 2012; Pinsky MR. *Chest.* 2002).

The study aimed to evaluate the effects of OSA and CVD on the central nervous system during sleep through quantitative EEG analysis of polysomnography (PSG) data.

Materials and methods: A total of 154 patients aged 18–75 years were enrolled in the study.

According to the study design, participants were divided into four groups: conditionally healthy controls (n = 39), patients with significant (AHI ≥ 15 events/h) OSA (n = 23), patients with CVD (n = 25), and patients with both significant OSA and CVD (n = 67).

Quantitative EEG analysis of PSG recordings included wavelet bicoherence calculation (Zhuravlev M. et al. *Clocks Sleep.* 2024). Wavelet bicoherence was computed for the entire recording period pairwise between 6 EEG channels across 14 frequency bands (Table 1). These bands corresponded to typical EEG rhythms observed during sleep.

Results: Interhemispheric brain connectivity:

Occipital (O2–O1): Significant decrease in OSA patients across low-frequency bands (0.2–8.0 Hz, $p < 0.05$), most pronounced at 1.0–4.0 Hz ($p = 0.001$). Patients with CVD and comorbid patients showed a similar trend, but without significant differences compared to healthy controls.

Central (C4–C3): Significant decrease in OSA and OSA+CVD groups across a wide frequency range (Δf_1 – Δf_8 , Δf_{12}), with the strongest differences at 1.0–4.0 Hz and 4.0–6.0 Hz ($p < 0.001$). In CVD patients, significant reduction was observed at 6.0–8.0 Hz.

Frontal (F4–F3): A general trend toward reduced connectivity across all patient groups compared to healthy controls; significant only at 0.2–1.0 Hz ($p = 0.034$).

Left frontal – right occipital (F3–O2): Increase in patients with CVD and OSA+CVD compared to controls across Δf_5 – Δf_7 ($p < 0.001$).

Significant patterns of intrahemispheric brain connectivity:

Right fronto-occipital (F4–O2): Increase in patients with OSA+CVD across a wide frequency range (Δf_2 – Δf_{14} , $p < 0.05$). Patients with OSA showed an increase predominantly in alpha range (8.0–14.0 Hz, $p < 0.05$).

Left fronto-occipital (F4–O2): Increase in patients with OSA+CVD across a wide frequency range (Δf_2 – Δf_{10} and Δf_{12} – Δf_{14} , $p < 0.05$).

Conclusions: The study demonstrated that patients with OSA and CVD exhibit distinct alterations in EEG functional connectivity during sleep. Interhemispheric connectivity was reduced in frontal, central, and occipital regions, particularly in low-frequency bands, while intrahemispheric connectivity showed compensatory increases, especially in comorbid patients. These findings highlight disrupted neural

communication in OSA and CVD and suggest that quantitative EEG measures such as wavelet bicoherence may serve as useful markers of brain functional alterations in these pathologies.

Characteristics of Obstructive Sleep Apnea Syndrome in Patients with Chronic Obstructive Pulmonary Disease

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Introduction: The combination of chronic obstructive pulmonary disease (COPD) and obstructive apnea syndrome during sleep is called the overlap syndrome.

Objectives: To describe the clinical features and clinical approach of COPD patients without or with obstructive apnea syndrome during sleep (overlap syndrome). And: To assess the polygraphs among two groups.

Materials and methods: A descriptive study in 60 patients with COPD who were chosen in the Respiratory Center at Bach Mai Hospital in 8 months.

Results: Proportion of the Epworth score ≥ 10 in patients with sleep apnoea syndrome (overlap) 32.5%. Rate SAS/COPD: 66.7%. Median AHI of the overlap: 16.6 ± 10.2 . SpO₂ min in group overlap is lower than COPD without sleep apnoea syndrome (79.9 ± 13.9 and 86.3 ± 7.8 ; $p < 0.05$). The difference of pulmonary artery pressure between the groups was statistically significant: AHI < 5 : 41.2 ± 10.1 ; $5 \leq \text{AHI} < 15$: 36.2 ± 7.5 ; $15 \leq \text{AHI} < 30$: 38.9 ± 9.3 ; AHI ≥ 30 : 75.7 ± 21.1 ; $p < 0.005$.

Conclusions: The association between SAS and COPD increased the risk of night-time hypoxemia and pulmonary arterial hypertension.

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Characterization of Craniofacial Skeletal Phenotype of Adult Obstructive sleep apnea

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Introduction: To analyze three-dimensional craniofacial characteristics influencing the severity of obstructive sleep apnea (OSA) and to investigate the differences in craniofacial features and various polysomnography (PSG) indices indicating OSA severity between craniofacial skeletal phenotype (CSP) and non-craniofacial skeletal phenotype (N_CSP).

Materials and methods: The frequency distribution of three-dimensional skeletal patterns was analyzed based on Sex, BMI, and OSA severity using CBCT of 142 adult OSA patients. Among them, demographic, PSG, and CBCT characteristics of the final 100 patients were classified by sex, OSA severity, and skeletal pattern, and comparisons were made between groups. Multiple linear regression analysis was performed to characterize the three-dimensional craniofacial features of CSP.

Results: Sagittally, patients with skeletal Class II pattern exhibited more severe OSA severity compared to those with Class I, despite being younger. Vertically, patients with hyperdivergent pattern showed higher OSA severity than those with normodivergent pattern, despite being younger and less obese. Transversely, the group with Transverse Skeletal Discrepancy (TSD) showed more severe OSA severity. After adjusting for age, sex, and obesity, multiple linear regression analysis revealed that ANB, Pharyngeal Minimal Cross-Sectional Area (PMCA), and Transverse Discrepancy Index (TDI) were craniofacial predictors of OSA severity. CSP_{2D} group exhibited higher OSA severity in all PSG variables except the hypopnea index compared to N_CSP group, despite being younger and less obese. CSP_{3D} group, which included TSD, showed more severe OSA severity than CSP_{2D} group, with smaller nasal airway volume and PMCA, and longer pharyngeal airway length.

Conclusions: This study is the first attempt to comprehensively analyze TSD and to characterize CSP_{2D} and CSP_{3D} OSA groups by incorporating three-dimensional information of both the nasal / pharyngeal airways and relating upper airway features to PSG variables. This provides evidence for a phenotype-

based precision approach, which should be the foundation for the diagnosis and treatment of OSA patients.

Characterizing blood pressure responses to sleep apnea by sleep stage and sleep position

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Introduction: Obstructive sleep apnea (OSA) events trigger a cascade of physiological responses that involve autonomic system, leading to fluctuations in blood pressure (BP). These fluctuations, combined with sustained autonomic changes, can contribute to the development of hypertension and increase the risk of cardiovascular complications. Conventional belief is that at the end of an apneic event, BP increases as a result of sympathetic surge. However, our observation has been that BP responses to OSA event are heterogeneous. Given different autonomic modulation across sleep stages and OSA intensity across sleep positions, we hypothesized that post-apneic BP responses would differ by sleep stages and sleep positions.

Materials and methods: Prospectively enrolled patients with a history of OSA underwent research home polysomnography studies. Continuous BP was estimated by pulse arrival time using a commercially available software (DOMINO software). For the purpose of this analysis, post-event period was defined by the period from the onset of an apneic event to first 10 seconds post-event. Pre-event period was defined by 10 second period preceding the onset of an apneic event. The outcome of interest was the systolic BP (SBP) (peak BP in either direction during apneic and post apneic period minus mean SBP during pre-apneic period). Changes were classified as drop (≤ -1 mmHg), modest rise (1–10 mmHg), or large rise (> 10 mmHg). Events were categorized by sleep stage, sleep body position, and pre-event baseline BP (hypertension: SBP >140 vs. Normotensive: SBP 90–140 vs. hypotensive: SBP <90 mmHg).

Results: We included 24 subjects (mean age: 48 years, female 25%) with various OSA severity (median Apnea hypopnea index [AHI] 10/hr), contributing a total of 2086 apneic events (either apnea or hypopnea). Overall, the most common pattern of BP response was modest rise (63.1%), followed by large rise (20.7%), and decrease (16.2%). The distribution of post event BP pattern was not different across sleep stages (N1: 68 vs. 20.3 vs. 11.7%; N2: 62.5 vs. 21.1 vs. 16.4%; N3 62.1 vs. 21.2 vs. 16.7%; REM: 60 vs. 20 vs. 20%, $p=0.76$). Similarly, the distribution of post event BP pattern was not different across sleep positions (supine: 62.8 vs. 21 vs. 16.2%; left: 66.2 vs. 17.6 vs. 16.2%, ; right: 57.8 vs. 25.9 vs. 16.4%, $p=0.236$). However, the distribution was different based on the pre-event baseline BP status. (hypertension: 56.8 vs. 25.4 vs. 17.9%; normotensive: 69.2 vs. 14 vs. 16.8%; hypotensive: 17.9 vs. 82.1 vs. 0%, $p<0.0001$). Pre-event baseline hypotension was associated with the absence of post-event BP decrease.

Conclusions: BP responses to apneic events were heterogeneous but largely showed the expected rise. Modest rise was the most common post-event BP response, followed by large rise, and decrease. This finding was consistent across sleep stages or sleep positions. In contrast, post-event BP pattern was significantly different based on the pre-event BP level.

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Chronic Intermittent Hypoxia Impairs Genioglossus Activity and Alters Upper Airway Negative Pressure Reflex in a Rat Model

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Introduction: This study aimed to investigate the effects of chronic intermittent hypoxia (CIH) on upper airway neuromuscular regulation in a rat model. Electromyographic activity of the genioglossus muscle was recorded to assess functional changes. Additionally, graded negative pressure was applied to the pharyngeal cavity to evaluate alterations in the negative pressure reflex, providing insight into how CIH may influence upper airway stability in sleep-disordered breathing.

Materials and methods: In this study, 34 healthy male Sprague-Dawley rats were randomly assigned to either a control group (n=10) or a CIH group (n=24). Chronic intermittent hypoxia (CIH) was induced by exposing rats to alternating hypoxic/normoxic conditions (7%–21% O₂) for 8 hours daily (9:00–17:00) over a 10-week period. Custom-designed unilateral nasal blockers of varying sizes were used to increase inspiratory effort by partially obstructing nasal airflow, thereby simulating increased negative pharyngeal pressure. Pharyngeal pressure gradients under different obstruction conditions were recorded. Electromyographic (EMG) activity of the genioglossus muscle was measured at baseline and under graded negative pressure stimulation applied to the pharyngeal cavity at weeks 4, 7, and 10. The control group was maintained under normoxic conditions. At the end of the study, all rats were euthanized, and genioglossus muscle samples were harvested for histological analysis via hematoxylin and eosin (HE) staining.

Results: At week 4 of CIH exposure, genioglossus EMG activity significantly increased ($96.36 \pm 6.78 \mu\text{V}$ vs. $59.55 \pm 3.76 \mu\text{V}$, $P < 0.001$), indicating compensatory activation. However, EMG activity declined significantly by week 7 ($64.36 \pm 3.30 \mu\text{V}$), and returned to baseline by week 10 ($58.64 \pm 17.17 \mu\text{V}$, $P > 0.05$). In both control and CIH groups, EMG activity increased in response to graded negative pharyngeal pressure ($P < 0.05$), though this reflex weakened over time in the CIH group. Histological analysis revealed that CIH caused muscle fiber disarray, irregular morphology, and disrupted nuclear distribution in the genioglossus.

Conclusions: Upper airway negative pressure enhances genioglossus activity in a pressure-dependent manner. Short-term CIH induces compensatory neuromuscular activation, but prolonged hypoxic exposure impairs this response and leads to structural muscle damage. These findings highlight the time-dependent impact of CIH on upper airway dilator muscle function, providing insights into the pathophysiology of OSA-related upper airway collapse.

Clinical Application of Pediatric Sleep Endoscopy: An International Survey

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Introduction: To investigate through an international survey the actual clinical application of drug-induced sleep endoscopy (DISE) in pediatric patients with obstructive sleep apnea (OSA) and to clarify the use, application, clinical indications, and protocol of pediatric DISE.

Materials and methods: A specific survey about pediatric DISE was initially developed by five international otolaryngologists with expertise in pediatric sleep apnea and drug-induced sleep endoscopy and was later spread to experts in the field of sleep apnea, members of different OSA-related associations.

Results: A total of 101 participants who answered all the survey questions were considered in the study. Sixty-four sleep apnea experts, equivalent to 63.4% of interviewed experts, declared they would perform DISE in pediatric OSA patients. A total of 81.9% of responders agreed to consider the DISE as the first diagnostic step in children with persistent OSA after adenotonsillectomy surgery, whereas 55.4% disagreed with performing DISE at the same time of scheduled adenotonsillectomy surgery to identify other possible sites of collapse. In the case of young patients with residual OSA and only

pharyngeal collapse during DISE, 51.8% of experts agreed with performing a velopharyngeal surgery. In this case, 27.7% disagreed and 21.4% were neutral.

Conclusions: Pediatric DISE is internationally considered to be a safe and effective procedure for identifying sites of obstruction and collapse after adenotonsillectomy in children with residual OSA. This is also useful in cases of patients with craniofacial malformations, small tonsils, laryngomalacia or Down syndrome to identify the actual site(s) of collapse. Despite this evidence, our survey highlighted that pediatric DISE is not used in different sleep centers.

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Clinical Characteristics and Management Outcomes of Congenital Central Hypoventilation Syndrome: A Single-Center Case Series

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Introduction: Congenital central hypoventilation syndrome (CCHS) is a rare disorder of autonomic nervous system dysregulation caused by mutations in the PHOX2B gene. It manifests with central alveolar hypoventilation, cardiac arrhythmias, gastrointestinal dysmotility, and neurocognitive impairment. Although typically presenting in the neonatal period, atypical presentations such as obstructive sleep apnea (OSA) prior to hypoventilation have been reported. Advances in early genetic diagnosis, multidisciplinary ventilatory strategies, and annual respiratory evaluations have significantly improved outcomes. This study aimed to describe the clinical characteristics, genetic findings, ventilatory management, comorbidities, neurocognitive outcomes, and long-term outcomes of patients with CCHS treated at King Chulalongkorn Memorial Hospital, Thailand.

Materials and methods: This retrospective chart review included patients diagnosed with CCHS between July 2005 and June 2025, confirmed by PHOX2B genetic testing. Data collected included demographics, genotype, initial clinical presentations, ventilatory modalities, associated comorbidities, neurodevelopmental assessments, and outcomes from annual respiratory evaluations. Descriptive statistics were used to summarize findings.

Results: A total of seven patients were included. The median age at diagnosis was birth. Six patients were diagnosed in the neonatal period, and one was diagnosed at 7 years of age. Four patients (57.1%) were male. Genetic testing revealed that all patients (100%) had polyalanine repeat mutations (PARMs); no non-polyalanine repeat mutations (NPARMs) were identified. Initial manifestations included neonatal hypoventilation and desaturation. Six patients (85.7%) initially required positive-pressure ventilation via tracheostomy (PPV-T). Three patients (50%) successfully transitioned to noninvasive ventilation (NIV) following structured protocols, with a mean transition age of 6.5 years. Comorbidities included Hirschsprung disease (14.3%) and neurodevelopmental delays (57.1%), while no cardiac arrhythmias were observed. Annual respiratory evaluations led to modifications in ventilatory management in all patients (100%). At the latest follow-up, six patients (85.7%) required nighttime-only ventilation, while one patient (14.3%) remained on continuous support. No deaths were observed.

Conclusions: CCHS presents with a heterogeneous and evolving clinical phenotype. Early identification of PHOX2B mutations, vigilant monitoring for autonomic comorbidities, neurodevelopmental surveillance, and proactive respiratory management are essential for optimizing long-term outcomes.

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Combined anterior palatoplasty with barbed suspension pharyngoplasty in the treatment of obstructive sleep apnea

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Introduction: Surgery is an alternative treatment to positive airway pressure therapy for obstructive sleep apnea (OSA) patients. Various palatal surgical techniques have been developed. However, medical literature has limited accounts on the use of a combination of these techniques to improved outcomes.

Materials and methods: Data of OSA patients who underwent a combined anterior palatoplasty (AP) with barbed suspension pharyngoplasty (BSP) between July 2020 to May 2024 were retrospectively reviewed. The surgical outcomes, including apnea-hypopnea index (AHI), lowest oxygen saturation (LSAT), snoring scores, Epworth Sleepiness Scale (ESS), and post-operative complications were collected.

Results: Twenty-four patients which showed retropalatal or oropharyngeal obstruction were included in our study, with thirteen patients (54.2%) underwent post-operative polysomnography with a mean follow-up time of 5.8 ± 2.2 months. The median (IQ-IIIQ) AHI decreased non-significantly from 27.3 (19.8-53.2) to 20.2 (14.4-37.0) events/h ($p = 0.216$) post-operatively. The median (IQ-IIIQ) snoring scores significantly improved from 6.0 (4.0-8.0) to 3.0 (0-4.0) ($p < 0.001$) and ESS decreased from 11.0 (9.2-14.8) to 6.5 (4.0-9.8) ($p < 0.001$). LSAT did not change in this study. There were no serious post-operative complications.

Conclusions: The combined technique of AP and BSP was safe and significantly improved snoring scores and reduced daytime sleepiness in OSA patients with retropalatal and oropharyngeal obstruction. Improvement in AHI was observed in some patients.

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Combined Hypoglossal Nerve and Ansa Cervicalis Stimulation Outperforms Single Interventions in Maintaining Airway Patency in Patients with Obstructive Sleep Apnea

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Introduction: Ansa cervicalis stimulation (ACS) is emerging as a promising neurostimulation therapy for obstructive sleep apnea (OSA). ACS enhances pharyngeal patency by mimicking the caudal tracheal traction effect. Research indicates that ACS is particularly effective at reducing airway collapsibility in the palatal, oropharyngeal lateral wall, and epiglottic regions, whereas hypoglossal nerve stimulation (HNS) primarily targets tongue-driven airway obstruction at the tongue base and velopharynx. Given their distinct mechanisms, we hypothesize that ACS and HNS may interact to further enhance airway stability. This study aims to determine whether combining ACS and HNS improves airway patency more effectively than either method alone in patients with OSA.

Materials and methods: Fifty-three participants with moderate-to-severe OSA (Age: 55.4 ± 10.2 years; Male: 36; body mass index [BMI]: $32.1 \pm 3.2 \text{ kg/m}^2$; apnea-hypopnea index [AHI]: 39.8 ± 19.9 events/hour) underwent unilateral HNS and bilateral ACS via hook-wire percutaneous electrodes during drug-induced sleep endoscopy. Stimulation was individually titrated to optimize airway dilation without causing arousal. Maximum inspiratory airflow (V_{imax}) was measured with a pneumotachometer during flow-limited breathing while lowering nasal pressure (P_N) in a stepwise fashion. The V_{imax} vs. P_N relationship was constructed to quantify pharyngeal collapsibility as the critical closing pressure (P_{CRIT}) and the opening pressure (P_{OPEN}). A linear mixed-effect model was used to evaluate airflow changes per breath, and univariate regression to assess the influence of patient characteristics—including age, sex, BMI, and AHI—on P_{CRIT} and P_{OPEN} responses.

Results: Combining HNS and ACS significantly reduced airway collapsibility, decreasing P_{CRIT} (median [Q1, Q3]: -4.1 [-7.5, -2.4] cmH_2O) and P_{OPEN} (-5.7 [-7.4, -3.2] cmH_2O) from baseline ($p < 0.001$). The decreases were greater than those observed with HNS alone (ΔP_{CRIT} : -2.1 [-5.2, -1.0] cmH_2O , $p = 0.004$; ΔP_{OPEN} : -3.2 [-5.6, -0.7] cmH_2O , $p < 0.001$) and ACS alone (ΔP_{CRIT} : -2.1 [-3.7, -1.1] cmH_2O , $p < 0.001$; ΔP_{OPEN} : -2.8 [-5.4, -1.4] cmH_2O , $p < 0.001$). In 10 patients, combined stimulation completely abolished

flow limitation, bringing P_{CRIT} and P_{OPEN} below atmospheric pressure. The mixed-effect model exhibited a significant increase in V_{max} by 301.7 mL/s ($p < 0.001$) compared to baseline, surpassing the improvements achieved with ACS (145.2 mL/s, $p = 0.006$) and HNS (85.7 mL/s, $p < 0.001$). The enhancement in airway stability during combined stimulation was superior to either stimulation alone ($\Delta\Delta P_{CRIT} = -1.7$; $\Delta\Delta P_{OPEN} = -2.3$ cmH₂O for ACS, $\Delta\Delta P_{CRIT} = -1.0$; $\Delta\Delta P_{OPEN} = -1.8$ cmH₂O for HNS, $p < 0.005$). Patient characteristics did not significantly impact the combined stimulation response.

Conclusions: The combined use of HNS and ACS significantly reduced pharyngeal collapsibility beyond the effects of either intervention alone. Importantly, its efficacy remained independent of baseline BMI and AHI, highlighting its potential for widespread application across diverse patient groups. These results further support the feasibility of combined HNS and ACS as an effective neurostimulation therapy for OSA.

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Combined Ventilatory Control and Upper Airway Mechanical Therapy for Obstructive Sleep Apnea: A Randomized-Controlled Mechanistic Trial

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Introduction: Treatment of obstructive sleep apnea (OSA) is hampered by poor adherence to continuous positive airway pressure therapy. Although OSA arises from both upper airway collapsibility and ventilatory control instability, few randomized trials have addressed both mechanisms simultaneously. We evaluated whether combining a ventilatory control intervention (supplemental oxygen) with a mechanical intervention targeting the upper airway (mandibular advancement device, MAD) could enhance treatment effectiveness.

Materials and methods: In a multicenter randomized crossover trial, 41 individuals with moderate-to-severe OSA (apnea-hypopnea index [AHI] >20 events/hour, scored without requiring oxygen desaturations) underwent polysomnography across four single-night interventions: supplemental oxygen (4 L/min), mandibular advancement device (MAD), combination therapy, and sham (air). The primary analysis assessed the percent change in AHI from baseline, comparing combination therapy with MAD monotherapy. Secondary outcomes included the arousal index and sleep quality as rated by a visual analog scale (VASSQ). Baseline pathophysiological traits, measured using gold-standard methods (oronasal mask and pneumotach plus esophageal pressure catheter), facilitated mechanistic subgroup analyses.

Results: Of the 41 patients randomized (14 female, 27 male; baseline AHI: 49 [29, 62] events/hour; median [interquartile range]), 38 completed all intervention nights. Compared to sham, AHI was reduced with oxygen (estimate [CI]: -33% [-46, -17]), MAD (-54% [-64, -41]), and the combination therapy (-68% [-77, -57]); the combination yielded a significantly greater reduction than MAD alone (-14% [-23, -4], $P = 0.009$). Similar improvements were observed using AHI scored with 3% desaturation or arousal criteria (-73% [-81, -62] vs. sham; -17% [-25, -7] vs. MAD). Combination therapy also reduced arousal index (-36% [-43, -27] vs. sham, -6.5% [-13.9, 1.6] vs. MAD), improved self-reported sleep quality (VASSQ: +0.98 [0.39, 1.58] vs. sham; +0.3 [-0.3, 0.9] vs. MAD), plus exploratory outcomes including reduced stage 1 sleep proportion (-10.9% [-15.7, -6.1] vs. sham; -2.7% [-7.4, 2.1] vs. MAD), lowered morning mean arterial blood pressure (-2.7 [-5.3, -0.1] mmHg vs sham, -2.9 [-5.5, -0.3] mmHg vs MAD), and improved EEG-based measure of wake-versus-sleep likelihood (-0.45 [-0.88, -0.03] units vs. sham; -0.19 [-0.61, 0.23] units vs MAD); note only morning blood pressure was improved by more with MAD alone. Combination therapy effects were most pronounced in participants with higher loop gain and greater upper airway collapsibility. Further mechanistic analysis revealed that MAD monotherapy responders had distinctly different traits compared with oxygen monotherapy responders. Formal assessment of interactions illustrated a additive effects of oxygen and MAD, with no less-than-additive component.

Conclusions: Combining a ventilatory control intervention (supplemental oxygen) with an upper airway intervention (MAD) is a promising approach to markedly attenuate OSA severity beyond that offered by each intervention alone. This treatment approach yields additive results and provides a novel strategy to benefit patients with the most severe ventilatory control and upper airway mechanical deficits who are otherwise the most challenging to treat.

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Comparative Analysis of Three Hypoxic Burden Calculation Methods and Their Association with Incident Congestive Heart Failure

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Introduction: The apnea-hypopnea index (AHI) is a widely used metric for assessing obstructive sleep apnea (OSA) severity but has limitations in capturing the physiological burden of intermittent hypoxia. Hypoxic burden (HB), which quantifies the depth of all oxygen desaturations, is a better marker of cardiovascular risk. However, HB calculation methods vary between studies and have not been standardized. Some argue that only oxyhemoglobin saturation (SpO₂) levels below 90% are relevant for prediction of cardiovascular risk. This study compares the prognostic performance of AHI and three different HB calculation methods in predicting incident congestive heart failure (CHF) in a large, population-based cohort.

Materials and methods: We analyzed data from 5,791 participants in the Sleep Heart Health Study (SHHS), excluding those with prior CHF, treated apnea or missing data, resulting in a final cohort of 5,256. HB was automatically derived from overnight SpO₂ signals using three methods: (1) HB-1, calculated as the area between the desaturation curve and a linear interpolation from the SpO₂ value at desaturation onset to the recovery point; (2) HB-2, calculated as the area between the desaturation curve and a horizontal baseline defined by the highest SpO₂ value within 100 seconds prior to desaturation onset; and (3) HB-3, calculated as the area above the SpO₂ curve and below a fixed 90% SpO₂ threshold. Time-to-event analyses were performed using Cox proportional hazards models, adjusted for age, sex, and race to assess the association between each HB and incident CHF. Both HB and AHI were examined as continuous variables using log₁₀-transformation to address nonlinearity. Model predictive performance was assessed using concordance (C) statistics. Hazard ratios (HR), 95% confidence intervals (CI), and p-values were calculated to assess variable-outcome associations, with significance set at p-value <0.05.

Results: The analysis revealed that all three HB methods were significantly associated with incident CHF. In the adjusted model, HB-1 (HR 1.802, 95% CI: 1.187–2.735; p=0.006) demonstrated a stronger association with CHF compared to AHI (HR 0.804, 95% CI: 0.553–1.169; p=0.253). Similar findings were observed for HB-2 (HR 1.774, 95% CI: 1.195–2.634; p=0.005) versus AHI (HR 0.802, 95% CI: 0.554–1.159; p=0.240). HB-3 (HR 1.135, 95% CI: 1.013–1.271; p=0.023), was also significantly associated with CHF, although less predictive than HB-1 and HB-2. AHI (HR 1.110, 95% CI: 0.861–1.430; p=0.422) showed no significant association and with lower predictive power compared to the other HB methods. C-statistics for the adjusted model showed a high concordance (C=0.807, SE=0.008), indicating that the model had strong predictive performance. HB-1 and HB-2 remained significant predictors of CHF, HB-1 being the most predictive. In comparison, AHI did not show a significant association with CHF, emphasizing that HB was a better and more reliable predictor than AHI.

Conclusions: The method used to calculate HB significantly influences its predictive value for incident CHF. The restriction of SpO₂ levels below 90% (HB-3) has a worse performance than previous reported methods (HBI-1 and HBI-2). Our findings confirm that HB is a superior predictor of cardiovascular outcomes compared to AHI.

Acknowledgments: Cohort data provided by SHHS.

Comparative Assessment of Diaphragm Morphofunctional Alterations in Obstructive Sleep Apnea, Chronic Obstructive Pulmonary Disease, and Overlap Syndrome

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Introduction: Obstructive Sleep Apnea (OSA) and Chronic Obstructive Pulmonary Disease (COPD) are both prevalent respiratory disorders globally. Their coexistence as Overlap Syndrome (OS) imposes a higher risk of nocturnal hypoxemia, morbidity, and mortality. While diaphragm dysfunction is well-established in COPD, its morphofunctional status in OS patients remains unclear. This study aimed to systematically compare diaphragm morphology and function among OSA, COPD, OS patients, and healthy controls using ultrasonography.

Materials and methods: We conducted a single-center cross-sectional study at the Sleep Center of a general hospital. Participants underwent overnight polysomnography (PSG) and spirometry. Based on PSG and pulmonary function test results, participants were categorized into four groups: OSA (n=50), COPD (n=22), OS (n=15), and healthy controls (n=16). Diaphragm morphology (thickness and thickening ratio) and function (mobility during quiet and deep breathing) were assessed using standardized ultrasonography protocols by experienced operators blinded to clinical data. Sleep indices, pulmonary function parameters, and diaphragm metrics were compared among groups. Spearman correlation analysis was performed to examine the associations between diaphragm parameters, AHI, and pulmonary function indicators.

Results: COPD patients exhibited significantly reduced diaphragm thickness and mobility compared to all other groups ($P<0.001$). OS patients showed preserved diaphragm thickness but impaired diaphragmatic mobility versus healthy controls ($P<0.05$). AHI positively correlated with diaphragm thickness ($r=0.572$, $P<0.01$), while FEV1/FVC and FEV1%pred were significantly associated with both diaphragm thickness and mobility ($P<0.001$). OS patients demonstrated the longest duration of nocturnal $SpO_2<90\%$, highlighting their unique hypoxemic burden.

Conclusions: COPD patients exhibited significantly reduced diaphragm thickness, which was inversely correlated with pulmonary function severity. In contrast, OS patients showed preserved diaphragm morphology, including thickness and thickening ratio comparable to healthy controls, but demonstrated significantly reduced diaphragmatic mobility, indicating functional impairment despite morphological preservation. These findings highlight the distinct diaphragm morphofunctional profiles among OSA, COPD, and OS patients, underscoring the need for targeted diaphragm function assessment in OS patients to guide early interventions.

Comparative Effects of Nasal and Oronasal Masks on Airway Collapse and Oxygenation During CPAP-Assisted DISE

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Introduction: Mask type can influence the effectiveness of CPAP therapy in patients with obstructive sleep apnea (OSA). However, how nasal versus oronasal masks differ in their anatomical and physiological effects remains unclear. We aimed to compare their impact on site-specific upper airway collapse and oxygen saturation during CPAP titration using drug-induced sleep endoscopy (DISE).

Materials and methods: In this randomized crossover study, 30 patients with OSA underwent DISE and polysomnography using both nasal and oronasal masks. CPAP was delivered in incremental steps (0–20 cmH_2O), and airway collapse at four VOTE regions (Velum, Oropharynx, Tongue base, Epiglottis) was scored at each pressure level. Pharyngeal opening pressure (PhOP) was defined as the pressure required to reduce VOTE score 2 obstruction. Oxygen saturation was simultaneously monitored.

Results: Nasal masks significantly improved obstruction at the velum, oropharynx, and tongue base at 10 cmH_2O , whereas oronasal masks improved only oropharyngeal collapse. The PhOP required to alleviate velum obstruction was significantly lower with nasal masks (Vap: 6.0 [4.0–10.0] vs 16.0 [11.0–

22.0] cmH₂O, $p < 0.001$). Nasal masks also yielded significantly higher SpO₂ between 6–12 cmH₂O. No mask type adequately resolved epiglottic collapse.

Conclusions: Compared to oronasal masks, nasal masks more effectively resolved airway obstruction and improved oxygenation during CPAP titration. These findings support the preferential use of nasal interfaces when feasible and suggest the need for individualized mask selection based on anatomic response and physiological outcome.

Comparative efficacy, safety and benefit/risk of alerting agents for excessive daytime sleepiness in patients with obstructive sleep apnoea: A network meta-analysis

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Introduction: Obstructive sleep apnoea (OSA) is a common chronic respiratory disease associated with a high burden of disabilities related to sleepiness and reduced quality of life. Despite first-line treatment with continuous positive airway pressure (CPAP) therapy, many patients experience residual EDS. Pharmacological treatment options authorised in Europe and/or the United States are modafinil/armodafinil, solriamfetol, and pitolisant. In the absence of head-to-head trials, the relative efficacy and safety of these agents is largely unknown.

Materials and methods: Randomised controlled trials (RCTs) that compared the efficacy and safety of authorised medications for OSA were analysed using network meta-analysis. The primary efficacy endpoint was combined Epworth Sleepiness Scale (ESS) and Oxford Sleep Resistance (OSLER)/Maintenance of Wakefulness Test (MWT) Z-scores. Quality of life (QoL), overall and cardiovascular safety, and benefit-risk ratios were calculated.

Results: Of 4017 studies identified, a total of 20 RCTs involving 4015 subjects were included. Analysis of combined subjective (ESS) and objective (OSLER/MWT) efficacy outcome Z-scores showed that solriamfetol (150 mg; effect size [ES]=0.66 [95% CI: 0.36, 0.96]), and pitolisant (20 mg; ES=0.66 [95% CI: 0.44, 0.88]), modafinil (200 mg; ES=0.53 [95% CI: 0.33, 0.73]); 400 mg; ES=0.53 [95% CI: 0.42, 0.64]) had a clinically meaningful improvement in efficacy. P-scores ranked placebo, then pitolisant, modafinil 200 mg, modafinil 400 mg and solriamfetol for overall safety; and pitolisant, then solriamfetol, modafinil 400 mg and modafinil 200 mg for benefit-risk ratio.

Conclusions: Pitolisant, solriamfetol and modafinil had comparable efficacy for maintaining wakefulness in patients with OSA. Pitolisant had a better safety profile and benefit-risk ratio compared with solriamfetol and modafinil. The overall and cardiovascular safety risk ratios suggest that pitolisant might be the best candidate for OSA patients with multiple cardiovascular comorbidities.

Comparative study of the prognostic value of hypoxic burden, nocturnal desaturation and apnea-hypopnea index on incident cardiovascular events. The HARPA score

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Introduction: Several retrospective, population-based studies suggest that hypoxic burden (HB) provides greater prognostic value for cardiovascular events (CVE) than traditional indices such as the apnea-hypopnea index (AHI) or oxygen desaturation index (ODI) in patients with obstructive sleep apnea (OSA).

HB is a novel metric that integrates the cumulative impact of nocturnal desaturations considering their frequency, depth, and duration, and may offer superior predictive accuracy.

We aimed to compare the prognostic performance of HB with conventional polygraphic parameters, including AHI and nocturnal desaturation, for incident CVE in patients with OSA.

Materials and methods:

We conducted a single-center, prospective, longitudinal study in consecutive patients with OSA, excluding those on well-tolerated CPAP therapy. Sleep studies were performed using respiratory polygraphy, and HB was calculated with dedicated software as the total area under the oxygen desaturation curve from a pre-event baseline, accounting for the number, depth, and duration of respiratory events. Participants were classified into tertiles according to HB, AHI, oxygen desaturation index $\geq 3\%$ (ODI3%), and percentage of sleep time with saturation $< 90\%$ (Tsat90%) for comparative analysis.

The primary outcome was a composite of ischemic heart disease, stroke, pulmonary embolism, heart failure, atrial fibrillation, and hypertensive crisis (fatal or non-fatal). Incident CVE were recorded over a median follow-up of 15 months (IQR 13–17). Cox proportional hazards models were used to assess the prognostic value of HB, AHI, ODI3%, and Tsat90% for CVE risk. Patients were followed until the pre-specified minimum of 85 CVE was reached.

Results: Of the 739 patients included, 93 patients experienced at least one CVE, of which 85 were first-ever events: 39 hypertensive crises, 19 heart failures, 18 atrial fibrillations, 17 ischemic heart diseases, and 8 strokes. There were 15 deaths (5 cardiovascular).

Those patients in the highest tertile of HB showed a significantly greater risk of CVE compared to lower tertiles (HR 3.11; 95%CI 1.91-4.09; p 0.0001), outperforming AHI in prognostic value. Tsat90% also independently predicted CVE (HR 2.68; 95%CI 1.11-3.9; p 0.023).

A new prognostic score, the HARPA Score, was developed based on HB and Tsat90% values, age (> 63 years), hypertension, and previous CVE, this score showed strong prognostic value (AUC-ROC 0.86), exceeding that of its individual components, and demonstrated good discriminative capacity in patients with OSA.

Conclusions: Hypoxic burden and nocturnal desaturation (Tsat90%) are valuable independent predictors of cardiovascular events in OSA patients, capturing distinct aspects of intermittent and sustained hypoxemia. The HARPA Score, combining these metrics with established cardiovascular risk factors, provides robust prognostic capability for incident cardiovascular events.

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Comparing apnea and hypopnea is akin to comparing apples and oranges

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Introduction: Sleep being recognized as sixth vital sign and obstructive sleep apnea (OSA) is attaining pandemic proportions with ever increasing lifestyle disorders. Assessing severity of OSA holds key in appropriate management of this global health crisis. However widely accepted "AHI scale" for severity

assessment uses apnea or hypopnea as a single unit without correlating physiological impact caused by each event. It is very clear that an event of 10 seconds duration may not result in heart rate variability or drop in saturation to the extent as compared to an event of 40 seconds duration. In background of this fundamental flaw in severity assessment of OSA, we undertook this study to analyze varying physiological impacts of apnea/hypopnea based on duration of these events.

Materials and methods: Confirmed cases of OSA following overnight level 1 polysomnography (PSG) were included. PSGs were recorded at a tertiary care hospital. Sleep study data including AHI, apnoea frequency and duration, hypopnea frequency and duration, number of relative desaturations, mean SPO2 recorded in sleep, minimum SPO2 recorded in sleep, minimum, average and maximum heart rate in sleep, sleep onset, total sleep time, sleep efficiency were retrieved from the system. A total of 853 events out of 1458 events were analyzed to obtain equal sample size between apnea and hypopnea and events were randomly chosen. Non parametric Kruskal Wallis test between apnoea and hypopnea events with respect two direct objective measures namely changes in oxygen saturation (SPO2) and Heart rate (HR) were studied. While assessing SPO2, delta SPO2 and maximum drop in SPO2 was studied. In case of heart rate change in heart rate (delta HR) and direction (increase or decrease in heart rate) was taken to account

Results: In our study we found that correlation coefficient between AHI and mean SPO2 in sleep is - 0.4542 which is moderate correlation and correlation between AHI and minimum SPO2 is - 0.45577 which is again only a moderate correlation. We found in our study that statistically significant difference between apnoea and hypopnea with respect to delta SPO2 ($p=0.002$) and maximum drop in SPO2 ($p=0.035$) for each event. Duration of apnoea has a moderate correlation with mean and minimum SPO2 in sleep. Regression analysis with one way ANOVA was applied to 20- 40 second events and compared with delta heart rate of apnoea and hypopnoea showed statistically significant difference. Similarly for apnoea and hypopnea events of more than 40 second there was statistical significant difference for delta heart rate.

Conclusions: Apnoea or hypopnea can have varying physiological consequences. Further based on duration of the each event physiological consequences like heart rate variability and drop in oxygen saturation varies with statistical significance. For precise severity assessment of OSA, there has to be distinction between apnoea and hypopnea events. Further apnoea/hypopnea events has to be segregated based on their duration and factor accordingly in severity scoring

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Comparison of SONNO® home sleep test with in-laboratory polysomnography in the diagnosis of obstructive sleep apnea syndrome

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Introduction: In-laboratory, polysomnography (PSG) is the gold standard for diagnosing obstructive sleep apnea syndrome (OSAS). However, the long waiting lists, inconvenience of sleeping away from home and high costs of testing make patients hesitate to undergo the examination, thereby delaying diagnosis. The home sleep test (HST) enables subjects to be tested at home, a familiar and comfortable environment, without a long waiting list and at much less cost. This study investigated the accuracy of SONNO® HST in diagnosing OSAS and identified factors affecting the diagnostic accuracy.

Materials and methods: This prospective study included 57 patients with clinically suspected OSAS. All patients were studied with the PSG and HST on the same night. The apnea-hypopnea index (AHI) measured through PSG was used as the standard. The sensitivity, specificity, and accuracy of the HST in diagnosing and evaluating the severity of OSAS were analyzed.

Results: Among the 57 patients, no significant difference was noted in the average AHI values obtained using PSG and the HST ($p = 0.08$). The AHI obtained from HST was significantly correlated with that obtained from PSG, with the correlation coefficient being 0.79 ($p < 0.01$). The sensitivity, specificity, and accuracy of the HST in diagnosing OSAS were 93.2%, 84.7%, and 91.0%, respectively. In diagnosing moderate to severe OSAS; sensitivity, specificity, and accuracy of the HST was 82.5%, 96.1%, and 77.6%. Furthermore, the difference in AHIs measured using the two tests were positively correlated with the severity of sleep apnea.

Conclusions: The SONNO® HST used in the screening of patients with suspected OSAS achieved an accuracy of >90%. For patients with moderate to severe OSAS, the accuracy was below 90%. Therefore, for patients who receive an OSAS diagnosis through the HST, in-laboratory PSG is recommended for assessing severity of the OSAS and appropriate treatment recommendations.

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Comparison of the 1st Half of the Night Polysomnography (3 Hours) vs. Full Night Analysis in Asian Population: A Cohort Study

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Introduction: Although full-night polysomnography (FN-PSG) is the gold standard for diagnosing obstructive sleep apnea (OSA), split-night polysomnography (SN-PSG) is generally used in practice given the limitations in resource and time. However, the diagnostic accuracy and cut-off threshold of the SN-PSG remains unclear, particularly in Asian populations. This study aimed to study the correlations of apnea-hypopnea index (AHI) analyzed from the SN-PSG to that of the FN-PSG. Diagnostic accuracy was analyzed using various AHI cut-off thresholds.

Materials and methods: Three-hundred-and-ninety-seven FN-PSGs conducted with the NOX-A1 system during November 2020–August 2024 at Ramathibodi Sleep Disorders Center were identified. To represent SN-PSG, data from the FN-PSG were divided for the first 3-hours to be analyzed and re-generated. Sleep and respiratory parameters between the first 3-hour-SN-PSG and FN-PSG were compared using concordance correlation coefficients (CCC). Analyses for specific phenotype including REM/NREM AHI, supine/non-supine AHI were performed. Sensitivity and specificity were calculated for 3-hour-AHI and oxygen desaturation index (ODI) against FN-PSG data.

Results: The CCC between 3hour-AHI and FN-AHI was 0.93 with higher correlation for NREM-AHI (CCC = 0.95) than REM-AHI (CCC = 0.79). The higher correlation was seen in supine-AHI (CCC = 0.89) than non-supine-AHI (CCC=0.60). Across severity of OSA the CCC were 0.71, 0.63, 0.60, and 0.86. for no-OSA, mild, moderate, and severe OSA respectively.

Sensitivity and specificity for 3hour-AHI cut-off threshold of ≥ 5 , ≥ 15 , and ≥ 30 events/hour were 72.7%/87.2%, 70.6%/91.3%, and 93.3%/96%, respectively. Sensitivity and specificity for 3-hour-ODI cut-off threshold of ≥ 5 , ≥ 15 , and ≥ 30 events/hour were 69%/91.5%, 75.5%/97.4%, and 94.7%/99.7%, respectively. The combination of 3hour-AHI with 3hour-ODI at the cut-off threshold of ≥ 15 improved specificity to diagnose moderated OSA to 98.3%, with lower sensitivity of 18.7%.

Conclusions: Overall, 3hour-AHI provide a reliable estimate of full-night-AHI, particularly for severe OSA. The high correlation of 3hour-AHI occurred for NREM-AHI, and supine-AHI but not for REM-AHI and non-supine -AHI. The best accuracy for OSA diagnosis were at the cut-off threshold of ≥ 30 for both 3-hour-AHI, and 3-hour-ODI. However, combining 3-hour-AHI with 3-hour-ODI at the threshold of ≥ 15 improved specificity markedly. This data may guide the decision to perform SN-PSG in the real-world practice.

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Comparison of the impact of nasal and pharyngeal surgery on CPAP treatment parameters and quality of life

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Introduction: It has been reported that approximately 30% of patients with obstructive sleep apnea (OSA) have upper respiratory tract diseases such as nasal disease or enlarged palatine tonsils. Although continuous positive airway pressure (CPAP) therapy is the first-line treatment for patients with

moderate or severe OSA, there have been few reports comparing CPAP therapy and patient quality of life before and after nasal or pharyngeal surgery. In this study, we retrospectively compared the effects of CPAP application and treatment parameters and subjective symptom changes before and after surgery in patients who underwent nasal or pharyngeal surgery during CPAP treatment.

Materials and methods: We retrospectively analyzed CPAP use before and after surgery and the Japanese version of the Epworth Sleepiness Scale (JESS), which measures daytime sleepiness, in patients who underwent OSA nasal or pharyngeal surgery at Atsugi City Hospital between April 2022 and September 2024 (nasal surgery: 13 cases, pharyngeal surgery: 8 cases).

Results: Postoperative CPAP pressure and postoperative leakage were significantly lower in both pharyngeal surgery groups. The nasal surgery group showed no significant difference, but there was a trend toward an increase in postoperative use for more than 4 hours. JESS, a measure of daytime sleepiness, tended to improve in the nasal surgery group. Furthermore, subjective symptoms such as xerostomia and nasal obstruction tended to improve after surgery, but not in patients undergoing pharyngeal surgery.

Conclusions: Nasal and pharyngeal surgery for patients on CPAP may have an additional effect of improving sleepiness and reducing CPAP pressure. When patients complain of subjective symptoms such as drowsiness, nasal obstruction, or xerostomia during routine CPAP treatment, it is important to examine whether nasal or pharyngeal surgery is indicated and to explain to patients that CPAP may improve their therapeutic effects and quality of life.

Computational fluid dynamics analysis of differences in airflow dynamics in upper airways between maxillo-mandibular advancement and genioglossus advancement

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Introduction: Maxillomandibular advancement (MMA) surgery and Genioglossus advancement (GA) surgery as a sleep surgery is useful for treating patients with obstructive sleep apnea (OSA). However, preoperative analysis and evaluation to make decisions about the direction and distance of maxillomandibular movement has previously consisted primarily of morphological analysis, and physiological functions have not been evaluated. In our study, we performed computational fluid dynamics (CFD) analysis of airway changes associated with MMA+GA to evaluate the effectiveness of MMA+GA.

Materials and methods: In this study, CFD simulation was conducted for 9 patients who had undergone MMA and MMA+GA surgery, had undergone 3D-CT and rhinomanometry before surgery and more than one year after surgery, and had given informed consent to participate. To evaluate jaw and airway morphology before and 1 year after surgery, 3D-CT was carried out using the Asteion Super 4 (Toshiba Corporation). A CFD mesh was prepared using HEXPRESS™ (version 11.2; NUMECA International). CFD simulation was carried out using FINE™/Open (version 11.2; NUMECA International). The airway model created by CFD was divided into six boundary sections, and the cross-sectional area of each boundary section was measured. In addition, at the boundary section where the change in cross-sectional area was the greatest, the airflow velocity, static pressure, total pressure, and airway resistance were measured and compared. This study was approved by Nihon University School of Dentistry Ethics Committee (Tokyo, Japan; approval no. EP16D007).

Results: After MMA and MMA+GA, the airway cross-sectional area from the upper end of the palate pharynx to the upper end of the epiglottis clearly increased. In addition, the airway flow rate decreased, the flow rate became uniform throughout the upper airway, and the airflow rectification was also observed. In particular, at the lowest point of the soft palate, where an increase in cross-sectional area was observed, static pressure and total pressure decreased significantly, and airway resistance also decreased. Compared to MMA, MMA+GA showed greater effects.

Conclusions: It was suggested that MMA and MMA+GA reduce the force tending to collapse the airway wall, making the airway more stable and less likely to collapse, and facilitating ventilation within the airway, providing evidence that they are effective treatments for OSA. CFD analysis makes it possible to identify areas of airway narrowing and areas of high static pressure before surgery, and is

thought to be able to warn of the possibility of airway obstruction and provide useful predictive data for considering the amount and direction of surgical movement.

Concomitant Instantaneous heart rate decrease, and proximal skin temperature increase during apnea events

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Introduction: Apnea events during sleep, trigger autonomic (sympathetic and parasympathetic) nervous system responses that result in heart rate and vascular tone fluctuations. The instantaneous heart rate (HR) during apnea events can decrease due to higher vagal tone or baroreceptor reflexes responding to changes in blood gases and intrathoracic pressure. The sudden absence of airflow and the buildup of carbon dioxide signal the parasympathetic system to slow heart rate. Concurrent changes in vascular tone help redistribute blood to vital organs.

Materials and methods: Sleep data from eighteen participants (9M/9F, mean age of 44.5 [SD: 6.7] years-old) that spent two nights in a sleep lab were used in this study. The dataset included polysomnography signals (PSG), and skin temperature measured at two sites: on the foot (distal) and near the left-collar bone (proximal). Sleep stages and respiratory events were annotated by a sleep expert.

To evaluate the correlation between changes in instantaneous heart rate (IHR) and changes in both distal and proximal skin temperature (DST and PST respectively), apnea events with duration $\geq T$ ($T=20$ and 30 seconds) were considered.

For each apnea event, we considered the IHR curve within a 40-second window (20 seconds before to 20 seconds after the event onset), with a sampling rate of 1 Hz. In contrast, PST and DST curves were considered within a 360-second window (180 seconds before to 180 seconds after event onset), also sampled at 1 Hz. The shorter analysis interval for IHR reflects its more rapid variability compared to PST and DST.

Baseline correction to IHR, PST and DST curves was applied by subtracting the corresponding mean values across the 20-second pre-event window. Baseline-corrected curves were smoothed using Locally Weighted Scatterplot Smoothing. Post minus Pre changes were then calculated for IHR, DST, and PST.

The Spearman correlation (r), the statistical significance thereof, and the coefficient of determination (R^2) were calculated for 1) IHR-change versus DST-change, and 2) IHR-change versus PST-change.

Results: For $T=20$ seconds:

A significant ($p=0.04$) correlation between IHR-change and PST-change was found $r=-0.22$ and $R^2=0.05$.

A non-significant ($p>0.05$) correlation ($r=0.169$ and $R^2=0.03$) between IHR-change and DST-change was found.

For $T=30$ seconds:

A trending ($p=0.06$) correlation between IHR-change and PST-change was found $r=-0.44$ and $R^2=0.19$.

A non-significant ($p>0.05$) correlation between IHR-change and DST-change was found $r=-0.24$ and $R^2=0.05$.

Conclusions: We examined the relationship between IHR and temperature fluctuations at distal and proximal locations during apnea events that last at least 20 and 30 seconds. For the former, a significant negative correlation was found between IHR changes and proximal skin temperature (PST) changes suggesting that increased parasympathetic activity during these events is associated with reduced PST. No significant correlations were observed between IHR and distal skin temperature (DST). The results indicate that PST may be a more sensitive biomarker for autonomic responses during severe apnea episodes.

Continuous Positive Airway Pressure Air Leak Phenotypes In A Cohort Of Obstructive Sleep Apnea Patients

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Introduction: Nasal masks are first-line options for obstructive sleep apnea (OSA) treatment with continuous positive airway pressure (CPAP). Excessive leak during nasal CPAP is common and is associated with poorer adherence. Excessive leak can occur due to mask and mouth leak. Mouth leak has a distinct overnight graphical profile characterized by sharp increases in leak followed by an abrupt resolution of leak. Those oscillations are caused by mouth opening, during sleep transition, and closing, precipitated by arousals from sleep. The distinction between mask and mouth leak has important clinical significance as they require different treatment approaches. We hypothesized that distinct air leak phenotypes can be detected through the analysis of overnight leak profiles.

Materials and methods: CPAP and patient demographic data from a cohort of OSA patients under nasal CPAP treatment were retrieved from the online CPAP data platform. Subjects that were using oronasal masks or a chinstrap and those that were not using CPAP during any of the last 30 days were excluded. Thirty-day CPAP data summary and detailed CPAP data of the last 7 nights were retrieved from each subject. Unintentional leak, residual apnea-hypopnea index and 30-day adherence were recorded. Mouth leak (ML) episodes were determined by the identification of abrupt leak reductions ($>10\text{L/min}$ per drop) during each overnight leak profile graph. ML index was defined by the total number of ML episodes divided by hours of CPAP use. Excessive leak was defined as a 95th leak percentile $\geq 15\text{L/min}$. Mask leak was defined as $\text{ML index} < 1/\text{h}$ and the presence of excessive sustained leak. Mouth leak was defined as $\text{ML index} \geq 1/\text{h}$ in the absence of sustained excessive leak. Mixed leak was defined as $\text{ML index} \geq 1/\text{h}$ and the presence of sustained excessive leak. A multiple linear regression model was used to test age and CPAP level as independent predictors of ML index. These variables have been shown to predict overall excessive leak.

Results: A total of 385 CPAP users were evaluated. Of these, 154 were excluded due to the use of CPAP devices lacking telemonitoring capability. Forty-six patients were excluded for using oronasal masks ($n=11$), chin straps ($n=26$), or for not using CPAP on at least 7 of the last 30 days ($n=9$). Oral leak occurred in 121 (60.2%) individuals - 60 with exclusive mouth leak and 61 with combined mouth and mask leak. Only 44 patients (21.9%) did not have excessive leak. Four CPAP leak phenotypes were identified: no leak, mask, mouth and mixed ([Table 1](#)). Multiple linear regression models considering 95th Percentile or ML index as dependent predictors and age and CPAP level ($R^2=0.211$, $p<0.001$).

Conclusions: Analysis of overnight CPAP leak profile allowed the distinction of 4 different phenotypes. More episodes of mouth leak were observed among elderly individuals and those with higher CPAP levels. Distinguishing between the different causes of excessive air leak allows appropriate treatment of the underlying cause.

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CPAP compliance trends from Cloud data: Who is on Cloud Nine?

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Introduction: Positive Airway Pressure (PAP) therapy is the preferred treatment for managing moderate to severe obstructive sleep apnea (OSA), but adherence varies. This study analyzes remotely accessed data from the Cloud on patients using ResMed device with an aim to explore factors which may affect PAP compliance including sex, age, mask type, daily usage patterns, and comorbidities.

Materials and methods: We analyzed data from 107 OSA patients (96 males, 11 females; mean age 56.7 years, range 24–86) over 364 days in 2024. Data included usage days, average daily usage (hours), maximum pressure, 95th percentile leak, maximum leak, mask type (nasal mask, full face mask, nasal pillow), and comorbidities (Obesity, hypertension, diabetes and coronary artery disease). Compliance was assessed across sex, age groups (20–39, 40–59, 60–69, 70+), mask types, daily usage duration (<4 ,

4–5, 5–6, 6–7, 7–8 hours), total usage (<70% vs. ≥70% of days), and comorbidities. Bayesian ANOVA was used, with Bayesian factor (BF_{10}) indicating the likelihood of reported interpretations.

Results: No significant sex-based differences in compliance were found. Age impacted usage: patients aged 60–69 used PAP for fewer hours daily ($BF_{10}=2.23$), had lower maximum pressure ($BF_{10}=14.42$), and higher 95th percentile and maximum leaks ($BF_{10}=4.03, 1.92$) compared to younger patients in the 20–39 age group. Patients over 70 had increased 95th percentile leaks ($BF_{10}=4.12$). Mask type influenced adherence: full face mask (FFM) ($BF_{10}=4.16$) and nasal mask (NM) users ($BF_{10}=2.7$) had longer total usage days than nasal pillow (NP) users; NM users also noted to have longer hours of daily usage ($BF_{10}=51$). Daily usage duration affected compliance: 6–7 hours/day users had longer total usage than <4 or 4–5 hours/day users ($BF_{10}=8.99, 513.73$). Those using 7–8 hours/day had longer total usage ($BF_{10}=3.03, 51.56$), higher maximum pressures ($BF_{10}=2.55$), and lower leaks ($BF_{10}=4.96, 1.82$) compared to 4–5 hours/day. Total usage (<70% vs. ≥70%) showed no differences in leaks or pressures. Obese patients used PAP longer ($BF_{10}=22$) and ≥70% during the year ($BF_{10}=50.72$) compared to non-obese, though daily usage time was similar.

Conclusions: Age, mask type, daily usage duration, and obesity significantly affect PAP compliance. Obese patients had higher compliance. Older patients (60–69, 70+) show reduced usage and increased leaks. FFM and NM users, and those with 6–8 hours daily usage duration, exhibit overall better adherence. Remote monitoring of compliance to identify issues earlier and providing personalized strategies will help to better manage patients with OSA.

CPAP Effect on Sleep Regularity, Blood Pressure Variability, and Cardiovascular Biomarker: A Randomized Trial

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Introduction: Studies showed continuous positive airway pressure (CPAP) had differential effect on circadian pattern of blood pressure in obstructive sleep apnea (OSA). It is unknown if CPAP effect on BP depends on sleep/wake regularity. This open-label randomized trial evaluated the CPAP effects on sleep regularity, 24-hour ambulatory blood pressure (ABP), and cardiovascular biomarker.

Materials and methods: Patients with OSA were randomized (1:1) to 12-week CPAP or inactive control. The outcomes included actigraphy-measured sleep/wake regularity (onset, offset, midsleep time, and sleep regularity index [SRI]) and ABP, along with their variability (via standard deviation), and biomarkers. CPAP effects were assessed as baseline-adjusted between-group differences using intention-to-treat analysis. A sensitivity analysis of completers was also performed.

Results: Of 52 randomized participants, 45 completed the study. Compared to control, CPAP had no effect on sleep/wake regularity and absolute ABP value, it reduced variability of awake systolic ($P=0.026$), diastolic ($P=0.024$), mean ($P=0.013$), asleep systolic ($P=0.033$) BP. The reduction in BP variability was observed in subgroup of early midsleep time but not than late midsleep time. No change was observed in plasma norepinephrine, natriuretic peptide, and inflammatory biomarker.

Conclusions: Our findings that CPAP reduced ABP variability, particularly in those with early midsleep times, suggest that midsleep time may influence the ABP response to CPAP. Our findings support the importance of monitoring sleep/wake regularity during CPAP follow-up.

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CPAP to reduce the risk of cancer in OSA? – a meta-analysis of 3 RCTs

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Introduction: Obstructive sleep apnea (OSA) has been hypothesized to promote cancer via intermittent hypoxia and assessing what happens when OSA is controlled by continuous positive airway pressure (CPAP) may provide valuable insight. To date no randomized controlled trials (RCTs) have been specifically designed to address this question however, exploring and utilizing data from RCTs with adverse event data on cancer may provide a useful option if meta-analyzing this data. This also provides a superior option to meta-analyzing data from observational studies which are inherently prone to selection bias and, by design, addresses a different research questions than a meta-analysis of RCTs. The three large RCTs, all assessing CPAP for OSA, can provide an opportunity to We aimed to test whether controlling OSA via CPAP reduces cancer incidence inside a robust randomized design with a control group.

Materials and methods: We conducted a meta-analysis of three randomized controlled trials (SAVE [NCT00738179], RICCADSA [NCT00519597], and ISAACC [NCT01335087]) assessing cancer incidence from adverse event data on neoplasms, among OSA patients randomized to continuous positive airway pressure (CPAP) versus control.

Results: Within the SAVE trial, a total of 42 (3.1%) cancers were reported in the CPAP arm and 34 (2.5%) in the control arm ($p=0.36$). The RICCADSA trial reported 2 (1.6%) events in the CPAP group versus 1 (0.8%) in the control group ($p=0.56$). Finally, the ISAAC trial reported 15 (2.4%) events in the CPAP arm and 24 (3.8%) in the control arm ($p=0.05$). Thus across trials, cancer incidence was not different between groups, and meta-analysis showed no statistically significant difference (CI 0.55 to 1.68).

Conclusions: Treating sleep apnea with CPAP in high-quality randomized controlled trials does not appear to markedly reduce (or worsen) the risk of incident cancers thereby offering no support to the hypothesis that OSA causes or accelerates cancers. The result of this meta-analysis is clearly an unsatisfying answer as the confidence limits are quite wide because these trials are too short/underpowered to provide a definitive answer. However, in the absence of any large suitable RCT currently recruiting, this uncertainty is likely the answer we will have to live with for the foreseeable future.

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CPAP Treatment Coverage and Adherence for Obstructive Sleep Apnea in French Polynesia: A Geographical and Health System Perspective

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Introduction: The effective management of Obstructive Sleep Apnea (OSA) with Continuous Positive Airway Pressure (CPAP) faces logistical and geographical challenges in remote regions. French Polynesia, a French overseas territory, is composed of 118 islands scattered over 4 million square kilometers in the Pacific Ocean, with a population of approximately 260,000. Despite this vast and sparsely populated area, CPAP treatment is supported by a health system modeled after the French national system. This study investigates whether CPAP treatment coverage and adherence remain satisfactory in this unique context, and examines their association with geographical isolation from the capital, Papeete, where the main homecare service providers are located.

Materials and methods: We conducted a cross-sectional retrospective analysis of CPAP treatment data across several islands in French Polynesia. Two primary indicators were assessed: (i) prevalence of CPAP equipment provision for diagnosed OSA cases, and (ii) adherence rates based on telemonitoring data (≥ 4 hours/night on $\geq 70\%$ of nights). We also analyzed the correlation between these indicators and the distance from Papeete using geospatial mapping and regression models.

Results: Preliminary findings indicate relatively high rates of CPAP coverage and adherence across the islands, with moderate variability. Islands closest to Papeete showed slightly higher adherence rates, but no strong linear correlation was found between distance and adherence. Notably, some remote islands achieved adherence rates comparable to central islands, suggesting compensatory factors such as local health support and patient education.

Conclusions: The study suggests that CPAP treatment can be effectively deployed and maintained in ultra-peripheral territories when supported by a robust and centralized healthcare system. Despite the extreme geographical dispersion, coverage and adherence remain acceptable, highlighting the resilience and adaptability of the French model in this unique setting. These findings may inform strategies for delivering sleep medicine care in other isolated or underserved regions.

Acknowledgments: We thank the healthcare providers and technical teams in French Polynesia who supported data collection and patient follow-up. This project is part of a broader reflection on access to care and health equity in remote regions, supported by Bordeaux University.

Craniofacial Phenotype of Responders to Position-Responding Mandibular Advancement Device in Patients with Obstructive Sleep Apnea: A Prospective Study

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Introduction: Obstructive sleep apnea (OSA) is a disorder characterized by recurrent upper airway collapse during sleep, leading to impaired respiratory function. Generally, positive airway pressure (PAP) is known as the treatment of choice for OSA patients with excessive daytime sleepiness, impaired sleep-related quality of life, or hypertension. However, despite the high efficacy of CPAP in eliminating respiratory events, its effectiveness is lowered by inadequate adherence to CPAP therapy. In the present study, we evaluated the clinical efficacy of a newly developed MAD that autotitrates depending on its position in patients with OSA. This study also aimed to evaluate the effectiveness of an auto-titrating mandibular advancement device (AMAD) by analyzing cephalometric changes and polysomnographic outcomes in OSA patients.

Materials and methods: A prospective, single-arm study was conducted on 16 OSA patients. The study included polysomnography and cephalometric measurements before and three months after AMAD treatment. Polysomnography included assessments of apnea-hypopnea index (AHI), respiratory disturbance index (RDI), arousal index (AI), oxygen desaturation index (ODI), and minimum oxygen saturation (SpO₂). Cephalometric analysis included measurements of hyoid-mandibular plane distance (H-MP), anteroposterior airway width (AP), square area (SA), and airway cross-sectional area (AWA), sella-nasion-point A (SNA) angle, sella-nasion-point B (SNB) angle, point A-nasion-point B (ANB) angle, maxillomandibular plane (MMP) angle, distance from the posterior nasal spine to the mandibular plane (PNS-MP), distance from the posterior nasal spine to the hyoid (PNS-H). Also in the sagittal view of the CT, soft palate length, soft palate thickness, and tongue cross-sectional area were measured.

Results: AMAD significantly reduced AHI (33.4 ± 20.5 to 15.2 ± 11.2 , $p < 0.05$), RDI (35.6 ± 19.8 to 16.6 ± 11.6 , $p < 0.05$), AI (34.8 ± 19.4 to 17.4 ± 8.6 , $p < 0.05$), and ODI (26.4 ± 20.5 to 11.9 ± 8.7 , $p < 0.05$), while minimum SpO₂ increased ($80.1 \pm 6.2\%$ to $83.9 \pm 5.3\%$, $p < 0.05$). Cephalometric analysis showed a significant decrease in H-MP (1.73 ± 0.72 cm to 0.96 ± 0.51 cm, $p < 0.05$), along with increases in AP (1.42 ± 0.43 cm to 1.64 ± 0.39 cm, $p < 0.05$), SA (3.76 ± 2.13 cm² to 4.77 ± 1.94 cm², $p < 0.05$), and AWA (2.45 ± 1.48 cm² to 3.13 ± 1.17 cm², $p < 0.05$). In the responder and non-responder

groups, H-MP significantly decreased from 2.05 ± 0.75 cm and 1.58 ± 0.46 cm before treatment to 0.98 ± 0.45 cm and 0.98 ± 0.53 cm after treatment, respectively. The change in H-MP was -1.07 ± 0.53 cm in the responder group and -0.60 ± 0.33 cm in the non-responder group, with a statistically significant difference between the two groups. Tongue cross-sectional area significantly decreased in the responder group from 32.67 ± 4.35 cm² to 30.41 ± 3.02 cm² after treatment, while no significant change was observed in the non-responder group.

Conclusions: AMAD could be an effective alternative for the treatment of OSAS and has been found to significantly improve several PSG parameters such as AHI, lowest oxygen saturation, and arousal index. AMAD improved polysomnographic parameters by elevating the hyoid and expanding the airway space, suggesting its potential as an alternative treatment for OSA patients who are intolerant to PAP therapy.

Cumulative brain desaturation: time to consider brain derived parameter to measure daytime sleepiness in obstructive sleep apnea

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Introduction: The change in cerebral hemodynamics induced by sleep apneas and hypopneas may contribute to the daytime sleepiness in patients with obstructive sleep apnea (OSA). However, previous studies failed to discovery their relationship. We propose and test a new parameter, the cumulative brain oxygen desaturation, which may contribute to OSA patient's daytime sleepiness.

Materials and methods: 22 patients with severe OSA (apnea-hypopnea index (AHI) at diagnosis [mean $\pm$ standard deviation, std.]: 52.1 ± 21.6 /h, median: 45.1/h, interquartile range: 34.4–60.2/h) were monitored by polysomnography during routine continuous positive airway pressure titration. The reductions of brain tissue oxygen saturation (StO₂) in all respiratory events at baseline sleep were measured by frequency-domain near-infrared spectroscopy (NIRS). The cumulative brain desaturation was calculated as AHI times the mean StO₂ desaturation. Similarly, the cumulative peripheral desaturation was also calculated, i.e., AHI times the mean reduction of peripheral arterial oxygen saturation (SpO₂). The correlations between Epworth sleepiness scale (ESS) and AHI, the mean StO₂ desaturation, the cumulative brain desaturation, and the cumulative peripheral desaturation were tested, respectively. Linear regression was applied to predict ESS using the cumulative brain and peripheral desaturation, with age and BMI as covariates.

Results: ESS significantly correlates to the cumulative brain desaturation (Pearson's correlation coefficient: 0.68, $p=0.00056$), not the other parameters. Regression analysis only finds significant association between ESS and the cumulative cerebral desaturation ($p=0.00195$) but not the cumulative peripheral desaturation ($p=0.71$).

Conclusions: The cumulative brain oxygen desaturation, which comprehensively combines total sleep time, the frequency of apnea and hypopnea events, and the severity of cerebral oxygen desaturation, may be a new indicator for daytime sleepiness in severe OSA.

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Decline in CD4⁺ Naïve T Cell Levels Correlates with OSA Severity in Adult and Pediatric Patients

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Introduction: Studies on naïve T cells in Obstructive sleep apnea (OSA) patients still remain limited. This study was designed to explore the circulating levels of CD4⁺ naïve T cells in patients with OSA across ages.

Materials and methods: The study involved participants from both adult and pediatric populations. For adult patients, we applied the CIBERSORT deconvolution algorithm to infer the relative abundance of

cell types based on microarray data. For children, we leveraged the previous pediatric single-cell transcriptome data to quantify cell type proportions. Weighted gene co-expression network analysis (WGCNA) was performed to explore potential significant gene modules associated with CD4⁺ naïve T cells. The correlation analysis was utilized to explore the relationship between CD4⁺ naïve T cell levels and OSA severity. Functional enrichment analyses were conducted to elucidate potential cell biological processes of CD4⁺ naïve T cells in both adult and pediatric patients.

Results: The CD4⁺ naïve T cell subset exhibited a decline trend and was closely linked to the characteristics of OSA in both adult and pediatric patients. The levels of CD4⁺ naïve T cells were negatively correlated with Apnea-Hypopnea Index (AHI) in adults ($R = -0.441$, $p = 0.017$) and pediatric patients ($R = -0.559$, $p = 0.010$). Functional enrichment analyses revealed that oxidative stress was a common biological feature in CD4⁺ naïve T cells shared by adult and pediatric patients with OSA.

Conclusions: CD4⁺ naïve T cells exhibited an age-independent depletion in OSA patients and correlated with OSA severity.

Deep Learning-based Identification of Severe Obstructive Sleep Apnea using Sagittal MRI Images

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Introduction: Obstructive sleep apnea (OSA) is a common disorder caused by repeated upper airway obstruction during sleep, often due to soft tissue collapse. It results in oxygen desaturation, daytime sleepiness, and cardiovascular complications. The gold standard diagnostic test, polysomnography (PSG), requires overnight hospitalization and is affected by the first night effect, where an unfamiliar environment alters sleep patterns. Imaging-based methods have been studied to complement PSG. X-ray cephalometry is useful for skeletal features but cannot clearly depict soft tissues, even though enlarged soft tissue often causes airway obstruction. Magnetic resonance imaging (MRI) visualizes soft tissue well, yet there is no standard method to interpret its relation to OSA severity, and diagnosis still depends on physician experience.

The aim of this study was to design a lightweight and transparent convolutional neural network (CNN) for classifying severe OSA from MRI images, and to evaluate its performance against standard deep CNN models such as VGG16 and ResNet-50.

Materials and methods: We analyzed 132 patients with OSA at Hakodate Medical Center, including 66 severe cases (apnea-hypopnea index, AHI ≥ 30) and 66 non-severe cases. All patients underwent PSG and MRI. The tongue region was extracted from MRI and resized to 224×224 pixels, with augmentation by rotation and translation.

Our CNN consisted of a single convolutional layer with a 29×29 kernel, followed by batch normalization, ReLU activation, and max pooling. Feature maps were divided into severe and non-severe groups, then aggregated by global average pooling and passed to a 2-unit softmax layer. Each unit corresponded to one filter with fixed weights, improving transparency. Dropout and L2 regularization were applied to reduce overfitting.

The model was trained with Adam optimizer (initial learning rate 0.005, decayed exponentially) for 300 epochs, with a batch size of 10. Performance was evaluated by 10-fold cross-validation repeated five times. For benchmarking, transfer learning with VGG16 and ResNet-50 was also performed.

Results: The proposed CNN had about 23,000 parameters, compared to 138 million in VGG16 and 25 million in ResNet-50. Despite being lightweight, our model achieved an average accuracy of 76% in classifying severe vs. non-severe OSA, comparable to both VGG16 and ResNet-50.

The variance of accuracy was slightly larger in our model, reflected by a higher standard deviation, but overall classification performance was maintained. Importantly, the transparent structure of our CNN allows direct association between filters and classes, providing the potential to analyze clinically relevant features after training.

Conclusions: This study demonstrates that accurate classification of severe OSA from MRI can be achieved not only with large deep CNNs but also with a lightweight and transparent CNN model. Although performance was similar among the three models, our model required far fewer parameters, offering efficiency and interpretability.

These findings suggest that CNN-based MRI analysis may provide an objective method for OSA assessment and reduce reliance on physician experience. Future work will focus on analyzing learned

filters to clarify the relationship between soft tissue morphology and OSA severity, aiming to support clinical diagnosis.

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Demographic and Baseline Disease Characteristics of SynAIRgy: A Phase 3 Trial of Aroxybutynin and Atomoxetine (AD109) in Obstructive Sleep Apnea

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Introduction: AD109 is a combination of a novel antimuscarinic, aroxybutynin (aroxy; R-enantiomer of oxybutynin), and the selective norepinephrine reuptake inhibitor atomoxetine (ato). We report the sample characteristics of the fully enrolled SynAIRgy trial, a Phase 3 study to examine the efficacy, safety, and tolerability of AD109 (aroxy 2.5mg/ato 75 mg) in OSA.

Materials and methods: SynAIRgy (NCT05813275) is a randomized, double blind, placebo-controlled, 6-month parallel-arm clinical trial in adults with OSA who do not accept or adhere to positive airway pressure therapy. Participants were enrolled over the full range of OSA severity as measured by apnea-hypopnea index with 4% desaturation (AHI₄) >5 with no upper limit. Participants must have had a Patient Reported Outcomes Measurement Information System (PROMIS) -Fatigue raw score ≥17, and a body mass index (BMI) between 18.5–40 kg/m² for men, or 18.5–42 kg/m² for women. The primary efficacy endpoint is the change from baseline in AHI₄ at Week 26. Secondary efficacy endpoints include change from baseline in oxygen desaturation index based on 3% desaturation (ODI₃), PROMIS-Fatigue, hypoxic burden based on 4% desaturation (HB₄), and PROMIS-Sleep Impairment (a measure of functional impairment during daytime).

Results: SynAIRgy enrolled 646 participants that were randomized to AD109 or placebo. At baseline, the mean (SD) age was 57.1 (11.0) years, and mean BMI (SD) was 32.3 (5.0) kg/m² with a balanced proportion of female (n=317, 49.1%) and male (329, 50.9 %) participants. The study enrolled a population representative of the diverse demographic composition of the United States with 67.2% being White, 20.4% Black/African American, 7.4% Asian, 1.1% American Indian/Alaskan Native, and 0.6% Native Hawaiian/Other Pacific Islander. The mean (SD) AHI₄ at baseline was 22 (11) with 34.4%, 42.4%, and 23.2% of participants having mild (AHI₄ 5–<15) moderate (AHI₄ 15–<30), or severe (AHI₄ ≥30) OSA, respectively. The mean (SD) ODI₃ was 29.0 (13.0), mean (SD) PROMIS-Fatigue T-score was 59 (7), mean (SD) HB₄ was 43 (40), and mean (SD) PROMIS-Sleep Impairment T-score score was 59 (7).

Conclusions: The baseline demographic characteristics of participants enrolled in SynAIRgy are representative of the general population of adults living with OSA, and the baseline AHI₄ scores and symptom profiles reflect those of a typical sleep clinic referral OSA population.

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Demographic profile and burden of comorbidities in patients with Obstructive Sleep Apnea (OSA)

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Introduction: Obstructive sleep Apnea (OSA) is commonly associated with comorbidities such as Hypertension (HTN), type 2 Diabetes Mellitus (DM), Heart Disease (HD), and Obesity. Despite an estimated 11% prevalence in India (~104 million), detailed demographic and comorbidity profiling is limited. This study compares OSA demographics, comorbidities, and correlations in Indian patients.

Materials and methods: Retrospective study of patients diagnosed with OSA from a tertiary sleep center between the years 2022 and 2024. Data collected included demographic details, Body Mass Index (BMI), Apnea Hypopnea Index (AHI), along with comorbidities. OSA was classified based on the AHI values. Patients were classified as children (<18 years), young adults (18 to 39 years), middle aged (40 to 64 years), elderly (65 to 79 years) and old (>80 years). The comorbidities considered were

obesity, overweight status, HTN, DM, thyroid disorders, and HD.

Bayesian statistical analysis (JASP Version 0.19.3) was applied to evaluate the likelihood of the hypothesis using Bayes Factor (BF_{10}). Bayesian Mann-Whitney test was used for continuous variables, and Bayesian Contingency tables were used for discrete variables.

Results: Among 1,041 OSA patients, 79.9% were males. Majority were middle-aged (60.7%), followed by young adults (22.1%), elderly (14.8%), with children and the old making up ~1% each. Compared to males, females presented later (56 vs 49 years, $BF_{10}=113.77$), had a higher BMI (35.9 vs 31.0 kg/m², $BF_{10}=98.98$), and a higher prevalence of obesity (61% vs 44%, $BF_{10}=1657$). There were no significant differences between the sexes in AHI (42.4 vs 35.3 low $BF_{10}=1.6$), hypertension (49.7% vs 40.7%), diabetes (36.3% vs 28%), or heart disorders (9.57 % vs 9.38%). Thyroid disorders were more in females (32.06% vs 10.71 %, $BF_{10}=23.31$). Females had higher rates of moderate (30.6% vs 21.6%, $BF_{10}=26.07$) and mild OSA (23.9% vs 17.8%, $BF_{10}=22.79$) whereas severe OSA was more in males (58.7% vs 44%, log (BF_{10}) =145). Unclassified cases were ~1.6% in both sexes. Children had a relatively even distribution of mild (36.36%), moderate (27.27%), and severe (27.27%) OSA. In contrast, severe OSA predominated in young (52.17%), middle-aged (56.42%), and elderly (61.04%) adults. The oldest group (>80) showed a decrease in severe OSA (50.00%) and an increase in mild OSA (28.57%).

Conclusions: The higher mean age of OSA presentation and greater burden of comorbidities among females may be attributed to postmenopausal status. Obesity was the most prevalent comorbidity, followed by hypertension, overweight status, diabetes, thyroid dysfunction, and heart disease. Females more often had obesity and thyroid disorders, but milder OSA, while males presented earlier with more severe disease. The significant gender disparity in diagnosis indicates potential under recognition of OSA in women, highlighting the need for improved awareness and targeted interventions given the high prevalence of obesity and comorbidities observed in females.

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Determining the Minimum Nights Required for Reliable Wearable-Based Assessment of Sleep Architecture and HRV in OSA, Insomnia, and COMISA

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Introduction: Single-night polysomnography (PSG) often fails to capture the full spectrum of sleep architecture and autonomic variability due to night-to-night variability, particularly in patients with OSA, insomnia, or co-morbid insomnia with obstructive sleep apnea (COMISA). While wearable devices now provide a scalable solution for multi-night assessment, the optimal number of nights required for reliable measurement remains uncertain. This study aims to determine the minimum number of nights needed to achieve stable estimates of sleep parameters and heart rate variability (HRV) metrics using the Belun Ring (BR) in individuals with OSA, insomnia, or COMISA.

Materials and methods: A cohort of 123 adults (median age: 61 years; 52% female; median BMI: 24.7; 30% OSA, 52% insomnia, 18% COMISA) underwent multi-night BR monitoring (median: 6 nights; IQR: 5-7; ≥ 100 minutes/night) following screening by a clinical psychologist and pulmonologist. Insomnia was defined by an Insomnia Severity Index (ISI) ≥ 15 or a diagnosis per ICSD-3 criteria, and COMISA was defined as meeting insomnia criteria with AHI ≥ 15 events/h. Sleep metrics included total sleep time (TST), sleep efficiency (SE), REM sleep, wake time, sleep onset latency (SOL), wake after sleep onset (WASO), and HRV time-domain metrics. Reference values were derived from the average of all available nights. The concordance correlation coefficient (CCC) was used to evaluate agreement between N-night averages and reference values, with 1,000 bootstrapped simulations performed for each N-night scenario.

Results: Across all participants, most metrics achieved a lower 95% CI of CCC ≥ 0.85 by the third night, with simulations confirming that three nights were sufficient for stable estimates. SOL exhibited the highest variability, requiring more than six nights to reach comparable precision. Stratified analyses revealed that participants with insomnia or COMISA required three nights for reliable estimation of insomnia-related metrics, whereas OSA patients required four or more nights for WASO to reach CCC

≥ 0.85 . While two nights of recording substantially improved accuracy, three nights effectively minimized night-to-night variability in both sleep architecture and HRV metrics.

Conclusions: This study is the first to establish evidence-based recommendations for the minimum number of nights required for reliable wearable-based assessment of sleep and HRV in patients with OSA, insomnia, and COMISA. Our findings demonstrate that three nights of wearable monitoring provide robust and stable estimates, offering a practical and scalable alternative to single-night PSG. These results have significant clinical implications for optimizing insomnia management and enhancing COMISA detection in both psychiatric and sleep medicine practice.

Development and Validation of a Facial-Recognition-Based Screening App for Obstructive Sleep Apnea (OSA)

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Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder affecting nearly 1 billion individuals worldwide. Although polysomnography (PSG) remains the diagnostic gold standard, its high cost and operational complexity limit its accessibility in primary care and home settings. This study proposes and validates a contactless, facial-recognition-based mobile application for rapid OSA screening, aiming to provide a scalable and user-friendly solution.

Materials and methods: We constructed a machine learning model based on a dataset of 3,265 facial images paired with corresponding sleep monitoring data collected during 2023–2024. Facial landmarks (106 key points) were extracted using the InsightFace framework and aligned via affine transformation. A face segmentation algorithm was then applied to isolate key regions covering the lower face and neck.

Image features were extracted using a modified ResNet50 architecture, followed by classification using a support vector machine (SVM) to assess OSA risk. Five-fold cross-validation was conducted for performance evaluation. To enhance interpretability, we employed Grad-CAM to visualize model attention and examine its alignment with known anatomical risk factors.

Based on this model, we developed a smartphone app for fast screening. The app incorporates a 3D pose estimation algorithm to automatically capture facial images at optimal angles, ensuring image quality while maintaining ease of use.

Results: The model demonstrated strong performance in identifying patients at moderate to high risk of OSA, with a sensitivity of 79.4% and a specificity of 84.1%. Grad-CAM visualization revealed that the model's attention focused primarily on anatomical regions relevant to OSA, such as the lower jaw and neck width.

The trained model has been successfully integrated into a public-facing app named "Sleepok" enabling users to complete screening in less than 10 seconds by simply taking a photo with their mobile device.

Conclusions: This study presents a low-cost, efficient, and scalable alternative to traditional PSG-based screening through a facial-recognition-based OSA risk assessment model and mobile app. The tool supports at-home use and may significantly enhance early detection rates for OSA. These findings demonstrate the practical potential of artificial intelligence in preventive healthcare and early disease intervention.

Development and Validation of a Reversible Obstructive Sleep Apnea Pig Model Using Cross-Linked Sodium Hyaluronate

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Introduction: Obstructive sleep apnea (OSA), affecting >900 million adults globally, lacks translational animal models that accurately replicate human pathophysiology. Current models (e.g., rodents, canines, monkeys) suffer from anatomical mismatches, irreversibility, or ethical constraints. This study introduces a method to induce upper airway obstruction by injecting a cross-linked sodium hyaluronate

mixture into the pharynx and palate of Bama pigs, creating an animal model that simulates recurrent upper airway collapse in patients with OSA. This model features a definable and controllable obstruction plane with a reversible degree of obstruction. The modeling effect was evaluated by polysomnography (PSG), upper airway computed tomography (CT), and HIF-1 α , which provided assurance at the clinical presentation, imaging, and biochemical levels for subsequent studies in this animal model. Histopathologic analysis of various respiratory tract locations, combined with monitoring of TNF- α and IL-6 in upper airway secretions and serum, helped to determine the respiratory system response to OSA conditions.

Materials and methods:

- **Model Design:** Palatal-pharyngeal injections of sodium hyaluronate/iohexol/penicillin (19.25 ml avg.) in Bama pigs (n=4) under Zoletil®/Remimazolam anesthesia.
- **Validation Metrics:**
 - Polysomnography (PSG) quantifying AHI/ODI and SpO₂ desaturation.
 - Serial CT imaging measuring airway volume/cross-sectional area.
 - Histopathology (H&E/Masson staining) and ELISA for HIF-1 α , IL-6, TNF- α in serum/airway secretions.
- **Reversibility:** Longitudinal monitoring over 28 days post-injection.

Results:

1. **Effective Obstruction Induction:**
 - AHI surged to 23.25 ± 2.99 events/hr ($p=0.003$) post-injection, with minimum SpO₂ dropping to $72.25 \pm 14.18\%$.
 - CT confirmed airway narrowing (min. cross-section: 157.48 ± 29.14 mm² $\rightarrow$ 46.18 ± 10.91 mm², $p=0.0112$).
2. **Reversible Physiology:**
 - Gradual AHI normalization to 8.00 ± 1.41 events/hr by day 14, correlating with airway volume recovery ($5,420 \rightarrow 11,157$ mm³, $p=0.0308$).
3. **Inflammatory Pathways:**
 - Serum HIF-1 α and IL-6 surged acutely post-obstruction.
 - Histopathology revealed lymphocytic infiltration, alveolar septal thickening ($p=0.0118$), and pharyngeal hyperkeratosis.
4. **Key Correlations:**
 - AHI strongly linked to airway anatomy (cross-section: $R^2=0.7421$, $p<0.001$).
 - TNF- α in secretions correlated with AHI ($R^2=0.3949$, $p=0.003$).

Conclusions: In this study, we successfully established a reversible, safe, and reliable animal model of OSA using a novel technique involving the precise multi-point injection of a cross-linked sodium hyaluronate mixture into the palatopharyngeal region of pigs via the oral cavity. This model accurately simulates upper airway collapse, leading to obstruction, closely mimicking the pathophysiology of OSA in patients. Consequently, it serves as an invaluable tool for future research on OSA.

Development of a Wavelet-Based Classifier for Sleep Apnea Subtypes Using EEG and ECG

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Introduction: Sleep apnea is a common sleep disorder that negatively impacts health and quality of life. It includes distinct respiratory events such as obstructive sleep apnea (OSA), central sleep apnea (CSA), and hypopnea, each requiring specific diagnostic and therapeutic approaches. Accurate classification of these events is essential for effective management.

Materials and methods: We analyzed 201 full-night polysomnography (PSG) recordings. Electrocardiogram (ECG) and electroencephalogram (EEG) signals were segmented into non-overlapping epochs, filtered using a Butterworth bandpass filter, and normalized. Discrete wavelet transform (DWT) was applied to EEG, and wavelet packet analysis (WPA) to ECG signals to extract statistical and nonlinear features. Feature selection was performed using Neighborhood Component Analysis (NCA). Classification models were trained using ensemble bagged tree algorithms. Three models were developed: EEG-only, ECG-only, and a combined EEG-ECG model. Their performance was compared to a deep learning model trained on ECG spectrograms. Two classification strategies were tested: (1) three-class (OSA-hypopnea-normal or OSA-CSA-normal) and (2) binary (OSA vs hypopnea or OSA vs CSA), in both NREM and REM sleep stages.

Results: The combined EEG-ECG model consistently outperformed models using single signals or spectrogram-based deep learning across both sleep stages and classification tasks. In the three-class classification, the model achieved **93.0% accuracy** for distinguishing OSA, hypopnea, and normal events during REM sleep, with high sensitivity (91.2% for OSA, 87.3% for hypopnea) and specificity (up to 99.5% for normal). For the task of distinguishing OSA, CSA, and normal events, performance further improved, reaching **97.0% accuracy** in REM with an F1-score of **0.96–0.97** across all classes. In the two-class classification, the model achieved **84.7% accuracy** for separating OSA from hypopnea during NREM and **98.8% accuracy** for distinguishing OSA from CSA in REM sleep, with corresponding F1-scores of **0.86** and **0.99**, respectively. These results demonstrate the model's high precision and generalizability across sleep stages and apnea types.

Conclusions: The findings highlight the effectiveness of combining non-linear features from ECG and EEG signals for classifying various sleep-related events, offering improved reliability for real-world applications. A proposed machine learning model provides significantly precise classification.

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Diaphragmatic dimensions as predictors of severity of obstructive sleep apnea: A cross-sectional study

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Introduction: Obstructive Sleep Apnea (OSA) is a sleep disordered breathing that involves a decrease or complete halt in airflow despite an ongoing effort to breathe. The Apnea –hypopnea index (AHI) is the standard metric used to describe the severity of sleep apnea. It represents the combined number of apnea and hypopnea that occurs per hour of sleep. OSA is classified into mild, moderate and severe according to AHI.

Mild OSA : AHI 5 to <15

Moderate OSA : AHI 15 to <30

Severe OSA : > 30

USG or ultrasonography is a simple non invasive tool. In our study we have tried to establish the association between diaphragmatic dimensions like thickness, excursion and thickness fraction with the severity of OSA.

Materials and methods: Objectives

- To find the association of Diaphragmatic thickness, excursion and thickness fraction with Apnea-Hypopnea Index

Study design : Cross-sectional

Methodology

In this cross-sectional study 40 patients (between 18-70yrs age) diagnosed as OSA by overnight inlab polysomnography were recruited after written consent. Patients having neurological disorder, hemodynamic instability, other lung diseases, pregnant females or patients already on PAP therapy were excluded. USG of diaphragm has been carried out by experienced sonologist. Diaphragmatic

thickness measurement done by B Mode USG using linear transducer while participants in supine position. To record the thickness of Right hemidiaphragm liver has been used as window with probe placed between the midclavicular and midaxillary line in Right subcostal margin. For the left hemidiaphragm spleen was used as window with probe placed subcostally between anterior and post axillary lines. The diaphragm is identified by 3 layered structure with two parallel echogenic line. Diaphragmatic thickness has been measured on both side at peak of inspiration, expiration . Diaphragmatic excursion :M mode used to display motion of diaphragm along the above mentioned areas on right and left side. It was also measured in supine position. To measure excursion the calliper was first placed on the foot of the slope of diaphragm echoic line and second calliper was placed at the apex. The Spearmen r coefficient was used to measure the degree of association between diaphragmatic thickness, excursion and thickness fraction on both side with AHI.

Results: Data from a sample of 40 patients (62.5%male, 37.5%female) were analysed. Mean age group 47.48 ± 9.28 , mean BMI 33.05 ± 6.72 , mean neck circumference 41.09 ± 2.50 •

•Positive correlation has been found between Right hemidiaphragmatic thickness on end inspiration with AHI ($r=0.298$, $p=0.0654$).

•Statistically significant correlation has been found between end inspiratory thickness of left hemidiaphragm with AHI ($r=0.381$, $p=0.016$) and end expiratory thickness of left hemidiaphragm with AHI($r=0.342$, $p=0.0333$)

•Statistically significant correlation has been found between Right hemidiaphragmatic Thickness Fraction with AHI ($r=0.358$, $p=0.023$)

• No significant correlation has been found between diaphragmatic excursion and AHI.

Conclusions: Our study depicted inspiratory thickness of diaphragm positively correlated with AHI which is a severity marker of OSA. Positive association also have been found with right diaphragmatic thickness fraction with AHI. However our study has been limited of small sample size and parameters have been taken in supine and awake conditions, there might have variations of anatomical measurements during sleep.

Differences in physiological endotypes between REM related and NREM related obstructive sleep apnea: Results from Shanghai Sleep Health Study cohort

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Introduction: According to the occurrence of apnea or hypopnea during rapid eye movement (REM) and nonrapid eye movement (NREM) sleep stages, OSA can be divided into REM predominant OSA (REM_{OSA}), NREM (NREM_{OSA}) predominant OSA and uniform OSA. We aimed to evaluate the endotypic differences of different OSA subgroups and changes of endotypes with sleep stages in Chinese population.

Materials and methods: Within the Shanghai Sleep Health Study cohort, individuals with OSA were recruited and classified as REM_{OSA}, NREM_{OSA} or uniform OSA. Non-invasive assessments of endotypes, including ventilatory control (loop gain, [LG]), arousal threshold (ArTH), pharyngeal collapsibility (V_{passive}), and muscle compensation (V_{comp}) were calculated using polysomnography.

Results: 1363 subjects were included in the analysis. REM_{OSA} participants exhibited lower loop gain ($0.51 [0.43-0.61]$ VS $0.58 [0.48-0.69]$, $p=0.001$), arousal threshold ($129.35 [114.27-155.63]$ VS $143.16 [118.71-179.36]$ %Veupnea, $p=0.001$), and upper airway collapsibility (higher V_{passive}; $91.55 [85.94-94.72]$ VS $87.82 [79.02-93.29]$ %Veupnea, $p<0.001$) than NREM_{OSA}; but the muscle compensation ($9.54 [4.09-19.94]$ VS $8.20 [-1.60-20.92]$ %Veupnea, $p=0.070$) did not have significant difference. The effects of sleep stage changes on the endotypes were different among OSA subgroups. Compared with NREM sleep, upper airway collapsibility (lower V_{passive}; $82.78 [69.64-91.53]$ %Veupnea in REM and $93.27 [88.15-95.71]$ %Veupnea in NREM; $p<0.001$) tended to increase in REM_{OSA} participants during REM sleep while the ArTH ($151.69 [123.15-195.87]$ %Veupnea in REM and $123.13 [111.77-141.61]$ %Veupnea in NREM; $p<0.001$) and V_{comp} ($14.12 [2.91-32.86]$ %Veupnea in REM and $9.93 [4.71-20.89]$ %Veupnea in NREM; $p=0.001$) showed elevation. In NREM_{OSA} participants, the LG ($0.59 [0.46-0.71]$ in NREM and $0.43 [0.34-0.52]$ in REM; $p<0.001$) , ArTH ($141.80 [120.80-175.56]$ %Veupnea in NREM and $125.77 [108.50-152.37]$ %Veupnea in REM; $p=0.001$), upper airway

collapsibility (lower V_{passive} ; 87.42[80.19–93.57] %Veupnea in NREM and 91.33[81.53–96.68] %Veupnea in REM; $p=0.02$) were higher in NREM sleep than those in REM sleep, while V_{comp} (7.51[–2.31–21.67] %Veupnea in NREM and 9.10[3.13–20.61] %Veupnea in REM; $p=0.002$) decreased in NREM compared to that in REM sleep. Fully adjusted generally linear mixed model analyses showed that the interactions between subgroups and sleep stages were significant (P for interactions all <0.001), this further conformed that effects of NREM to REM sleep stage changes on endotypic traits were different between NREM_{OSA} and the other two subgroups. Uniform OSA had the highest loop gain, highest arousal threshold, most collapsible upper airway (lowest V_{passive}), lowest muscle compensation among the three subgroups.

Conclusions: The different endotypic traits and different effects of sleep stage changes on endotypes among OSA subgroups can facilitate the understanding of the mechanism in OSA subgroups.

Differential effects of drugs for Insomnia and Sleep apnea : A Focus on sleep macrostructure and microstructure in rat

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Introduction: Various drugs are used to treat insomnia, contributing not only to the induction and maintenance of sleep but also to improvements in sleep quality. These therapeutic effects are often characterized by changes in sleep macrostructure, such as increased total sleep time (TST), shortened sleep latency, and alterations in sleep architecture. However, macrostructure alone may not fully represent the qualitative aspects of sleep. Microstructural change such as sleep fragmentation, which is caused by interruptions due to arousals, is also considered to influence sleep quality. This is particularly important for sleep disorders like sleep apnea syndrome (SAS), where frequent arousals can disrupt sleep sufficiency and reduce overall sleep quality.

Focusing on microstructural changes may help reveal new therapeutic potentials and contribute to evaluate the appropriate drugs for specific sleep disorders. In this study, we examined several compounds, including those developed for insomnia and those studied for SAS, to assess their effects on both sleep macrostructure and microstructure.

Materials and methods: Rat electroencephalogram (EEG) from the frontal cortex and neck electromyogram (EMG) were obtained and sleep stages were scored using SleepSign. Recordings were conducted during the light phase, and drug effects were evaluated for five hours post-administration. Sleep parameters including total sleep time (TST), sleep latency, sleep architecture for the macrostructure, and sleep bout duration, number of arousals for microstructure. We also analyzed EEG power changes. Lemborexant was assessed as a drug for insomnia, and trazodone was evaluated as a drug studied for both sleep and SAS. Atomoxetine and acetazolamide were assessed as drugs studied for SAS.

Results: Lemborexant shortened sleep latency and showed a tendency to increase total sleep time (TST), without altering sleep architecture. Trazodone did not affect TST but increased NREM sleep. Regarding sleep microstructure, lemborexant did not change sleep bout duration or the number of arousals, whereas trazodone increased bout duration and reduced arousals. Atomoxetine and acetazolamide did not significantly affect sleep microstructure, but atomoxetine altered sleep architecture. Changes in delta power during sleep were observed in trazodone and atomoxetine, consistent with the alteration in sleep architecture.

Conclusions: Both lemborexant and trazodone modulate sleep, but their effects on sleep macrostructure and microstructure differ. Given that these drugs have different mechanisms of action, their distinct effects on sleep macrostructure and microstructure may suggest that each is suited to different types of sleep disorders. While macrostructural changes are considered important for insomnia, microstructural aspects may also play a meaningful role. In contrast, for other disorders such as SAS, microstructural changes such as sleep bout duration and the number of arousals may provide even more relevant indicators of treatment effects.

It is important to appropriately select assessment methods that correspond to the pathophysiology of each disorder. By focusing on both macrostructure and microstructure, we can gain deeper insights into promising pharmacological approaches for various sleep disorders.

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Digital Health Engagement and CPAP Adherence: Analysis of Patient Interaction with the myAir App

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Introduction: Adherence is a crucial indicator in assessing the efficacy of continuous positive airway pressure (CPAP) therapy for sleep apnea. Although telemedicine enhances adherence and mobile apps represent a viable approach, individual variations may exist in the level of engagement with these apps.

Materials and methods: A retrospective chart analysis was performed on patients utilizing the myAir app, compatible with ResMed CPAP devices, across four hospitals in Japan from January 2023 to April 2024. Patients can track their CPAP usage and obtain guidance on appropriate use by employing the app. The app has a function whereby patients receive a maximum of five inquiries monthly regarding their sleepiness, which they can evaluate on a five-point scale, and their responses are transmitted to medical institutions. We classified patients who did not respond within a one-month period as having poor engagement. We transformed responses on a 5-point scale about how sleepy they were into 1–5 points, with larger scores denoting more sleepiness. The average of multiple replies indicated post-treatment sleepiness. We extracted data on usage from medical records for the initial month following the beginning of treatment. Good adherence was characterized by using the device for four or more hours during a minimum of 70% of the observation period. Patients were divided into two groups according to adherence, and comparisons were made for background characteristics, app engagement, and pre- and post-treatment sleepiness.

Results: The study comprised 62 patients: 56 males and 6 females, with a mean age of 51.3 ± 12.3 years, a mean apnea-hypopnea index (AHI) upon diagnosis of 44.5 ± 18.4 events per hour, and a mean body mass index (BMI) of 28.3 ± 5.1 kg/m². Within one month of CPAP therapy, 27 patients had good adherence, while 35 exhibited poor adherence. Age, sex, AHI, and BMI were not significantly different between the groups. However, the group with poor adherence had significantly higher leak levels (10.4 vs 18.1 L/min, $p=0.002$) and a significantly higher percentage of poor app engagement (18.5% vs 42.9%, $p=0.042$). Excluding patients with poor app engagement, 22 individuals in the good adherence group and 23 in the poor adherence group reported on sleepiness via the apps. Post-treatment sleepiness scores were 2.0 and 2.8 points, respectively, on a 5-point scale, with the poor adherence group exhibiting significantly higher sleepiness ($p=0.009$).

Conclusions: Reduced leak levels and good app engagement were proposed as indicators of favorable short-term CPAP adherence. Furthermore, among patients exhibiting good app engagement, individuals in the poor adherence category demonstrated minimal improvement in sleepiness.

Distinct Salivary Microbial Signatures Associated with Anatomical Sites of Upper Airway Obstruction Caused by Lymphoid Hypertrophy in Children

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Introduction: Adenoid hypertrophy and tonsillar hypertrophy are the most common causes of upper airway obstruction in children and are major risk factors for pediatric obstructive sleep apnea (OSA). Clinical observations and previous studies have shown that children with obstruction at different anatomical site often exhibit distinct craniofacial morphological features. In addition, earlier research has identified characteristic salivary microbiota profiles in children with OSA compared to healthy controls. While these findings suggest a potential link between airway obstruction and biological signatures such as microbiota composition, the specific influence of the obstruction site on the salivary microbial environment remains unexplored.

Materials and methods: A total of 92 children (mean age 7.79 ± 2.41 years) were categorized into four groups: tonsillar hypertrophy (TH, $n=26$), adenotonsillar hypertrophy (ATH, $n=21$), adenoid hypertrophy

(AH, n=23), and healthy controls (n=22). Unstimulated saliva samples were collected and analyzed using 16S rRNA sequencing targeting the V3–V4 regions. Microbial diversity and composition were assessed and correlated with polysomnographic and hematologic parameters. Comparative analysis across obstruction sites was emphasized.

Results: Significant differences in α -diversity (Chao1, Faith's PD, Shannon, and Observed species) were observed among the groups, with TH group showing increased richness and diversity compared to AH, ATH and control groups ($p < 0.05$). β -diversity analysis revealed distinct microbial community structures associated with the site of obstruction ($p < 0.05$). Notably, *Firmicutes*, particularly genera such as *Gemella*, *Parvimonas*, and *Dialister*, were enriched in TH group. These findings suggest a potential link between microbial composition and immune activity at different obstruction sites. No substantial microbiota variation was found across different severities within the same anatomical site.

Conclusions: Salivary microbiota composition varies according to the location of upper airway obstruction in children, indicating that the anatomical site of hypertrophy plays a more pivotal role in shaping microbial profiles, offering novel perspectives for future related research.

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Distraction Osteogenesis Maxillary Expansion (DOME) in Isolated and Personalized Multilevel Surgery for Obstructive Sleep Apnea: The First Clinical Case Series in Thailand

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Introduction: Obstructive sleep apnea (OSA) is frequently associated with transverse maxillary deficiency, manifesting as a high-arched, narrow palate that compromises nasal airflow and contributes to tongue crowding. Distraction Osteogenesis Maxillary Expansion (DOME) enables skeletal midpalatal expansion in skeletally mature adults. This study presents the first clinical case series in Thailand utilizing DOME as part of a personalized, multilevel surgical strategy for OSA. We aimed to evaluate the one-year outcomes, safety, and feasibility of this approach.

Materials and methods: Six adult OSA patients (mean age: 31 years; 5 males, 1 female) with high-arched, constricted maxilla underwent DOME using customized bone-anchored palatal expanders secured with mini-implants. Minimally invasive osteotomies were performed to allow gradual midpalatal expansion. DOME was integrated into individualized treatment plans, and combined with site-specific procedures such as nasal surgery, tonsillectomy, uvulopalatopharyngoplasty, genioglossus advancement, or bimaxillary osteotomies, based on anatomical needs. Some procedures were staged separately when simultaneous surgery was not feasible due to anatomical or procedural constraints. Pre- and post-operative evaluations included polysomnography, dental arch analysis, and craniofacial measurements. Measured parameters included dental class, skeletal facial profile, intercanine and intermolar widths, maxillary base width, palatal expansion distances, and maximum diastema width. Occlusion and facial profiles were assessed clinically.

Results: All patients achieved successful midpalatal suture separation, with a median diastema width of 9.5 mm (range: 7–10 mm), confirming skeletal expansion. Mean maxillary skeletal base width increased from 63.60 mm to 67.81 mm; mean intermolar width expanded from 50.04 mm to 58.10 mm. Intercanine width increased across all cases, with an average gain of 7.4 mm. Palatal expansion at anterior, midline, and posterior points reached mean values of 10.15 mm, 7.29 mm, and 4.55 mm respectively.

Dental occlusion remained stable in five patients; one improved from Class III to Class I. Two patients experienced facial profile correction from convex to straight. Three device-related complications occurred: two required reoperation due to insufficient expansion from short midline screws, and one had posterior screw loosening resolved with screw replacement. No major complications were observed. Minor complications included transient numbness, which resolved without lasting effects. At one-year follow-up, median AHI decreased from 33.0 to 15.1 events/hour (55% reduction). Four patients achieved a >50% AHI reduction, with one reaching normalized AHI <5. Oxygenation improved in most cases (median ODI from 9.7 to 5.6 events/hour), and responders demonstrated increased REM sleep percentage (mean REM% from 14% to 26%). Quality of life, assessed by a VAS scale (–10 to +10), showed consistent improvement in all cases (median +7; range +5 to +9), with better sleep continuity,

reduced mouth breathing, and improved daytime functioning.

Overall, the combined approach resulted in anatomical, functional, and symptomatic improvements in the majority of patients.

Conclusions: DOME provides effective maxillary expansion with preservation of occlusion, supporting its integration into multilevel OSA surgery. This first Thai case series affirms DOME as a safe and effective modality to correct transverse maxillary deficiency in adult OSA. Larger studies are warranted to validate these findings.

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Distribution and characteristics of habitual snoring from a global population

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Introduction: Evidence suggests that occasional snoring varies significantly in prevalence, ranging from 2% to 86%, largely due to self-reported measurement methods. To better understand snoring features, studies using objective records from large population samples are essential. This research aimed to investigate the distribution and characteristics of snoring among general worldwide users of the Samsung Health application over a five-month timeframe, under real-life conditions.

Materials and methods: Data were sourced from Samsung servers, including users with sleep data updated from February to June 2024. Eligible users recorded at least one sleep session ≥ 20 minutes with a Samsung Galaxy Watch (version 4 or later) and updated demographic details (age, weight, height, and gender). Users < 20 years old were excluded. Users were categorized based on weekly snoring frequency: (1) Frequent snorers, individuals who experienced snoring on ≥ 3 days per week; and (2) Non-frequent snorers, including those who snored < 3 days per week or had no snoring events detected. Oxygen saturation (SpO₂) measurements were assessed in a sub-dataset. Statistical analyses used PySpark 2.4.7, with normalized data presented as frequency/percentage for categorical variables and mean $\pm$ SD for continuous variables. The Ordinary Least Squares test evaluated age and body mass index (BMI) significance ($p < 0.05$), while the Mann-Whitney U test analyzed SpO₂, snoring duration, and BMI, adjusted for Bonferroni correction.

Results: The analysis included 6,084,029 users: 5,397,593 non-frequent snorers and 686,436 frequent snorers, totaling 130,146,432 snoring sessions. From the total group, 58% were males and 48% were between 20-40 years old. The mean BMI was 27.3 ± 6.1 kg/m² (27.5 ± 5.1 for males, 27.1 ± 6.1 for females) and 62% were classified as pre-obesity to obesity III. Males presented a higher proportion (67%) in the BMI categories of pre-obesity to obesity III compared to females (55%). Users were geographically distributed across all continents, with Europe (39%), the Americas (30%), and Asia (27%) being the most represented. Frequent snorers comprised 11.3% of the total group (11.5% males, 10.9% females). For both males and females, snoring proportion increased with age up to the 50s, and frequency in males was higher in all of age groups. Pre-obesity to obesity III prevalence was 54% in females and 73% in males in the frequent snorers group. Snoring sessions duration and frequency progressively increased with BMI in both genders. SpO₂ levels during sleep were significantly ($p < 0.05$) lower in frequent snorers ($93.57 \pm 2.62\%$) compared to non-frequent snorers ($93.80 \pm 2.66\%$), with significant ($p < 0.05$) decreases in SpO₂ correlating with BMI severity in frequent snorers.

Conclusions: Global data from over 6 million wearable device users (with > 130 million snoring sessions assessed) showed that snoring was prevalent in both genders, with higher frequency and duration of the snoring sessions as BMI categories increases. These findings suggest that objective snoring data, measured by wearable devices used in real-world and free-living conditions, are reliable tools for understanding and monitoring snoring patterns, echoing previous controlled studies.

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Does enlarging the pharyngeal lumen or bony enclosure translate to better airflow in obstructive sleep apnea? A State-of-the-Art Review

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Introduction: This review aims to assess the efficacy of airway reconstructive surgeries—both intra-pharyngeal (soft tissue) and extra-pharyngeal (craniofacial)—in improving respiratory airflow and alleviating obstructive sleep apnea (OSA) symptoms.

Materials and methods: Data Sources: A literature search was conducted using databases such as PubMed, MEDLINE, and Scopus, focusing on studies evaluating uvulopalatopharyngoplasty (UPPP), maxillomandibular advancement (MMA), hyoid myotomy with mandibular suspension (HS), and hyoidthyroidpexy (HTP). Keywords included "OSA surgery," "airway enlargement," "respiratory airflow dynamics," and "pathophysiological mechanisms."

Methods: Selected studies were analyzed for evidence of airway structural changes, impact on airflow dynamics, and reductions in OSA severity. A simplified static respiratory geometric model, represented as a cylindrical conduit, was applied to synthesize the data and understand how each procedure influences airflow.

Results: Both intra- and extra-pharyngeal surgeries were found to induce structural modifications that reduce airway resistance and improve airflow. However, these interventions alone may not fully address the multifactorial nature of OSA. Factors such as airway collapse and occlusion persist despite surgical enlargement of the upper airway lumen.

Conclusions: Airway reconstructive surgeries contribute to improved respiratory airflow by reducing airway resistance. However, a comprehensive understanding of the underlying pathophysiological mechanisms is essential for optimizing treatment outcomes. Combining surgical interventions with adjunct therapies may offer a more holistic approach to managing OSA.

Does OSA severity reflect symptom burden? Clinical equivalence in REM- and non-REM-predominant OSA

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Introduction: REM-predominant Obstructive Sleep Apnea (REM-OSA) is often treated as a distinct clinical phenotype, yet evidence for clinically meaningful impacts on symptoms, comorbidities, or prognosis remains inconsistent. Moreover, traditional null hypothesis testing may be insufficient to address this knowledge gap. Equivalence testing may be helpful to assess whether people with REM-OSA differ from those without REM-predominant OSA (nREM-OSA) across common clinical and patient-reported outcomes.

Materials and methods: Data were drawn from 77 participants with suspected OSA from the Simplified Assessment and Monitoring of OSA (SAMOSA) observational cohort study. REM-OSA was defined as a REM/non-REM apnea-hypopnea index (AHI) ratio >2 and a non-REM AHI <15 events/h on polysomnography, while all others with a REM or non-REM AHI >5 events/h but not meeting REM-OSA criteria were classified as nREM-OSA. Participants with both REM and nREM AHI <5 events/h were excluded. Outcomes included the Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), Functional Outcomes of Sleep Questionnaire-10 items (FOSQ-10), the EQ-5D visual analogue scale (EQ-5D-VAS), mean systolic (SBP) and diastolic blood pressure (DBP), and self-reported diagnoses of depression and anxiety. To assess similarity, two one-sided tests of equivalence were conducted between REM-OSA and nREM-OSA groups on each outcome based on *a priori* minimally important differences (MIDs). These were defined as ESS=2 points, ISI=6 points, FOSQ-10=1.8 points, EQ-5D-VAS=5 points, SBP/DBP=2mmHg, and depression/anxiety=2-fold greater odds. Where equivalence was not established, group differences were compared using linear models. All analyses were run both unadjusted and adjusted for age and sex.

Results: Of the initial cohort, nine participants were excluded due to no REM or nREM OSA (AHI<5 events/h). 68 participants were included in final analyses (age[mean±SD] = 54±14 years; 51% male, 49% female). The REM-OSA group had significantly lower overall AHI (8±6 events/h) than the nREM-OSA group (32±29 events/h), $p<.001$. Despite this, REM-OSA was equivalent to nREM-OSA within predefined MIDs on outcomes of FOSQ-10 and ISI scores. Equivalence within MIDs was not established for ESS, EQ-5D-VAS, blood pressure, anxiety, and depression. Indeed, rates of self-reported anxiety were significantly higher in REM-OSA vs. nREM-OSA (48 vs.19%, $p=.02$). No significant differences between REM- and nREM-OSA were present for EQ-5D-VAS (70±21 vs. 73±14), SBP (122±11 vs. 127±12 mmHg), DBP (80±8 vs. 81±7 mmHg), or rates of depression (23 vs. 32%).

Conclusions: Using equivalence testing, we show that insomnia severity and sleep-related daytime functional impairment in REM-OSA are equivalent to nREM-OSA within MIDs, despite substantially lower overall AHI values in the people with REM-OSA. Moreover, rates of self-reported anxiety were higher in REM- compared to nREM-OSA. These findings challenge assumptions that lower OSA severity determined by the overall AHI necessarily translates to lower symptom burden. These results highlight the potential for high symptom burden in REM-predominant OSA, irrespective of overall OSA severity, that is phenotypically distinct from non-REM-predominant OSA.

Dramatic Improvement of Obstructive Sleep Apnea Following Kidney Transplantation in an ESRD Patient: A Case Report

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Introduction: Obstructive sleep apnea (OSA) is a prevalent condition in patients with end-stage renal disease (ESRD), with estimated prevalence rates nearing 50%. Recent research suggests a bidirectional relationship between OSA and chronic kidney disease (CKD), in which renal dysfunction contributes to OSA pathophysiology and vice versa. However, clinical evidence demonstrating improvement of OSA following restoration of renal function remains limited. This case highlights a patient with ESRD whose OSA significantly improved following kidney transplantation.

Materials and methods: A 51-year-old male with ESRD on peritoneal dialysis presented with severe snoring, fragmented sleep, and excessive daytime sleepiness. Despite prior surgical intervention (uvulopalatopharyngoplasty and tonsillectomy), symptoms persisted. Initial polysomnography (PSG) confirmed severe OSA. The patient underwent treatment with multiple modalities of positive airway pressure (PAP) therapy, including automatic (APAP), continuous (CPAP), and bi-level (BiPAP) devices, but showed minimal subjective or objective improvement over a six-month period.

Results: Sixteen months after the second PSG, the patient underwent deceased donor kidney transplantation. Postoperatively, he reported spontaneous and sustained improvement in sleep quality and resolution of apnea-related symptoms. Follow-up PSG showed a marked reduction in AHI and oxygen desaturation index (ODI), with severity improving from severe to mild OSA. The patient continues to be monitored under APAP therapy, though pressure requirements and symptom burden have significantly decreased.

Conclusions: This case supports the hypothesis that renal dysfunction plays a contributory role in the pathogenesis and persistence of OSA. The improvement observed following kidney transplantation—despite the failure of prior PAP therapies—suggests that fluid overload and uremic status may be key reversible factors. Clinicians should consider underlying renal pathology when evaluating OSA severity and treatment response in ESRD patients. Additionally, ODI may serve as a useful complementary marker alongside AHI in assessing disease burden in this population.

Dynamic Changes in Pulse Propagation Time Following Respiratory Events are Associated with Cortical Arousals in Obstructive Sleep Apnea

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Introduction: Cortical arousals significantly impact obstructive sleep apnea (OSA) pathophysiology and cardiovascular consequences, often mediated by sympathetic activation. While pulse oximetry (PPG) provides an accessible reflection of autonomic responses such as changes in pulse rate (PR) and pulse wave amplitude (PWA), the dynamic influence on other vascular indices remains less explored. Pulse Propagation Time (PPT), (interval from the systolic to the diastolic peak of the PPG pulse wave) is known to reflect modulation in vascular stiffness during sleep. This study examines dynamic changes in PPG-derived PPT following respiratory events (apneas/hypopneas) and evaluates the association with EEG-based cortical arousals in patients with OSA.

Materials and methods: Polysomnography data from 87 patients referred for suspected OSA were analyzed. A total of 18,275 apnea and hypopnea events were identified. Beat-to-beat PPG signals were processed to extract percentage changes in PWA, PR, and PPT following each respiratory event, alongside changes in SpO₂. EEG-based cortical arousals coinciding with event termination were manually scored. Statistical comparisons (t-tests) and logistic mixed-effect models were used to assess the association between PPT parameter changes and EEG arousals, controlling for age, gender, BMI, event type, SpO₂ change, and other PPG parameters.

Results: The mean percentage change (shortening, vascular stiffening) of the PPT following respiratory events was significantly greater when accompanied by an EEG arousal compared to events without arousal (-20.1% vs. -17.3%, $p < 0.001$; $N=18275$ events). This difference remained significant when analyzing apneas (-21.0% vs -17.9%, $p<0.001$) and hypopneas (-19.4% vs -17.0%, $p<0.001$) separately. In the multivariate logistic model, the change in PPT emerged as an independent predictor of EEG arousal presence ($p < 0.001$ with scaled odds ratio: 0.87; 95% CI: 0.83-0.92), after accounting for changes in PWA, PR, SpO₂, and other covariates.

Conclusions: Dynamic, short-term changes in PPG-derived PPT are significantly associated with cortical arousals following respiratory events in OSA patients. This parameter provides independent predictive information beyond established PPG metrics like PWA and PR, potentially reflecting rapid, arousal-induced alterations in vascular tone. These findings highlight a novel PPG-based marker that could contribute to non-EEG based assessment of arousal responses in OSA.

Effectiveness of drug-induced sleep endoscopy in improving outcomes of barbed pharyngoplasty for obstructive sleep apnea surgery: a prospective randomized trial

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Introduction: To observe the effectiveness of preoperative drug-induced sleep endoscopy in improving surgical results of patients undergoing single-level barbed pharyngoplasty surgery for OSA, using a prospective randomized model.

Materials and methods: A single-center randomized controlled trial with two prospective arms was carried out to compare functional results in patients treated with barbed reposition pharyngoplasty (BRP) surgery without a preoperative drug-induced sleep endoscopy (DISE) evaluation vs patients treated with BRP surgery performed after DISE evaluation of sites/patterns of collapse.

Results: We compared 50 patients who underwent BRP without a preoperative DISE evaluation (Group A) and 42 patients (Group B) treated with BRP surgery but preoperatively selected by means of a preoperative DISE. In this second group of patients, after DISE evaluation, 70% of patients were selected for single-level BRP surgery because they showed an isolated velopharyngeal collapse at the DISE evaluation, without obstruction at other upper airway levels evaluated. Both groups of patients showed a statistically significant difference between preoperative and postoperative values of AHI, ODI, and LOS ($p<0.05$ in all cases). Comparing Group A and Group B patients, the therapeutic success rate was found to be 60% in patients treated without preoperative DISE evaluation and 83% in patients treated with preoperative DISE ($p = 0.02$).

Conclusions: DISE appears to improve the surgical results of single-level velopharyngeal surgery due to the possibility of excluding patients with obstruction of the base of the tongue, the hypopharynx, and the epiglottis/larynx.

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Effectiveness of Inflatable Positional Therapy Device in Patients with Position-Dependent Obstructive Sleep Apnea

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Introduction: Continuous positive airway pressure (CPAP) remains the gold standard treatment for obstructive sleep apnea (OSA). However, a substantial proportion of patients exhibit poor compliance, particularly those with mild-to-moderate and oligosymptomatic disease, often associated with positional dependency. In such cases, positional therapy may be beneficial.

The main objective of this study is to evaluate the effectiveness of a novel positional therapy device (a pillow with an inflatable core) in patients with position-dependent obstructive sleep apnea (POSA).

Materials and methods: Eighteen ambulatory patients (17 males, 1 female; age: 48.6 ± 14.1 years; BMI: 28.5 ± 2.8 kg/m²) diagnosed with POSA were enrolled. POSA was defined as an apnea-hypopnea index (AHI) in the supine position at least twice that in the non-supine position, with non-supine AHI < 30 events/h.

Exclusion criteria included: 1. Other sleep disorders; 2. Significant somatic or psychiatric comorbidities and 3. <10% time spent in the supine position during total sleep time

Baseline home respiratory polygraphy was conducted using the NoxA1 system (NoxMedical, Iceland), with recordings scored according to standard guidelines (version 2.3 of the American Academy of Sleep Medicine criteria). Participants then used a TED BED EAD positional pillow (inflatable core, worn like a backpack) for 4–7 nights. A second polygraphy was performed under treatment conditions. Normality of differences (POST–PRE) was tested using the Shapiro–Wilk test. Paired t-test was applied for normally distributed variables and the Wilcoxon signed-rank test for non-normal distributed variables. A significance level of $p < 0.05$ was used. Normally distributed data are presented as Mean $\pm$ SD and non-normally distributed data as Median (25th–75th percentile). All comparisons are presented as (after vs before).

Results: Significant reductions were observed in AHI (9.4 ± 8.4 vs 21.7 ± 13.3 , $p < 0.001$), oxygen desaturation index (ODI) (6.4 (5.3 – 9.6) vs 15.6 (12.0 – 23.6), $Z = -3.724$, $p < 0.001$), and time of SpO₂ under 90% (SpO₂ < 90%) (0.6 (0.1 – 3.3) % vs 2.5 (0.6 – 12.4) %, $Z = -3.054$ $p = 0.002$).

These effects were primarily attributed to a significant reduction in supine sleep time (9.7 ± 12.3 % vs 46.4 ± 24.2 %, $p < 0.001$), while the total sleep time was not statistically different (415.1 ± 74.4 min with treatment vs 456.4 ± 54.7 min at baseline, $p = 0.074$).

Additionally, improvements in supine oxygenation levels were also found: ODI in supine position (6.3 (0 – 13.3) vs 29.7 (19.3 – 55.2), $Z = -2.865$, $p = 0.004$) decreased and the average SpO₂ (94.1 (92.4 – 93.4) % vs 93.2 (92.3 – 93.4) %, $Z = -2.486$, $p = 0.013$) and minimal SpO₂ (90.0 (86.0 – 92.5) % vs 83.0 (76.8 – 86.3) %, $Z = -3.177$, $p = 0.001$) in supine position increased. No significant differences were detected in non-supine oxygenation parameters.

Conclusions: A positional therapy pillow with an inflatable core significantly reduces AHI and improves oxygenation in patients with POSA, offering a promising alternative to CPAP therapy in selected cases.

Acknowledgments: We thank TED BED EAD for designing the positional therapy pillow with inflatable core.

Effect of adenotonsillectomy on lipid profile in children with obstructive sleep apnea

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Introduction: Limited evidence addressing effects of adenotonsillectomy (T&A) on lipid profiles in childhood obstructive sleep apnea (OSA). The aim of this study is to elucidate changes in lipid profiles after surgery in children with OSA.

Materials and methods: Children aged 4-16 years with clinical symptoms and polysomnography (PSG)-diagnosed OSA (apnea-hypopnea index, AHI >1) were recruited from a tertiary medical center and received T&A as the treatment for OSA. All children had the postoperative PSG studies, and examined for lipid profiles (i.e. total cholesterol, triglyceride, low-density lipoprotein [LDL], and high-density lipoprotein [HDL]) before and 6 months after surgery.

Results: This study included 124 children (mean age, 6.3±3.0 years; 65% boy). T&A resulted in a significant reduction of the AHI from 12.3±17.9 to 2.9±5.7 per hour ($P < 0.001$). After surgery, total cholesterol (162.9 to 164.4 mg/dL, $P = 0.51$), triglyceride (79.3 to 79.9 mg/dL, $P = 0.87$), and LDL (97.0 to 96.5 mg/dL, $P = 0.75$) were not significantly changed. The HDL was significantly increased from 53.3 to 55.7 mg/dL after surgery ($P = 0.03$). Moreover, the LDL/HDL ratio was significantly decreased from 1.99 to 1.87 after surgery ($P = 0.004$).

Conclusions: Adenotonsillectomy (T&A) treatment may provide beneficial effects on lipid profiles in children with obstructive sleep apnea (OSA).

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Effect of Continuous Positive Airway Pressure on Intraocular Pressure in Patients with Obstructive Sleep Apnea – A Systematic Review and Meta-Analysis

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Introduction: While the association between Obstructive Sleep Apnea (OSA) and glaucoma has been well studied, the long-term effects of Continuous Positive Airway Pressure (CPAP) therapy on Intraocular Pressure (IOP) and glaucoma progression is less known. With the increasing prevalence of both OSA and glaucoma globally, along with varying reports in the literature of the effect of CPAP therapy on IOP, an in-depth review of existing literature in this present moment is of utmost clinical importance. Clarification of the relationship between CPAP therapy and IOP may help to guide patient management and improve health outcomes. This study aims to systematically synthesise evidence to clarify the association between CPAP therapy and IOP.

Materials and methods: PubMed, Embase, The Cochrane Library, CINAHL, Scopus and Web of Science were searched through 26 March 2025 for interventional studies evaluating the effect of CPAP on IOP among OSA adult patients. Two independent authors selected relevant articles, extracted data and evaluated the quality of evidence using the Newcastle-Ottawa Scale (NOS), Cochrane Risk-of-Bias Tool for Randomised Trials (RoB 2) and Grading of Recommendations Assessment, Development and Evaluation (GRADE). Inverse variance meta-analyses were conducted using random effects. I^2 values were used to evaluate for heterogeneity. To account for potential sources of heterogeneity, further

subgroup analyses were performed. Additional leave-one-out analysis and cumulative analysis were also conducted to evaluate the impact of omitting each study on the overall effect size and the stability of the pooled effect size over time respectively. To assess for publication bias, visual inspection for funnel plot asymmetry was conducted.

Results: This study included 16 studies, pooling a cohort of 602 patients. The risk of bias of studies ranged from low-moderate and the quality of evidence was moderate on GRADE. CPAP therapy significantly increased IOP levels overnight (MD: -4.14; 95% CI: -7.76, -0.52; $I^2=76\%$; $p=0.04$), and after one month (MD: -0.78; 95% CI: -1.21, -0.35; $I^2=0\%$; $p=0.60$). IOP levels remained unchanged with CPAP therapy of more than one month. Our findings remained significant and stable through the various subgroup and sensitivity analyses, with no publication bias noted.

Conclusions: While short-term CPAP therapy of one month or less in OSA patients was associated with elevated IOP, minimal long-term effects were observed after one month. Nonetheless, these findings underscore the importance of exercising caution when administering CPAP therapy on IOP especially in glaucomatous patients. Further studies are needed to investigate whether CPAP affects the risk of glaucoma directly.

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Effect of CPAP on Subjective and Objective Cognitive Deficits in Post-COVID Patients with Obstructive Sleep Apnea

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Introduction: Cognitive deficits are reported in up to 60% of patients with post-COVID syndrome. Obstructive sleep apnea (OSA), which commonly co-occurs in this population, may further exacerbate these cognitive symptoms. This study aimed to evaluate whether treatment of OSA with continuous positive airway pressure (CPAP) improves subjective and objective measures of cognitive fog in post-COVID patients with comorbid OSA.

Materials and methods: Patients meeting the WHO criteria for post-COVID syndrome, who reported cognitive fog and were diagnosed with OSA, were recruited for the study. Neuropsychological testing was conducted at baseline and again at 4 ± 2 weeks after initiating CPAP therapy. We assessed key domains of executive function, including working memory (Digit Span Backward), task switching (Trail Making Test Part B), and inhibition (Stroop Color-Word Test). Additional cognitive measures included Processing speed (Digit Symbol Substitution Test), Vigilance (Psychomotor Vigilance Test), and Episodic memory (Benson Complex Figure Delayed Recall Test). Patient-reported cognitive fog was evaluated using the PROMIS Cognitive Function scale.

Results: Among 17/20 recruited patients who completed the study, the mean age was 49 ± 14 years; 55% were women, 15% were Black, the median AHI was 12 (9.6–30), and the mean BMI was 34.5 ± 9.9 . The average nightly CPAP usage was 6 hours and 14 minutes ± 2 hours and 24 minutes. Executive functions improved following CPAP therapy across multiple domains: working memory assessed by the Digit Span Backward test (post: 8.1 ± 0.7 vs pre: 7.1 ± 0.4 ; $p = 0.08$), task switching by the Trail Making Test Part B (post: 60.8 ± 4.3 vs pre: 69.7 ± 5.3 ; $p = 0.06$), and inhibition by the Stroop Color-Word Test (post: 45.8 ± 2.9 vs pre: 40.7 ± 2.8 ; $p < 0.01$). There were significant improvements in other cognitive domains including Processing speed assessed with Digit Symbol Substitution Test (post: 59.8 ± 2.5 vs pre: 51.8 ± 2.7 ; $p < 0.01$), Episodic memory measured with Benson Complex Delayed Recall Test (post: 13.8 ± 0.5 vs pre: 12.2 ± 0.4 , $p = 0.02$) and substantial improvement in Vigilance measured by Psychomotor Vigilance Test-Mean Reaction Time (post: 238.3 ± 6.3 msec vs pre: 254.6 ± 7.5 msec, $p < 0.01$). Additionally, patient-reported cognitive function significantly improved as measured by the PROMIS Cognitive Function scale (post: 26.7 ± 2.1 vs pre: 17 ± 1.6 ; $p < 0.01$). Improvement in PROMIS scores correlated with nightly CPAP use ($r = 0.5$, $p = 0.04$).

Conclusions: Our findings suggest that treating comorbid OSA among patients with post-COVID syndrome can decrease cognitive fog in post-COVID patients.

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Effect of Neck-Bending on Upper Airway Caliber and Surrounding Soft Tissues in Controls and Apneics

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Introduction: Head and neck flexion and extension influence upper airway size, but the underlying mechanisms remain unclear. This study aims to investigate changes in airway caliber and the movement of surrounding soft tissues during head and neck flexion and extension in individuals with and without obstructive sleep apnea.

Materials and methods: Upper airway MRI was obtained in 24 controls (AHI<5; 1.5±1.5 events/hour) and 33 apneics (AHI≥5; 33.2±28.7 events/hour) with the neck in flexion, extension, and neutral positions. Differences in airway measures and soft-tissue movement were assessed.

Results: During extension, controls and apneics showed increased minimum cross-sectional area (CSA) and anteroposterior (AP) and lateral dimensions in the retropalatal ($p\leq 0.002$) and retroglossal ($p\leq 0.010$) airways. During flexion, both groups showed reduced lateral dimensions in the retropalatal ($p\leq 0.017$) and retroglossal ($p\leq 0.013$) airways; controls had reduced retroglossal CSA ($p=0.0001$) and apneics had reduced retroglossal AP dimension ($p=0.019$). In associations with degree of head/neck bending, moving from flexion to extension resulted in increased retropalatal/retroglossal airway sizes (all $p<0.0001$), less lateral wall narrowing ($p\leq 0.0001$), and more anterosuperior movement of soft palate and tongue ($p\leq 0.0001$). Results were generally consistent in controls and apneics, although each 1° change from flexion to extension resulted in greater increases in retropalatal airway size and more lateral movement of the lateral walls in controls (interaction $p\leq 0.005$).

Conclusions: Controls and apneics showed reductions in airway caliber during neck flexion and increases during extension, primarily due to movement of the soft palate, tongue, and lateral pharyngeal walls. These data provide important insights into the role of head and neck position on upper airway caliber.

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Effect of orofacial myofunctional therapy (OMT) on chewing efficiency, lip strength and tongue strength in participants of the "OMT with autofeedback for obstructive apnea" (OMTAOSA) randomized controlled trial

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Introduction: Obstructive sleep apnea (OSA) is a prevalent condition, estimated to affect nearly one billion people worldwide. OMT represents a novel, non-invasive approach to the treatment of OSA. Improving chewing function and oral muscle strength is a key objective in OMT. Accordingly, we hypothesized that chewing efficiency, lip- and tongue strength would improve after 12 weeks of OMT.

Materials and methods: The "OMT with autofeedback for OSA" multicenter randomized controlled trial (OMTAOSA RCT) included 104 newly diagnosed participants with mild to moderate OSA. Eligibility criteria included an apnea-hypopnea index (AHI) from 5 to 30 and body mass index (BMI) below 30. Participants adherent to a two-week electronic sleep diary pre-screening were randomized to a 12-week standardized OMT protocol or waitlist. Sleep was measured with self-applied polysomnography three consecutive nights at project start and end. Masticatory efficiency was assessed by a

standardized test measuring number of chewed particles (NP) and average particle size (PS), where higher NP and lower PS indicated better efficiency. Maximal anterior tongue strength (MTS) and maximal lip strength (MLS) were measured by the Iowa Oral Performance Instrument (IOPI) which measures pressure (kPa) exerted on a small air-filled bulb. Analyses followed the intention-to-treat principle. Between-group differences in effect of OMT were analyzed with independent t-tests and within-group changes with paired t-tests.

Results: Patients were randomized to a treatment group (n=52; mean age=46,3 years; BMI=26,4; AHI=13,77; 72,9% male) or a waitlist group (n=52; mean age=48 years; BMI=26,1; AHI=15,10; 66,0% male). Randomization was successful with no significant differences in age, BMI, AHI or gender. Between-group differences in post-intervention outcomes were not significant for NP (treatment: 493 vs. waitlist: 473; p=0,67), PS (31,9 mm² vs. 35,2 mm²; p=0,38), MTS (57,6 kPa vs. 57,6; p=1,00) or MLS (34,5 kPa vs. 33,3 kPa; p=0,38). Within-group analyses showed significant NP increase in both treatment (pre: 438; post: 493; p=0,02) and waitlist groups (pre=420; post=473; p<0,01), but no significant PS changes (treatment: p=0,40 vs. waitlist: p=0,14). MTS increased significantly only in the waitlist group (pre=55,4kPa; post=57,6kPa; p=0,04), but not in the treatment group (pre=56; post=57,6; p=0,18). No significant changes were observed in MLS within either group (treatment: pre=33,4kPa; post=34,5kPa; p=0,06 vs. waitlist: pre=33,4kPa; post=33,3kPa; p=0,83).

Conclusions: The hypothesis that twelve weeks of OMT would improve chewing function, lip strength, or tongue strength was not supported by the results. Surprisingly, there were very small differences between groups. Future analyses are pre-specified and will examine per-protocol and subgroup potential effects after adjustment for treatment adherence and baseline OSA severity.

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Effect of Self-Viewing Sleep Videos on CPAP Adherence: A Prospective Real-World Study in Patients with Sleep Apnea Syndrome

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Introduction: Adherence to positive airway pressure (PAP) therapy in obstructive sleep apnoea (OSA) remains suboptimal. Previous cognitive behavioural therapy (CBT) has relied on passive education approaches and has yielded mixed results. To evaluate whether personalised video footage showing one's own sleep-disordered breathing events (Self-Viewing of Sleep Apnea Videos, SVSV) improves PAP adherence.

Materials and methods: In this randomised controlled trial, 228 treatment-naïve patients with moderate to severe OSA were assigned to either the SVSV or standard CBT-only (control) group. All participants received standard CBT before PAP initiation. The SVSV group additionally viewed video footage of apnoeas from their own diagnostic polysomnography. The primary outcome was good adherence, defined as ≥4 hours of sleep per night on ≥70% of nights for 90 days. Secondary outcomes included the number of days with adequate use, mean daily usage time, and apnoea-hypopnoea index (AHI) during PAP. Statistical analysis was performed using independent t-tests and chi-square tests. A p-value < 0.05 was considered statistically significant.

Results: Good adherence was achieved in 89.5% of the SVSV and 78.1% of the control group (absolute difference, 11.4%; 95% confidence interval (CI), 1.94% to 20.86%). Compared with the control group, the SVSV group had more days with adequate usage (mean difference of 9.05 days; CI, 2.29 to 15.81) and longer daily usage (mean difference of 0.55 hours; CI, 0.13 to 0.98). AHI during PAP therapy was similar between the two groups.

Conclusions: This study supports the clinical utility of patient-specific visual feedback to improve PAP adherence. SVSV—a simple, low-cost, and scalable strategy—resulted in a higher proportion of patients achieving good adherence and greater nightly usage.

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Effect of Surgical Therapy of Sleep Apnea Syndrom in Patient Treated by Noninvasive Ventilation

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Introduction: The method of choice in patients with sleep apnea syndrome is Positive Airway Pressure (PAP - CPAP / BPAP), surgical intervention is usually a last resort. Some patients with PAP, who are treated suboptimally, may also benefit from concomitant surgery.

Materials and methods: The study included 25 patients with severe obstructive sleep apnea syndrome (age 17 - 72, baseline AHI 31 – 120, av. 66., baseline pressure on PAP 8-20 mbar) who were indicated for PAP therapy and whose treatment for various reasons was suboptimal. All patients underwent oropharyngeal surgery (tonsillectomy, uvulopalatopharyngoplasty, radiofrequency-assisted uvuloplasty, or a combination thereof). Two months after the operation, a controlled limited polygraphy and off-line retitration of the ventilation device were performed. Monitored parameters: 1. subjective difficulties, preventing further use of PAP treatment. 2. AHI before and after surgery. 3. The level of pressure on the PAP device before and after surgery.

Results: 1. None of the patients in our group had problems preventing further use of the ventilation device. 2. In all patients there was a statistically significant reduction in AHI after surgery ($p < 0.000012$). The mean reduction in AHI was 45 ($\pm 26,68$). Five patients did not continue treatment with CPAP / BPAP because it reached the limit of the indicative criteria for PAP (in Czech Rep. it is limit AHI 15), so their treatment can be considered successful. In seventeen of the remaining 20 patients, it was possible to reduce the pressure on the device after retitration, in three it was left at the original level. The mean pressure drop on the PAP device after retitration was 3,3 mBar (± 3.3), the average percentage reduction was 20% . The difference between the values before and after surgery is statistically significant ($p < 0.00294$)

Conclusions: The results of our pilot study show that patients with OSAS, who are treated with non-invasive ventilation and whose treatment is suboptimal, can benefit from concomitant surgical therapy. None of the patients in our cohort had problems with postoperative use of PAP therapy, while all had a decrease in AHI and most had a decrease in pressure on the PAP device.

Effect of waterless humidification via heat and moisture exchangers on long-term adherence to PAP therapy: a 12-month home-based study

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Introduction: Adherence to Positive Airway Pressure (PAP) treatment is essential to realising its full clinical benefits in patients with Obstructive Sleep Apnoea (OSA), including improved symptoms and long-term health outcomes. While humidification enhances comfort and may improve adherence, maintaining active humidification systems can be burdensome. Waterless humidification through heat and moisture exchangers (HMX) offers a low-maintenance alternative. This study aimed to evaluate the effect of HMX on 12-month PAP adherence and user experience in the home setting.

Materials and methods: This decentralised, prospective cohort study enrolled US-based established PAP users using cloud-connected devices, non-heated tubing and a patient-engagement app. Participants used an HMX device with their home PAP device and were followed remotely for 12 months.

Objective PAP therapy data including Apnoea-Hypopnoea Index (AHI), leak, pressure and usage were collected. Average nightly usage was assessed at baseline (3 months pre-enrolment) and tracked monthly during the 12-month follow-up. Usability, comfort, and ease of use were assessed monthly via 11-point Likert scale questionnaires. HMX discontinuation rates were assessed, and exploratory analyses examined the influence of seasonality, absolute humidity, and patient-app engagement. At study completion, participants were propensity-score matched to a retrospective control group using

active humidification. Analyses were conducted on intention-to-treat (ITT), per-protocol (PP), and as-treated (AT) populations using appropriate statistical methods.

Results: In the PP population (n=87), 12-month usage did not differ significantly from controls (6.8 vs. 6.7 hours/night; $p=0.64$), with a statistically significant increase from baseline (+18 minutes; $p=0.010$), although not clinically relevant.

In the AT population, consistent HMX users maintained PAP adherence comparable to controls ($\Delta=-12$ minutes; $p=0.39$), while non-users had significantly lower PAP adherence (5.2 vs. 6.9 hours/night; $\Delta=-108$ minutes; $p=0.0001$).

In the ITT population (n=164), average nightly usage at 12 months was significantly lower than in matched controls (5.6 vs. 6.5 hours/night; $\Delta=-54$ minutes; $p<0.0001$). Usage stabilised at approximately 5.5 hours/night after month 3, with early discontinuation (43.8%) occurring primarily in the first 3-4 months. Baseline usage <6 hours/night significantly predicted discontinuation ($p=0.021$).

Therapy parameters (AHI, leak, pressure) remained stable across all groups. No significant associations were found between adherence and seasonality, absolute humidity, or patient-app engagement. Positive usability ratings were sustained throughout 12-month follow-up, with participants rating the HMX favourably for breathing comfort, ease of use, and overall performance.

At study completion, 92.6% of participants preferred HMX during winter, 99.2% were satisfied with air temperature, and 87.6% with humidification. Participants were highly likely to recommend the HMX (Net Promoter Score [NPS]: 74), and moderately likely to purchase out-of-pocket (NPS: 25.6). No safety concerns were identified.

Conclusions: Patient populations that completed 12-month follow-up (PP) and consistently used HMX (AT) experienced no deterioration in long-term adherence, comfort, or therapy efficacy, with outcomes comparable to traditional humidification. Although early discontinuation affected the overall adherence in the full cohort, results suggest that HMX is a safe, low-maintenance alternative to active humidification for adherent users, particularly during colder months or for travel. These findings highlight the potential of HMX as part of a personalised approach to PAP therapy.

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Effects of acute exercise performed at different times of day on respiratory, blood pressure, and cardiac autonomic modulation outcomes in patients with obstructive sleep apnea: a randomized crossover trial

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Introduction:

Obstructive sleep apnea (OSA) is a prevalent sleep disorder associated with increased cardiovascular risk, including elevated blood pressure and impaired autonomic regulation. While physical exercise is recognized for its cardioprotective effects, the influence of exercise timing on sleep-related and cardiovascular outcomes in individuals with OSA remains unclear. This study investigated the acute effects of aerobic exercise performed at different times of the day on sleep respiratory parameters, blood pressure, and cardiac autonomic modulation in patients with OSA.

Materials and methods: In this randomized cross-over trial, 22 patients (age 57.4 ± 11.1 years old, body mass index 32.1 ± 6.1 kg/m²) with OSA (AHI 34.2 ± 23.8 events/hour) were recruited and completed four experimental sessions in random order: aerobic exercise and control in the morning (8:00- 11:00 AM) and in the afternoon (3:30-6:30 PM). Each exercise session consisted of 40 minutes of aerobic exercise on a treadmill at 54-59% heart rate reserve; each control session consisted of seated rest for 40 minutes. Measurements were taken in the supine position before and after each session for clinic and central BP and cardiac autonomic modulation (by heart rate variability). After each session, all patients underwent at-home polysomnography using a portable polygraph.

Results: Clinic systolic BP decreased following both morning (-16.1 mmHg; 95%CI = -22.5 to -9.7 mmHg; $p<0.001$) and afternoon exercise sessions (-11.4 mmHg; 95%CI = -16.8 to -5.9 mmHg; $p=0.03$). In addition, central systolic BP showed a decrease at both morning (-13.3 mmHg; 95%CI = -21.6 to -5.0 mmHg; $p=0.002$) and afternoon session (-13.9 mmHg; 95%CI = -20.1 to -7.7 mmHg; $p<0.001$). No significant changes were observed regarding diastolic BP, respiratory, or heart rate variability parameters ($p>0.05$ for all).

Conclusions: In conclusion, acute aerobic exercise has no effect on obstructive sleep apnea, but it does lead to a reduction in Clinic and Central BP, regardless of time of day.

Acknowledgments:

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Effects of adaptive servo-ventilation on sleep architecture in patients with central sleep apnoea and treatment-emergent periodic limb movements in sleep

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Introduction: In some patients with heart failure and reduced ejection fraction, adaptive servo-ventilation (ASV) is associated with an increase in periodic limb movements with arousal (PLMA). The aim of this study was to analyse the impact of ASV therapy on PLMA and to investigate the effects of treatment-emergent PLMA on sleep fragmentation and architecture in patients with central sleep apnoea (CSA).

Materials and methods: In 56 consecutive patients, three polysomnographies were retrospectively analysed (1. diagnostic, 2. on continuous positive airway pressure (CPAP), and 3. on ASV therapy). Patients with and without heart failure were included. Polysomnographic data were evaluated according to the 2017 criteria of the American Academy of Sleep Medicine. Treatment-emergent PLMA were defined as an increase in PLMA on ASV.

Results: Treatment-emergent PLMA under ASV occurred in 31 out of 56 patients (55%) (mean $\pm$ standard deviation: age 65 ± 12 years, body mass index 31 ± 5 kg/m², male 89%, heart failure 36%). The PLMA index increased significantly from the diagnostic night to the ASV night (median [25th; 75th percentile]: 5 [2; 7] vs. 7 [2; 16]/h, $p=0.018$), but not between the CPAP and ASV nights. From diagnostic to ASV PSG, patients without emergent PLMA showed a greater decrease in stage N1 sleep ($\Delta N1$: -13 [-25; -8]% vs. -5 [-16; 7]%, $p=0.015$) and greater increases in N3 and REM sleep ($\Delta N3$: 8 [1; 17]% vs. 3 [-8; 6]%, $p=0.003$; ΔREM 10 [4; 15]% vs. 5 [-3; 10]%, $p=0.043$) compared to patients with treatment-emergent PLMA. A further increase in N3 and REM sleep was observed from the CPAP night to the ASV night ($\Delta N3$: 4 [0; 12]% vs. 0 [-3; 6]%, $p=0.091$; ΔREM 3 [-1; 11]% vs. 0 [-6; 7]%, $p=0.057$ in patients without treatment-emergent PLMA compared to those with treatment-emergent PLMA).

Conclusions: Treatment-emergent PLMA on ASV affect more than half of patients with CSA, both with and without heart failure. ASV therapy significantly improves sleep architecture compared to the diagnostic night and showed an additional benefit over CPAP but only in patients without treatment-emergent PLMA. Treatment-emergent PLMA may be an important modifier for the effect of ASV on sleep architecture.

Effects of Continuous Positive Airway Pressure Treatment on Gut Microbiota and Metabolome in Obstructive Sleep Apnea Patients

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Introduction: Obstructive sleep apnea (OSA) is associated with gut dysbiosis and metabolic disturbances. Continuous positive airway pressure (CPAP) therapy is the standard treatment for OSA, but its impact on the gut microbiome and metabolome remains underexplored. This study aimed to investigate the effects of 6 - month CPAP treatment on fecal microbiota and metabolites in OSA patients and their correlations with clinical parameters.

Materials and methods: Fecal samples from 14 OSA patients were collected at baseline and after 6 months of CPAP treatment (n=28 in total). 16S rRNA gene sequencing was performed to analyze the microbiota, while untargeted metabolomics (LC-MS) identified metabolic profiles. Alpha and beta diversity indices were calculated, and group differences were assessed using PERMANOVA. Linear discriminant analysis effect size (LEfSe) identified differentially abundant bacteria, and orthogonal partial least squares discriminant analysis (OPLS-DA) was used to detect metabolic changes.

Results: CPAP treatment significantly increased gut microbiota alpha diversity ($p<0.05$) and altered the community structure (PERMANOVA, $p<0.01$). LEfSe analysis revealed that *Lachnospira* was the most discriminantly abundant genus (LDA score >4.0), with higher relative abundance after CPAP treatment. Particularly, the baseline abundance of *Lachnospira* was positively correlated with AHI ($r = 0.68$, $p<0.01$). Untargeted metabolomics detected 326 metabolites, of which 58 showed significant differences between baseline and post - treatment groups ($p<0.05$). Pathway analysis highlighted alterations in amino acid metabolism, lipid oxidation, and short-chain fatty acid (SCFA) biosynthesis pathways. Although canonical SCFAs were not directly identified, increased *Lachnospira* abundance may indicate enhanced SCFA production, potentially contributing to improved gut health.

Conclusions: CPAP treatment modulates the gut microbiota and metabolome in OSA patients. The positive correlation between *Lachnospira* and AHI highlights its potential as a biomarker for OSA severity. Further studies are warranted to elucidate the causal relationship between *Lachnospira* - associated metabolic alterations and OSA pathophysiology.

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Effects of CPAP on Neuroimaging Biomarkers and Cognition in adult OSA: A Randomized Controlled Trial

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Introduction: Obstructive sleep apnea (OSA) is associated with cognitive impairment. The effects of continuous positive airway pressure (CPAP) on neuroimaging biomarkers and cognitive performance among middle-aged patients with OSA and normal cognition remain unclear. The aim of our study was to investigate the effects of CPAP therapy over 12 months on neuroimaging biomarkers and cognitive performance.

Materials and methods: In this multicenter, randomized clinical trial, we randomly assigned 148 participants with normal cognition and an apnea-hypopnea index ≥ 15 /hour into two groups: patients receiving CPAP with best supportive care (BSC); and patients receiving BSC alone. The primary endpoint was the MoCA score at 6 months after enrollment. The secondary endpoints were intranetwork functional connectivity (FC) of the default mode network (DMN) and cortical thickness assessed by functional and structural magnetic resonance imaging, other neuroimaging biomarkers and neurobehavioral tests.

Results: Between 2017 and 2021, 148 patients were recruited from 5 hospitals. Linear mixed models showed that there was no significant difference in MoCA scores at 6 months between the CPAP and BSC groups (difference, -0.04, 95% confidence interval (CI), -0.72 to 0.65, $P=0.91$). However, there were significant differences in the FC of DMN (difference, -13.73, 95% CI, -23.40 to -4.06, $P=0.01$) and cortical thickness (difference, -0.06, 95% CI, -0.10 to -0.01, $P=0.02$) between the CPAP and BSC groups at 6 month after treatment. No serious adverse events occurred.

Conclusions: CPAP improved cortical thickness and FC of DMN, suggesting that patients with OSA may recover from brain atrophic processes following CPAP treatment. However, no improvement in MoCA scores was found.

Effects of Obstructive Sleep Apnea Treatment on Blood Biomarkers of Alzheimer's Disease: A Prospective Clinical Study

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Introduction: The relationship between obstructive sleep apnea (OSA) and Alzheimer's disease (AD) has attracted increasing attention. Intermittent hypoxia and sleep fragmentation associated with OSA may accelerate neurodegenerative changes and increase the risk of AD. This study aimed to investigate whether OSA treatment, particularly surgical intervention, influences blood biomarkers associated with AD and other neurodegenerative diseases.

Materials and methods: This three-year prospective, non-randomized study enrolled 73 patients with severe OSA (AHI ≥ 30) at Chiayi Chang Gung Memorial Hospital. Patients received either CPAP, sleep surgery, or conservative treatment, with an additional group of patients with dementia as a reference. Plasma levels of several biomarkers—including amyloid $\beta 1-40$ ($A\beta 1-40$), amyloid $\beta 1-42$ ($A\beta 1-42$), Tau protein, neurofilament light chain (NFL), and TDP-43—were measured at baseline and at 3, 6, and 9 months post-treatment using immunomagnetic reduction (IMR) technology.

Results: Significant reductions in the $A\beta 1-42/A\beta 1-40$ ratio were observed in both the CPAP and surgical groups at 6 and 9 months post-treatment ($p < 0.05$). In the surgical group, the ratio decreased by 18.4% at 6 months (95% CI: -30.7% to -6.0%) and 22.1% at 9 months (95% CI: -34.0% to -10.1%). In the CPAP group, reductions of 14.7% (95% CI: -28.6% to -0.9%) at 6 months and 19.5% (95% CI: -33.3% to -5.7%) at 9 months were noted. Additionally, the $A\beta 1-42$ concentration in the surgical group showed a significant decline of 17.9% at 9 months (95% CI: -29.8% to -6.0%). No statistically significant changes were observed in Tau, NFL, or TDP-43 across all groups and timepoints, suggesting limited short-term response.

Conclusions: This study indicates that effective treatment of OSA, especially through surgery, may help reduce blood-based biomarkers linked to Alzheimer's disease, particularly $A\beta 1-42$ and its ratio to $A\beta 1-40$. These findings suggest potential clinical value in AD prevention. However, changes in other neurodegenerative markers such as Tau and TDP-43 were not significant in the short term, highlighting the need for longer follow-up to elucidate long-term effects.

Effects of Reboxetine alone and in combination with Oxybutynin on quantitative electroencephalogram measures of alertness in obstructive sleep apnea

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Introduction: Obstructive sleep apnoea (OSA) often causes excessive daytime sleepiness, which can have major consequences on health, safety and productivity. Recent studies of noradrenergic and antimuscarinic agents to treat OSA have been promising, however subjective assessments of sleep quality and daytime sleepiness with these agents have shown inconsistent results. This study aimed to assess the effects of the noradrenergic agent reboxetine alone and in combination with the antimuscarinic oxybutynin on next-day alertness through objective assessment of quantitative electroencephalography (qEEG) power during resting wakefulness. We hypothesised that these agents would improve next day alertness through reduced wake EEG delta and theta power.

Materials and methods: 16 people with OSA from a double-blind, randomized, three-way crossover trial of 4mg reboxetine, placebo or 4mg reboxetine with 5mg oxybutynin completed morning and evening Karolinska Drowsiness Tests (KDT). Drug administration occurred after the evening KDT. Power spectral analysis of resting wake EEG data during eyes open and eyes closed conditions, and across the entire KDT was conducted with linear mixed models. EEG power in delta (0.5 – 4 Hz) and

theta (4 - 8 Hz) frequency ranges during the morning KDT tests were the primary alertness variables of interest.

Results: There was no significant main effect of treatment (Reboxetine vs placebo vs Reboxetine-Oxybutynin) on slow EEG frequencies during the morning KDT. There was no treatment by test time interaction, however there was a significant effect of testing time on EEG metrics. Delta EEG power during eyes open ($F[1, 54.3] = 35.9$; $p < 0.001$) and the entire KDT was significantly higher ($F[1, 58.8] = 32.5$; $p < 0.001$), during morning compared to the evening. Theta power was also higher during the eyes open condition in the morning ($F[1, 59.5] = 8.8$; $p = 0.004$).

Conclusions: Reboxetine with and without oxybutynin did not improve or impair morning alertness as measured by delta and theta EEG power during resting wakefulness. Despite the lack of improved alertness, these findings support the safety profile of these agents.

Acknowledgments: TJA contributed substantially to the acquisition of the data. CT, AV, DJE and TJA contributed substantially to the study design. All authors contributed to the data analysis, interpretation of the data and writing of the manuscript. All authors approve of the final version to be published and agree to be accountable for all aspects of the work.

Effects of strength training on blood pressure and arterial stiffness in adults with moderate to severe obstructive sleep apnea: a randomized controlled trial

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Introduction: Obstructive Sleep Apnea (OSA) is a sleep disorder characterized by partial (hypopnea) or complete (apnea) interruptions in airflow through the upper airways during sleep, leading to reduced oxygen saturation. OSA is closely associated with cardiovascular complications, such as elevated blood pressure (BP) and increased arterial stiffness—mainly driven by sleep fragmentation and intermittent hypoxia. Although continuous positive airway pressure (CPAP) is the first-line treatment for OSA, its effectiveness is often limited by poor adherence. Consequently, physical exercise—particularly strength training (ST)—has emerged as a promising non-pharmacological strategy to improve cardiovascular health in different populations. In individuals with OSA, ST may reduce body fat—especially in the cervical region—through exercise may alleviate upper airway narrowing. However, it remains unclear whether ST can reduce BP and arterial stiffness in adults with OSA. Thus, this randomized controlled trial aimed to evaluate the effects of an eight-week ST program on ambulatory, office, and central BP, as well as arterial stiffness, in adults with moderate to severe OSA.

Materials and methods: Participants aged 18 years or older with a confirmed diagnosis of moderate to severe OSA (based on the apnea-hypopnea index; AHI) were recruited from a sleep laboratory. Stratified by sex and OSA severity, participants were randomly assigned to either a ST group or a control group (CG). The ST group performed three sessions per week, consisting of eight resistance exercises, while the CG participated in two sessions per week of stretching exercises. OSA severity was assessed using full overnight polysomnography. Additionally, systolic and diastolic [BP (ambulatory, office, and central)] and arterial stiffness were evaluated. Generalized Estimating Equations (GEE) were used to analyze group-by-time interactions, with a significance level set at $p < 0.05$.

Results: A total of 26 adults (mean age: 54.6 ± 7.2 years; BMI: 36.1 ± 7.9 kg/m²; AHI: 52.2 ± 27.4 events/hour) were included. Significant group-by-time interactions were found for 24-hour systolic BP (CG: $+5.3 \pm 2.4$ mmHg vs. ST: -2.9 ± 3.2 mmHg; $p = 0.041$), daytime systolic BP (CG: $+4.6 \pm 2.5$ mmHg vs. ST: -2.8 ± 2.8 mmHg; $p = 0.050$), and daytime mean BP (CG: $+3.7 \pm 1.6$ mmHg vs. ST: -2.3 ± 2.0 mmHg; $p = 0.021$). In addition, a significant reduction was also observed in OSA severity (AHI CG: -3.5 ± 3.8 events/hour vs. ST: -20.9 ± 6.1 events/hour; $p = 0.015$). No significant differences were observed between groups regarding office and central BP, or arterial stiffness.

Conclusions: An eight-week strength training program significantly reduces ambulatory blood pressure and OSA severity in adults with moderate to severe OSA, even without changes in arterial stiffness. These findings support the role of strength training as a potential adjunct non-pharmacological intervention for cardiovascular risk management in this population.

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Effects of Transvenous Phrenic Nerve Stimulation in patients diagnosed with Central Sleep Apnea and Atrial Fibrillation

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Introduction: The prevalence of atrial fibrillation (AF) in patients diagnosed with central sleep apnea (CSA) has not been systematically studied. The purpose of this retrospective analysis is to report the prevalence of AF in a cohort of patients diagnosed with CSA and describe the potential effects of treatment of CSA with phrenic nerve stimulation (PNS) on patient symptoms in this cohort.

Materials and methods: In the randomized, double-arm, parallel group design pivotal trial of the implantable **remedē** System to treat CSA, all patients were implanted with the transvenous PNS system. The PNS therapy was activated in the active arm after 1 month and remained off in the control arm for 6 months. PNS was then activated in the control group and all patients were followed up to 12 months. Two quality of life metrics, Patient Global Assessment (PGA) and Epworth Sleepiness Scale (ESS), were evaluated.

In-laboratory polysomnograms were obtained at baseline to determine eligibility and after 6 and 12 months to determine effectiveness. All sleep studies were blindly scored by a central core laboratory.

Results: Of 151 participants diagnosed with predominant CSA and enrolled in the study, 42% (64/151) had AF, including 32 in the active arm and 32 in the control arm. The apnea hypopnea index and central apnea index decreased significantly from medians of 49 and 20 events/hour of sleep at baseline to 21 and 1/hour of sleep after 6 months of PNS therapy (within group change from baseline $p < .001$ for each test), respectively. In parallel, changes in arousal index (48 at baseline vs. 25/hour of sleep at 6 months, $p < .001$) and percent of sleep time with oxygen saturation less than 90% (8% vs. 4%, $p = 0.071$) improved. There were no significant changes in sleep metrics in the control group. Marked or moderate improvement on the PGA was noted by 54% of the active participants compared to 11% in the control group (between group $p < .001$). Although most patients did not report excessive daytime sleepiness at baseline, the ESS improved by 2.0 points in the active arm ($p = 0.025$) while there was no change in the control arm. After 12 months of therapy, the active participants had sustained improvements in the sleep metrics, PGA and ESS endpoints. The control group, who had therapy activated after the 6-month visit, experienced similar improvements as well. Serious adverse events related to the device, procedure or therapy were reported by 8% (5/64) of participants through 12 months and all events resolved without sequela. The events included an implant site infection, impending pocket erosion, lead displacement, feeling stimulation in area remote from diaphragm, and a concomitant device interaction.

Conclusions: Atrial fibrillation was highly prevalent in this cohort of patients diagnosed with CSA. Compared to the control arm, after 6 months of therapy with PNS, sleep metrics, quality of life, and daytime sleepiness improved significantly in this retrospective subgroup analysis. Similar improvements were observed in the control group after 6 months of active therapy and the safety profile was acceptable in both groups.

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Efficacy of Line Official Account on Adherence of PAP therapy in Obstructive Sleep Apnea Patients

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Introduction: Positive airway pressure (PAP) therapy is the mainstay treatment for obstructive sleep apnea (OSA), however, the compliance in the use of PAP machine is consistently low. Previous study

has shown that the benefits from using a PAP machine if it is used adequately and continuously. Good compliance is indicated by the patient uses the machine at least 70% of the total number of nights and least 4 hours/night. We study efficacy of Line official account on PAP adherence among OSA patients in Thailand.

Materials and methods: A randomized study was conducted in obstructive sleep apnea patients indicated in PAP therapy at outpatient in Phramongkutklao hospital. They were divided into two groups. The use of Line official account was added in the first group. The second group was treated with standard treatment. Both were followed up at the fourth week of treatment. Patients diagnosed with obstructive sleep apnea who received treatment at Phramongkutklao Hospital from March 2023 to February 2024. Inclusion Criteria: 1. Patients diagnosed with obstructive sleep apnea based on criteria for positive airway pressure machine usage 2. Patients aged between 20 and 80 years old. 3. Possession of a mobile phone capable of using the Line application. Exclusion Criteria: 1. Central sleep apnea . 2. Patients with contraindications for PAP machine usage.

Results: A total of 58 patients were enrolled, There was no difference between the basic characteristics of the two groups: mean age (51.14 ± 14.43 vs 51.86 ± 14.32 , $p = 0.849$), male (58.6% vs 62.1%, $p = 0.788$), neck circumference (38.61 ± 4.24 vs 40.84 ± 5.29 , $p = 0.082$), epworth sleepiness scale (9.24 ± 4.71 vs 8.41 ± 4.84 , $p = 0.512$). The average apnea-hypopnea index did not differ between the two groups. The Line official account group had less AHI than the standard treatment group (49.4 ± 26.2 vs 54.9 ± 33.7 ($p = 0.496$)), however both ranged in severe OSA. In addition, CPAP use > 4 hr/night was more than 70% of the use in the Line official account group 62.21%, compared to the standard treatment group 48.3% ($p = 0.291$).

At fourth-week follow-up, there was no significant different in % CPAP use > 4 hr/night between the Line official account group (70.73 ± 28.82) and the standard treatment group (61.5 ± 30.47), $p = 0.241$.

Conclusions: The use of Line official account did not significant differ from standard treatment in improving adherence of PAP therapy of patients with obstructive sleep apnea.

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Efficacy of Novel Oral Appliance and Novel Oral Positive Expiratory Pressure Accessory at reducing sleep apnea-specific hypoxic burden, a metric predictive of cardiovascular morbidity and mortality

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Introduction: Evidence suggests that moderate to severe OSA patients have increased risk of major adverse cardiovascular events (MACE; composite of coronary heart disease, heart failure, stroke, or cardiovascular mortality) and that sleep apnea-specific hypoxic burden (SASHB) is associated with increased risk of cardiovascular disease mortality. SASHB appears to be more predictive of OSA-related risk than AHI but has not been extensively studied as a measure of therapeutic efficacy in patients treated with oral appliance therapy.

O2Vent Optima is a novel oral appliance that incorporates both mandibular advancement to reduce pharyngeal collapsibility and an air channel that allows airflow through the device to circumvent nasopharyngeal obstruction. The ExVent is an optional accessory to the novel oral appliance and provides oral Expiratory Positive Airway Pressure (EPAP) to support upper airway by passive dilatation of the airway, which reduces flow limitation.

This is the first assessment of combination therapy with novel oral appliance combined with an Oral EPAP accessory to reduce SASHB, rather than AHI, to define therapeutic efficacy.

Materials and methods: Data obtained from a clinical study to assess efficacy of the combination therapy with novel mandibular advancement device and novel oral EPAP accessory in the treatment of OSA were analyzed. Forty-four study participants with OSA (moderate = 28, severe = 16) completed a diagnostic PSG study to obtain the baseline AHI and confirm a diagnosis of moderate to severe OSA. Subjects used the combination therapy at home for >3 months and logged usage hours. Subsequent to the home use, subjects underwent an in-lab PSG sleep night while using the combination therapy.

Results: Treatment with the combination therapy with novel mandibular advancement device and novel oral EPAP accessory reduced AHI from 28.5 ± 6.4 /hr. to 12.9 ± 2.7 /hr. ($p < 0.001$) and SASHB from 82.3 ± 31.1 %min/hr. to 16.7 ± 9.4 %min/hr. ($p < 0.001$). Average reduction in AHI with the combination therapy was 75%. Using an AHI-based definition of therapeutic efficacy (AHI < 10 /hr.), 81% of participants achieved efficacy with the combination therapy. However, when the risk based SASHB definition of therapeutic efficacy (SASHB < 53 %min/h) was utilized, therapeutic efficacy with combination therapy with novel mandibular advancement device and novel oral EPAP accessory increased to 92%.

Conclusions: Therapeutic efficacy with combination therapy with novel mandibular advancement device and novel oral EPAP accessory significantly improved to 92% by SASHB criteria as compared to 75% by AHI reduction criteria. Our study demonstrated that the use of AHI measurement would have misclassified a substantial number of individuals who responded to the combination therapy with novel mandibular advancement device and novel oral EPAP accessory based on more meaningful SASHB reduction of OSA-related risk.

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Efficient and Effective Telemonitoring System for CPAP Adherence Using Digital Transformation

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Introduction: In Japan, the national Health Insurance System began covering CPAP therapy with mandatory monthly clinic visits in 1998, later permitting visits once every two months in 2013 and every three months during the COVID-19 pandemic in 2022. These regulatory adjustments resulted in a substantial increase in CPAP users. Previously, our clinic depended predominantly on manual methods to collect adherence data from multiple providers, necessitating improvements in monitoring efficiency and effectiveness. To address these challenges, we developed the Remote Monitoring Network for CPAP Adherence. Additionally, we conducted a comparative analysis of CPAP usage between individuals demonstrating good and poor adherence before and after three months of enrollment in tele-monitoring to assess its impact.

Materials and methods: The Remote Monitoring Network for CPAP Adherence utilizes 3G connectivity (SIM) to integrate adherence data from CPAP devices into individual provider cloud servers. This data is efficiently transferred to medical charts using Application Programming Interfaces (APIs) and Robotic Process Automation (RPA). It enables a seamless flow of information and remote adjustment of CPAP pressure without in-person visits.

For analysis, patients were classified as good users ($\geq 70\%$ monthly CPAP use) or poor users ($< 70\%$). In line with insurance guidelines, physicians contacted poor users monthly to offer personalized support and address barriers such as mask discomfort, nasal congestion, and psychological resistance.

To minimize manufacturer-related bias, that could affect data collection and interpretation, our analysis focused exclusively on 1,589 Philips CPAP users from our total patient population. Of these patients 1,314 (82%) were categorized as good users and 273 (18%) as poor users. For assessment of the tele-monitoring impact, we selected random samples, comprising 473 good users and 142 poor users. These samples were not adjusted for gender and age, to maintain real-world representation in our patient population. We evaluated the adherence changes before and after three months implementation of tele-monitoring.

Results: Between June 2020 and April 2025, 67.2% (2,909 out of 4,330) of CPAP users transitioned to remote monitoring, exhibiting a consistent upward trajectory. Following tele-monitoring implementation, adherence remained stable among good users, with 83.5% (395 out of 473) maintaining their status and 16.5% (78 users) shifting to poor adherence. Among poor users, 63.4% (90 out of 142) sustained low adherence, while 36.6% (52 users) improved to good adherence.

Conclusions: Remote tele-monitoring for CPAP adherence is both feasible and effective, reducing clinic visit frequency and related costs, enhancing time management and operational efficiency for patients and healthcare providers alike with improving productivity. Disclosure of APIs and RPAs by each company is essential to the success of this initiative. The predominance of good users in our cohort may reflect the effectiveness of our clinical protocol.

Tele-monitoring did not notably affect patient attitudes toward CPAP adherence in this study. Defining adherence and motivating low-use patients remain ongoing issues, and integrating Digital

Transformation (DX) with Artificial General Intelligence (AGI) is needed to enhance care quality and efficiency.

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Electroencephalographic response to respiratory events is associated with all-cause mortality in obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA)-associated hypoxic burden (HB) has been shown to predict increased mortality. In those with increased HB, there is variability in electroencephalographic (EEG) response to respiratory events, with preliminary studies suggesting worse outcomes in those with a blunted EEG response. We hypothesized that those with a high HB but a blunted EEG response, are at increased risk of all-cause mortality when compared to: 1) those with low HB, and 2) those with high HB and high EEG response.

Materials and methods: The sample included participants in the Sleep Heart Health Study who underwent baseline polysomnography (PSG) with follow-up survival data. HB was quantified as the sum area under the event-related desaturation curve per hour of sleep. EEG responses to respiratory events were quantified by calculating the EEG power ratio (post-event power / pre-event power)) across frequency ranges (i.e., delta, theta, alpha, beta and gamma). The total event-related EEG response was defined as the sum of power ratios across all frequency ranges. Finally, the Brain Response to Event (BReTE) was defined as the mean within individual event-related EEG responses. We examined the risk of all-cause mortality in those with high HB (HB>60%min/h) (a previously defined threshold) and levels of BReTE (per quartiles) versus those with low HB (HB≤60%min/h). Finally, within the high HB subgroups, we compared the risk of all-cause mortality in those with lower quartiles of BReTE versus the highest quartile. Cox regression models were used to estimate the hazard ratios, controlling for relevant confounders including age, sex, race, BMI, baseline EEG, hypertension, diabetes, and smoking status.

Results: The sample (n=5592) had a median [interquartile range] age=63[55, 72] years and a mean ±standard deviation (SD) of follow-up time=11±3.1 years. Cox regression models revealed the highest hazard ratio for high HB/lowest quartile of BReTE vs. low HB (HR=1.44 [1.18,1.76]; p<0.001) with a dose-response relationship for other quartiles. Within the high HB group, the lowest quartile of BReTE exhibited a significantly higher mortality hazard ratio than the highest quartile of BReTE.

Conclusions: Within individuals with high OSA-related hypoxemia, the lowest EEG response was associated with an increased risk of all-cause mortality. Future studies are needed to understand whether blunted response to hypoxemia is a risk marker of accelerated aging or adaptation to untreated OSA, or is a direct risk factor for increased mortality.

Elevated level of pro-Brain Natriuretic peptide (pro-BNP) is associated with History of Major Adverse Cardiovascular Events (MACE) in subjects with Obstructive Sleep Apnea

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Introduction: Patients with untreated obstructive sleep apnea (OSA) are at increased risk for major adverse cardiovascular events (MACE). Additionally, sleep disturbance in non-OSA subjects and certain

clinical symptoms of OSA have also been associated with a higher risk for MACE. Finally, multiple biomarkers have been shown to be associated with increased risk for cardiovascular (CV) events. However, the association between OSA status, biomarker profile, sleep symptoms and MACE has not been carefully delineated. In this preliminary analysis of the ongoing WTCCOMISA study, we examined the association between sleep symptoms, OSA status, biomarkers of CV risk (highly sensitive c-Reactive Protein (hs-cRP), Troponin I and pro-BNP) and MACE.

Materials and methods: 172 subjects enrolled in the ongoing WTCCOMISA study were studied. OSA status was determined either by a prior history or was confirmed to be negative by home sleep testing. Sleep symptoms were determined on the basis of the Epworth Sleepiness Score (ESS) and the Insomnia Severity Index (ISI) and patients classified as: Asymptomatic (ESS<10, ISI<8), Sleepy (ESS>10) or Disturbed sleep (ISI>8). MACE (obtained by history) was defined as any of the following: Stroke, arrhythmia, coronary artery disease, cardiac procedure, myocardial infarction, congestive heart failure. Comorbid conditions, perceived stress levels, diet and physical activity, smoking status and medications as well as hs-CRP, Troponin I and pro-BNP were obtained from all subjects. Biomarker values were log-transformed as they were significantly right skewed. Data were analyzed using logistic and linear regression analyses, with adjustment for age, sex, BMI, cardiac risk factors and medications, where appropriate.

Results: 97 subjects without OSA (mean age: 62, 92.5% M, mean BMI: 30.7) and 75 subjects with untreated OSA were enrolled (mean age:61, 81.2% M, man BMI: 27.5). The proportion of asymptomatic, sleepy and disturbed sleep in OSA versus non-OSA subjects was 45.4% versus 52%, 23.7% versus 13.3% and 30.9% versus 34.7% . A history of MACE was present in 11.6% (20/172). No significant differences were present in subjects with and without OSA in history of MACE (12.3% versus 10.7%). No significant differences and no association was noted with a history of MACE in levels of hs-CRP and Troponin I in all subjects with or without OSA. In subjects with OSA and a history of MACE, adjusting for multiple covariates, log pro-BNP was significantly higher compared to non-OSA (mean (CI) 4.78 (4.27-5.30)versus 3.67 (3.14-4.20) or subjects with or without OSA without MACE. Log proBNP was significantly higher in asymptomatic subjects with OSA compared to symptomatic subjects (disturbed sleep or sleepy), and compared to those without OSA adjusting for multiple covariates.

Conclusions: Preliminary data from our ongoing WTC COMISA study suggests that elevated levels of novel cardiovascular biomarkers, such as pro-BNP is associated with a history of MACE in those with OSA without sleep symptoms.

Elevated levels of proBNP may reflect cardiac dysfunction in OSA subjects with a history of MACE. Elevated pro-BNP in asymptomatic OSA subjects, may serve as a marker of cardiac dysfunction.

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Endoscopic titration technique of mandibular advancement device treatment for obstructive sleep apnea

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Introduction: Mandibular advancement device (MAD) therapy is a treatment option for patients with obstructive sleep apnea (OSA). The treatment mechanism for MAD is to advance the mandible in order to reduce the collapsibility of the upper airway during sleep. Protrusion of the mandible with an MAD is the most important factor in achieving maximum treatment effects for OSA. Some studies have reported that more protrusion of the mandible leads to larger improvements in OSA. However, excessive mandibular protrusion leads to side effects, including temporomandibular joint, muscle, and tooth problems. This suggests that the degree of mandible protrusion needs to be titrated for each patient. Our group has reported that an increase of the airway volume at the velopharynx with mandibular advancement as shown by endoscopy is key to successful MAD therapy. This study presented the mandibular titration technique for MAD to effectively treat OSA by using endoscopy to evaluate the change in the airway at the velopharynx with simultaneous recording of mandibular position.

Materials and methods: This titration technique was applied to 83 consecutive OSA patients (Age=53.7±13.0 years old, BMI=25.4±5.2 kg/m², AHI=28.3±16.9/h) and the percentage of maximum

forward movement of the determined mandibular position was calculated. The titration technique using endoscopy is as follows: (1) Spray topical anesthesia (4% lignocaine) into one nasal passage. With the patient in the supine position in the dental chair, insert the flexible nasoendoscope (FNL-10RP3; Pentax) into the nostril to the velopharynx. (2) Position the occlusal registration tool (George gauge; Great Lakes Orthodontics Ltd) intraorally. This tool allows the degree of mandible protrusion to be measured and records the mandibular position with a millimeter indicator. The operator can preset the moveable incisal notches so that when the patient occludes into them, the mandible is automatically brought to the desired point on the protrusive path. (3) With the chin in a rest position, observe the cross-sectional area at the velopharynx with endoscopy. (4) Protrude the mandible from the rest position until the airway at the velopharynx widens and record the George gauge measurement.

Results: The percentage of mandibular position determined by this titration technique was $69.8 \pm 10.4\%$. The patients were divided into three groups based on the value of the percentage of mandibular forward movement ($<66.6\%$, $66.6\text{--}75\%$, $>75\%$) and compared for age, BMI, and AHI. There were no significant differences among the three groups in age and BMI, while AHI was significantly different among the three groups ($\text{AHI} = 21.4 \pm 10.3/\text{h}$ in $<66.6\%$, $30.0 \pm 18.3/\text{h}$ in $66.6\text{--}75\%$, $37.2 \pm 18.2/\text{h}$ in $>75\%$; $p = 0.0076$).

Conclusions: It was considered important to titrate the mandibular position for each patient using an objective measure of endoscopic airway assessment.

Endothelial-dependent vasodilation is associated with sleep apnea-specific blood pressure variations in patients with severe OSA

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Introduction: Obstructive sleep apnea (OSA) can lead to frequent acute blood pressure (BP) variations that may advance organ damage. However, a subset of patients with OSA can maintain nocturnal BP homeostasis. Data to disclose the underlying mechanisms for different clinical nocturnal BP phenotypes in patients with OSA are limited. We investigate the association between OSA event-triggered BP variation profiles and vascular function, including endothelial/smooth muscle vasodilation function and sympathetic activity in a cohort of patients with severe OSA without comorbidities.

Materials and methods: Brachial artery flow-mediated dilation (FMD) and nitroglycerine-induced vasodilation (NID) were measured to assess endothelial and smooth muscle function, respectively. Event-triggered BP variation parameters, including BP surges, nocturnal BP fluctuations (NBPFs), NBPF/apnea-hypopnea index (AHI), and BP peaks and valleys were collected. Comparisons between subgroups, stepwise multiple regression, and ordinal logistic regression analysis were used to explore factors associated with event-triggered BP variation.

Results: A total of 177 patients with severe OSA and without comorbidities were studied. In patients with normal endothelial function ($\text{FMD} \geq 10$), NBPFs, NBPF/AHI, and BP surges were significantly associated with FMD (all P s < 0.05). The relationships between nocturnal BP variations and vasodilation function were not significant in patients with impaired endothelial function ($\text{FMD} < 10$). However, sympathetic activity markers were independently associated with BP variations in both subgroups (all P s < 0.05). In ordinal logistic regression analysis, severe nocturnal BP variation in the normal endothelial function group was associated with increased sympathetic activity and higher FMD and drowsiness. In the impaired endothelial function group, only elevated sympathetic tone was associated with an increased risk of high BP variation.

Conclusions: This study has discovered that sympathetic activity is independently associated with OSA event-triggered BP variations regardless of vasodilation function. In patients with normal endothelial function, a high sleep apnea-specific BP variation may be partly associated with endothelial-dependent dilation.

Enhancement of slow wave sleep after bariatric surgery: OSA remission may not be the sole benefit after weight loss

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Introduction: Despite diverse etiopathogenic components, the prevalence of obstructive sleep apnea (OSA) ordinarily increases concomitantly with the increased prevalence of obesity. Altered sleep has been documented in both OSA and in obese patients without OSA. Possible OSA remission has previously been documented after substantial weight loss in obese OSA patients. Former evidence further suggests that bariatric surgery is often more effective than non-surgical treatments in severe or morbid obesity, particularly in case of prior failure of alternative weight reduction attempts. Whether a body mass index (BMI) reduction, following bariatric surgery, may also exhibit effects on sleep that are not necessarily related to OSA, remains yet to be determined.

Materials and methods: Within the framework of a cross-sectional study, we recruited 35 obese patients (24 females and 11 males ; mean age of 46.5), all with a BMI above 35kg/m². All included patients displayed clinically significant OSA with an obstructive apnea-hypopnea index (OAHI) >15/h. All patients underwent bariatric surgery by means of a gastric bypass (GBP). Full polysomnographies (PSG) were carried out at baseline (before GBP) and performed after bariatric surgery (at least 6 months after GBP). BMI, sleepiness levels (assessed with the Epworth Sleepiness Scale) and sleep variables (PSG) were compared between baseline (prior to surgery) and one year later (>6 months after GBP). Associations between variables were investigated exploratively.

Results: Expectedly, mean BMI decreased significantly from 39.7 to 26.7 (p<.005) after GBP. Concomitantly, both OAHI (from 46.7 to 8.6) and oxygen desaturation index (from 32.2 to 6.8) also dropped significantly after the surgical intervention (all p<.005). While improving numerically, after one year, sleepiness levels did not show statistically significant variations in our sample (Epworth scores reducing from 12.2 to 8.4). While total recorded sleep time and REM sleep durations did not significantly differ between both PSG measurements, sleep fragmentation and sleep efficiency significantly improved after GBP (p<.05). In addition, slow wave sleep (absolute duration and relative percentage of sleep time) significantly increased after GBP (p<.005).

Conclusions: Following GBP, the post-surgical weight loss, led to relative remission of OSA in most patients. Conversely, sleep fragmentation and efficiency also significantly improved in our sample. In addition, slow wave sleep durations expanded significantly within similar total sleep times. Hence, along with obvious metabolic upsides and improvements of ventilatory mechanics, our results also suggest that potential health benefits of surgically induced weight loss, may imply sleep-related neurological improvements way beyond respiratory parameters.

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Eupneic Submental EMG as a Marker of OSA Severity: KISS & MrOS Cohorts

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Introduction: Obstructive sleep apnea (OSA) is conventionally diagnosed and graded by the apnea-hypopnea index (AHI), yet event counts provide limited information on how the upper airway is stabilized during normal breathing. Submental surface electromyography (sEMG), routinely recorded during polysomnography but rarely quantified, may serve as a bedside marker of compensatory upper-airway muscle tone. We hypothesized that as pharyngeal collapsibility increases, median submental sEMG during event-free breathing rises monotonically with OSA severity. We tested this hypothesis in two large community cohorts (KISS and MrOS).

Materials and methods: We analyzed overnight polysomnography from 7,523 adults in the Korea Image-based Sleep Study (KISS) and 2,831 adults in the Osteoporotic Fractures in Men Study (MrOS).

sEMG signals were extracted during eupneic periods, defined as respiratory event- and arousal-free segments in supine or lateral positions across sleep stages (Wake, N1, N2, N3, REM). Signals were segmented into non-overlapping 1-second windows, and the mean absolute value (MAV) was computed. For each subject and stage, the median MAV across all windows was taken as the representative sEMG activity.

Results: Subjects were categorized into five OSA severity groups based on the apnea-hypopnea index (AHI): normal, mild, moderate, severe, and very severe (AHI ≥ 60). Eupneic submental EMG activity increased progressively with OSA severity, from 1.19 μV [1.00–1.56] in the normal group to 2.93 μV [2.09–4.10] in the very severe group in KISS, and from 1.25 μV [1.01–1.91] to 2.48 μV [1.65–3.50] in MrOS. When stratified by sleep stage, the same trend was observed, most prominently during N2 sleep (KISS: 1.30 μV [1.08–1.77] in normal vs. 3.26 μV [2.33–4.53] in very severe; MrOS: 1.41 μV [1.11–2.13] vs. 2.75 μV [1.84–3.85]). Similar stage-dependent increases were also noted in N1, N3, and REM sleep.

Conclusions: In conclusion, sEMG activity increased with OSA severity, reflecting elevated global muscle tone and possibly upper airway muscle tone. Notably, this pattern persisted even when stratified by sleep stage. The presence of heightened activity during eupneic, event-free periods suggests adaptive compensatory mechanisms in OSA patients. These findings highlight submental EMG as a promising non-invasive biomarker for disease severity and pathophysiology.

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Evaluating Patient-Reported Outcomes and PAP Adherence in Obstructive Sleep Apnea Treatment Using an Interactive Care Plan

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Introduction: Patient-reported outcome measures (PROMs) are underutilized in obstructive sleep apnea (OSA) management, often overshadowed by compliance with positive airway pressure (PAP) therapy and residual apnea-hypopnea index (AHI). This study investigates the utility of the PROMIS-10 score (physical and mental domains) and the Epworth Sleepiness Scale (ESS) in assessing health outcomes before and after PAP therapy initiation. An interactive care plan (ICP) that interacts with our electronic health record and delivered via an internet portal was used to deliver education, motivation, and to monitor patient adherence and health outcomes.

Materials and methods: This retrospective analysis included 181 OSA patients enrolled in an ICP upon PAP therapy initiation. The ICP provided educational resources, tracked task completion, and enabled clinician intervention. PAP adherence was defined as ≥ 4 hours of use on $\geq 70\%$ of nights over 30 days, measured using PAP device data. The study assessed adherence during an initial 30-day period, compared baseline and post-PAP therapy PROMIS-10 and ESS scores with paired t-tests, and used linear regression to evaluate potential associations of compliance data with changes in PROMIS-10 scores.

Results: 181 patients diagnosed with OSA and enrolled in the ICP were identified. A total of 123 had ESS data and 100 had PROMIS-10 scores, of which 78 had complete compliance data and PROMIS-10 scores. The mean compliance rate for the initial 30-day period was 27.1 out of 30 days (SD = 4.3). The average 4-hour compliance rate was 79.8% (SD = 22.2%), with an average of 6.2 hours of PAP use per night (SD = 1.5 hours). There was no significant change in the PROMIS 10 scores following initiation of PAP therapy (physical: $p = 0.46$ and mental: $p = 0.43$), whereas the ESS significantly decreased ($p = 0.02$). Neither AHI, nor 4-hour compliance percentage were significantly associated with a change in physical or mental PROMIS-10 scores after adjusting for the first PROMIS-10 score and days between PROMIS-10 scores (respectively, AHI - physical: $p=0.84$ and mental: $p=0.34$, 4-hour compliance percentage physical: $p=0.55$ and mental: $p=0.75$).

Conclusions: Despite high PAP adherence rates, further improvements in patient engagement may be necessary. The ICP was valuable for patient education and digital interaction, promoting data collection and supporting adherence. However, the lack of significant association between adherence and

improvements in PROMIS-10 scores suggests the need for additional or alternative metrics to assess the broader benefits of PAP therapy. It is also likely that focusing only on airway-directed therapy may not address all symptoms and manifestations of OSA. Tailored education, multi-modal treatments, and proactive follow-up are critical for optimizing treatment outcomes and long-term disease management. Future studies should incorporate control groups to evaluate the impact of structured support on adherence and treatment effectiveness, focusing on metrics that capture a broader spectrum of health improvements.

Exploring the Intensity of Arousals in Patients with Obstructive Sleep Apnea: Based on Odds Ratio Product

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Introduction: Obstructive sleep apnea (OSA) is characterized by recurrent upper airway obstruction during sleep, resulting in frequent arousals and sleep fragmentation. However, traditional frequency-based metrics are inadequate to precisely quantify the intensity of arousal events. The Odds Ratio Product (ORP), a validated electroencephalographic marker that provides a continuous measure of sleep depth, offers a novel approach for quantifying arousal intensity in OSA patients. This study aims to establish the feasibility and clinical utility of ORP-derived arousal intensity and to explore its associations with respiratory event characteristics and subjective sleepiness.

Materials and methods: We retrospectively analyzed data from 1,057 untreated OSA patients (median age 52.0 years; BMI 30.74 [IQR 27.17–36.19] kg/m²; AHI 34.40 [20.20–54.30]/h) from the APPLES cohort. EEG (C3/C4) power spectra in the δ , θ , α - σ , and β frequency bands were processed every 3 seconds to compute ORP values across the sleep period. Arousal intensity was quantified for each annotated arousal event using the positive area deviation (PAD) of the ORP curve compared to the pre-arousal baseline. Associations of arousal intensity with respiratory event characteristics (type, duration), sleep stage, and inter-individual variability were analyzed using mixed-effects models. The relationship between baseline (subject-level) arousal intensity and subjective daytime sleepiness (Epworth Sleepiness Scale, ESS) was evaluated with multivariate regression.

Results: A total of 258,121 arousal events were identified, of which 171,346 were linked to respiratory events. The mean arousal intensity was 2.25 ± 3.28 , exhibiting significant inter-individual variability ($\eta^2 = 0.257$, $p < 0.001$). Arousal intensity increased progressively with the duration of preceding respiratory events (obstructive apnea: ORP +0.84; mixed apnea: +0.78; central apnea: +0.70; all $p < 0.001$). All apnea subtypes induced significantly stronger arousals than hypopneas. Central and mixed apneas were associated with more pronounced and variable arousal responses than obstructive events. Deepening sleep stage significantly attenuated arousal intensity ($\beta = -0.765$, $p < 0.001$). Baseline arousal intensity at the individual level was independently associated with increased daytime sleepiness ($\beta = 0.072$, $p = 0.023$, adjusted for confounders). The mixed effects explained 16.9% of the variance in arousal intensity.

Conclusions: ORP-derived arousal intensity offers a robust and objective biomarker for the quantification of sleep fragmentation in OSA. Arousal intensity is closely governed by respiratory event type and duration, sleep stage, and inter-individual neurophysiological traits. Furthermore, heightened baseline arousal intensity independently predicts greater subjective sleepiness, underscoring its clinical significance. These findings support the use of ORP as a quantitative tool in sleep research and facilitate a deeper understanding of the mechanistic links between arousal dynamics, sleep quality, and neurocognitive outcomes in OSA.

Exploring the Synergistic Impact of Obstructive Sleep Apnea and Mental Health Conditions on Cardiometabolic Risk: Insights from the Canadian Longitudinal Study on Aging

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Introduction: Obstructive sleep apnea (OSA) and mental health conditions have complex, bidirectional relationships and are each recognized as risk factors for cardiometabolic morbidity. However, the combined effects of these conditions on cardiometabolic health remain unexplored. This study evaluates whether the combined presence of high risk for OSA and mental health conditions increases cardiometabolic risk and, if so, whether this co-occurrence has synergistic clinical relevance.

Materials and methods: We conducted a secondary analysis of the Canadian Longitudinal Study on Aging, a national cohort study collecting information on the biological, medical, psychological, social, lifestyle, and economic aspects of middle-aged and older adults (aged 45-85 at baseline), utilizing data from Baseline Comprehensive Survey (2011-2015) and Follow-up 1 (2015-2018).

Individuals with at least two self-reported symptoms of snoring, daytime somnolence, being observed to stop breathing in sleep, or hypertension were categorized as **high risk for OSA (OSA+)**. **Mental health conditions** were defined based on a combination of standardized questionnaires (Center for Epidemiologic Studies Short Depression Scale [CESD-10] ≥ 10 and Kessler Psychological Distress Scale [K10] ≥ 20), self-reported clinical diagnoses and taking medication for depression (Mental Conditions+). **Cardiometabolic morbidity** was defined through relevant self-reported clinical diagnoses (diabetes, heart disease, peripheral vascular disease, angina, cerebrovascular accident) and medications.

We used multivariable logistic regression models to compare odds between four mutually exclusive groups: (1) OSA+ Mental Conditions+; (2) OSA+ Mental Conditions-; (3) OSA- Mental Conditions+, and (4) OSA- Mental Conditions- (reference for comparison). Relative excess risks due to interaction (RERI) were calculated to test for additive interaction. We assessed how these exposure groups were associated with prevalent cardiometabolic conditions (at baseline and follow-up separately) and incident cardiometabolic conditions (in participants without cardiometabolic conditions at baseline), controlling for covariates (sociodemographic and lifestyle measures, medical conditions, sleep complaints and other sleep disorders aside from OSA).

Results: We included 26,945 baseline participants (6,958 [25.8%] OSA+; 9,220 [34.2%] mental conditions+; and 6,493 [24.2%] with cardiometabolic conditions) and 24,575 follow-up participants (7,348 [29.9%] OSA+; 7,968 [32.4%] mental conditions+; and 6,610 [27.0%] with cardiometabolic conditions). Among the 16,678 participants free of cardiometabolic conditions at baseline, 1,251 (7.5%) reported new cardiometabolic conditions at follow-up.

In all statistical models, OSA+ Mental Conditions + was associated with the greatest odds of prevalent or incident cardiometabolic conditions (odds ratios [ORs] 1.50-1.93; 95% confidence intervals [CIs]: 1.23-2.14) compared to each exposure considered separately (OSA+ Mental Conditions-: ORs 1.24-1.52; 95% CIs: 1.04-1.66; OSA- Mental Conditions+: ORs 1.05-1.24; 95% CIs: 0.96-1.45), using OSA- Mental Conditions- as a reference. RERI estimates above zero (0.03-0.19) suggested a positive additive interaction, but were not statistically significant.

Conclusions: In this national community-based study of middle-aged and older adults, individuals at higher risk for OSA with comorbid mental health conditions were at higher cardiometabolic risk compared to either exposure condition alone. While estimates of additive interaction were positive, suggesting potential synergy, they were not statistically significant, warranting further investigations. These findings underscore the importance of integrated screening and management strategies to mitigate cardiometabolic risks in individuals with these coexisting conditions.

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Exploring the treatment journey of Obstructive Sleep Apnoea: A scoping review on the perspectives of Chinese patients

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Introduction: Globally, obstructive sleep apnoea (OSA) is a common sleep-related breathing disorder, thought to affect up to 23.6% of patients of Chinese ethnicity. However, little is known about the perspectives of the Chinese patient population and the key factors underpinning their health behaviours and treatment engagement. This scoping review aims to systematically synthesise the literature to understand Chinese patient perspectives towards OSA and its management.

Materials and methods: A systematic search was conducted in Jul 2023 and May 2024 across CINAHL, Embase, Medline, PsycINFO, and Scopus in Chinese and English for studies including the concepts: obstructive sleep apnoea, adult Chinese patients, treatments (CPAP, surgery, mandibular devices, pharmacotherapy, positional therapy, complementary therapies, lifestyle changes), and psycho-social-behavioural factors. Search results were screened and data extracted by 2 independent reviewers. Publications meeting the following criteria were included in this review: adult patients (≥ 18 years) self-identifying as Chinese with OSA (sample); patient experiences of various OSA treatments (phenomenon of interest); primary studies published in a peer-reviewed journal and written in English or Chinese (design); inclusion of a patient-reported outcome related to their OSA treatment at any stage of the treatment trajectory (evaluation).

Results: From the 976 results, 49 studies were retrieved, comprising of 16,239 adults (mean age: 47 years, 80% male); conducted primarily in China, Hong Kong, Taiwan and Singapore. Studies were broadly synthesised into the following patient-centred domains: beliefs about OSA, treatment preferences, acceptance, satisfaction, and adherence. Considerable heterogeneity was observed in the measurement of treatment acceptance and satisfaction, coupled with insufficient reporting of factors influencing treatment preference. Notable limitations included the under-representation of older women and migrant Chinese populations and the limited coverage of health beliefs and health behavioural change.

Conclusions: Factors influencing patient engagement with OSA treatments are multifactorial. Patients' health beliefs and sociocultural factors play an important role in treatment acceptance and adherence. Future research should focus on patient-centred approaches to identify strategies to promote behavioural change and provide culturally sensitive care.

Facial Aesthetic Outcomes of Counterclockwise Maxillomandibular Advancement in Asians with Obstructive Sleep Apnea: An Objective Analysis

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Introduction: Counterclockwise maxillo-mandibular advancement (CCW-MMA) is the most effective surgical management to enlarge the pharyngeal airway space in obstructive sleep apnea. However, the facial aesthetic consequences in Asians whose craniofacial morphology and cultural ideals differ from Western norms remain under represented.

Materials and methods: A retrospective cohort of 54 Asian adults (18 years and above; apnoea-hypopnoea index > 5) treated with CCW-MMA were reviewed. Pre-operative (T0) and 6-months post-operative (T1) lateral cephalograms were analysed. Soft-tissue landmarks including pogonion (Pog'), subnasale (Sn'), upper lip (ULs'), lower lip (LLs'), and nasion (N') positions were measured relative to the Zero Meridian Line (ZML) and E-line. Facial angles including nasolabial, Z-, facial-convexity and gonial angles were also measured. Patients were stratified by skeletal class I, II, and III. Soft tissue deviations from the Caucasian normative values were recorded. Intra-rater reliability was verified (intraclass correlation coefficient > 0.90). Paired t-tests were used to assess T0-T1 changes. Postoperative soft tissue changes and facial angles across all skeletal classes were compared to the Caucasian normal values using paired t-tests. ANOVA and multivariate regression was then used to examine between skeletal classes.

Results:

There were significant changes in the soft tissue landmarks between T0 and T1 across all skeletal classes with mean ($\pm$ SD) anterior translation of Pog' 5 ± 2 mm, Sn' 3 ± 1 mm, ULs' 3 ± 1 mm, and LLs' 3 ± 1 mm. The facial convexity angle decreased by $4^\circ \pm 2^\circ$, while the nasolabial angle increased by $8^\circ \pm 2^\circ$, indicating forward rotation of the lower face and profile straightening. Postoperatively, 85% of subjects had Pog' within the Zero meridian harmony. The Z-angle improved from a mean of 65° to the

aesthetic ideal of 75–80°, confirming enhanced chin–lip projection. Class II patients showed the greatest Pog' advancement (8 ± 2 mm), with 90% of subjects achieving Pog' alignment within ± 2 mm of the ZML. In Class III patients, a notable reduction in Pog' (-5 ± 2 mm) and LLs' (-5 ± 2 mm) was observed, while Sn' and ULs' showed notable forward movement toward the ZML. Class I subjects demonstrated a forward shift of Pog' relative to the ZML, which significantly exceeded the expected normative variation. They also displayed significant changes in the Z-angle, facial convexity angle, and gonial angle. Other landmarks did not show significant changes or deviations from the Caucasian norm.

Conclusions: Although facial angles and soft tissue profiles demonstrated balanced and improved projection comparable to Caucasian norms, Class I Asian patients exhibited slight overprojection of the facial profile as a compensatory outcome for pharyngeal airway enlargement. These findings highlight the importance of skeletal class-specific surgical planning to optimize both functional and aesthetic outcomes, particularly in Asian OSA patients. Further research incorporating subjective aesthetic assessments is warranted to better define ideal facial aesthetics within Asian populations.

Factors affecting level II polysomnography (PSG) outcomes in a tertiary referral sleep centre in Australia: A retrospective cohort study

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Introduction: Obstructive sleep apnoea (OSA) has a significant prevalence and associated healthcare cost in Australia and globally. In Australia Level II polysomnography (PSG) studies, provide an accessible and affordable way to help diagnose OSA. However, level II PSG's often have higher failure rates than in-lab sleep studies with recent data from Australia and New Zealand showing failure rates of 5-8%. Factors that may contribute to failed level II PSG have not been clearly identified in the literature with limited anecdotal evidence guiding clinician decisions with their patients. We conducted a single centre retrospective cohort study to assess which factors are more prevalent in failed level II PSG compared to successful tests with the aim to establish a more robust evidence base in this area to ultimately improve the success rate of level II PSG.

Materials and methods: The study population included 496 from patients > 18 years of age who had performed a level II PSG through our hospital's sleep laboratory between January 2022 and January 2024. Failed tests identified using a standardised criteria by the sleep technician analysing the test. Factors to be assessed included clinical factors (Age, gender, weight, BMI, co-morbidities, smoking status, Epworth score, STOP-BANG score) environmental factors (season, average daytime temperature, distance from the sleep laboratory in km) and technical factors (test unit used). Comorbidities were categorised into none, one or more than one and included asthma, hypertension, diabetes, gastro-oesophageal reflux disease (GORD), atrial fibrillation, heart disease and chronic obstructive pulmonary disease (COPD). Statistical tests comparing factors of failed and successful tests included t-tests for continuous variables and chi-square tests for categorical variables. The statistical significance level was set at $p < 0.05$.

Results: Of the 496 studies analysed, there were 16 (3.2%) failed tests and 480 (96.8%) successful tests. There were 254 (51.2%) female patients and 242 (48.8%) male patients with an average patient age of 52.41 (SD +/- 16.2) years. There was no significant difference between the failed and successful tests for the clinical factors of age ($p = 0.96$), BMI ($p = 0.81$), gender ($p = 0.54$), smoking status ($p = 0.49$), Epworth score ($p = 0.69$), STOP-BANG score ($p = 0.22$) and co-morbidities ($p = 0.52$). In regard to environmental factors there was a significant difference between seasons ($p = 0.05$), with 14/16 (87.5%) failed tests occurring in autumn or winter. There were no significant differences for distance from the sleep laboratory ($p = 0.90$), daytime temperature ($p = 0.16$), or which sleep unit was used ($p = 0.31$).

Conclusions: Although the failure rate of the level II PSG in our study was lower than previous studies, analysis of relevant factors found no differences between the failed and successful tests except for season which showed that autumn and winter seasons in the local area were more highly associated

with failure. This suggests that aspects related to colder seasons such as increased bedding or clothing may be attributable for the failure rate but this requires further research

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Factors Associated with Worsening of Sleep-Disordered Breathing in Patients with REM Sleep Behavior Disorder

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Introduction: REM sleep behavior disorder (RBD), like obstructive sleep apnea (OSA), is more prevalent in older adults and males. Although OSA is frequently comorbid with RBD, it has been reported that due to the presence of REM sleep without atonia (RWA), the severity of OSA tends to be mild in these patients. In this study, we investigated the factors associated with worsening sleep-disordered breathing (SDB) in patients with underlying RBD.

Materials and methods: We retrospectively analyzed patients diagnosed with RBD who underwent multiple polysomnographic (PSG) studies for follow-up, with a baseline apnea-hypopnea index (AHI) <20/h, which is below the indication for CPAP therapy in Japan. Worsening of OSA was defined as an increase in the severity category (e.g., from mild to moderate, or from moderate to severe). Patients were divided into two groups: those with worsening OSA and those without. Background characteristics were compared using the Mann-Whitney U test. Multivariate regression was performed to identify factors associated with OSA worsening, using sex, BMI change, interval between PSGs (age change), and clonazepam use as covariates.

Results: Among 61 RBD patients (46 males; mean age 66.1 years; BMI 23.2 kg/m²; ESS score 6.4), the mean interval between PSG studies was 5.3 years. The AHI significantly increased from 4.7 ± 4.3 to 8.5 ± 9.6/h (mean ± SD, $p < 0.001$). Worsening of OSA was observed in 23 patients (38%). No significant differences were found in sex or BMI between the worsening and non-worsening groups; however, age tended to be higher (68.0 ± 8.4 vs. 65.0 ± 6.3 years, $p < 0.08$) and interval between PSGs was significantly longer (6.0 ± 2.2 vs. 4.8 ± 1.8, $p < 0.04$). Multivariate regression analysis showed that only interval between PSG studies were significant predictors of OSA worsening.

Conclusions: AHI may increase even when RWA increases over time. Aging plays a significant role in the worsening of OSA in patients with underlying RBD. Even in the absence of weight gain, periodic reassessment of OSA is warranted in this population.

Five-year, prospective, multicenter, real-world study to assess initial delivery, management and long-term effectiveness of a CAD/CAM, 3-D printed oral appliance in the treatment of obstructive sleep apnea: Interim Analysis Update

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Introduction: Oral appliance therapy (OAT) continues to be a mainstay of therapeutic options in the treatment of obstructive sleep apnea (OSA). The provision of OAT requires a multidisciplinary approach to care involving a qualified sleep dental provider and a prescribing sleep specialist. This trial supports this methodology in a real-world, observational, longitudinal study of the Panthera D-SAD. The patients' therapeutic journey will be followed by providing data from first-time fit and delivery to ongoing adherence. Long-term adherence is essential for any OSA therapy to contribute to overall health and well-being. This study will fulfill French reimbursement requirements. Ethics committee approval was obtained.

Materials and methods: OAT naïve individuals with moderate OSA (AHI 15-30) or those with severe OSA (AHI > 30) who decline CPAP and meet all other criteria will be included. Sites will follow the standard of care in France to provide OAT. The Panthera D-SAD is a CAD/CAM, 3D printed biocompatible nylon appliance allowing for a patient-matched design. Fifteen centers in France will enroll 217 participants via consecutive sampling. A Somnologist will assess participants for entry

criteria, and a prescription for OAT obtained. A dental evaluation for suitability is conducted (V0). Initial OAT fitting occurs at Visit 1. Evaluation time points are (V2) three to six months (medical/sleep/dental), yearly follow-up to four years (dental visit/phone calls), and five years (medical/dental). Secondary endpoints include side effects, oxygenation metrics, quality of life, self-reported adherence, and subjective symptoms.

Results: Enrollment is complete (n=257). Baseline demographics n=239 (mean/SD): Age 50.7 (12.8), BMI 26.6 (4.7), F 49%, AHI 22.7 (9.0), ODI 17.0 (11.4), lowest SpO₂ 84.6% (6.8), ESS >10 42.4% (n=198). No changes to the OAT at delivery were required in 84.3%, with 82.3% of participants indicating that the device was comfortable and that only minimal adjustments were required. Within two post-delivery visits, 88.3% of participants were fully titrated. Change from baseline in sleep respiratory variables (n=179) to sleep testing (3-6 Mos): AHI reduction $\geq 50\%$ (60.3%). Additionally, 87.8% of moderate and 83.4% of severe transitioned to a lower AHI classification, with AHI <15 (80.9%), <10 (58.5%), <5 (20.8%). ODI decreased to 9.7 (8.4). Daily usage of ≥ 4 hours per night was reported by 96.2% of participants at three months and 94.8% at six months. During the routine annual call, 94.7% confirmed wearing the device all night. The average number of nights per week with device usage was 6.6 (1.2) at 3 months, 6.4 (1.4) at 6 months, and 6.2 (1.7) at one year, demonstrating sustained adherence over time. Satisfaction with treatment was 82.8% at three months and improved at one year (91.9%). At three months, ESS >10 24.5% (n=139).

Conclusions: These data represent insight into an ongoing, real-world observational study. Participants had improvement in their OSA and high satisfaction levels regarding wearing the device. The continued robust self-reported adherence confirms sustained therapy over time. Limitations include variances from site to site. However, in an observational study, these are expected findings. The last participants enrolled have not finalized titration. Additional data will be forthcoming.

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Flow Reduction Indicator: A Novel Metric for Predicting Cardiovascular Mortality in Sleep Apnea Patients

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Introduction: Obstructive sleep apnea (OSA) is a well-established risk factor for cardiovascular morbidity and mortality. However, its standard severity metric, the Apnea-Hypopnea Index (AHI), has limited predictive power for these outcomes, as it merely counts respiratory events without considering their duration and degree of flow reduction. Hypoxic Burden (HB) captures only the cumulative hypoxic stress of OSA. Ventilatory Burden (VB) measures inspiratory flow limitation using a fixed 50% threshold, which may fail to detect subtler events that nonetheless elicit cardiovascular responses, including heart rate elevation and arousal. To overcome aforementioned limitations, we propose the Flow Reduction Indicator (FRI). FRI quantifies the severity of airflow reduction by measuring the magnitude of reductions and the duration of each event.

Materials and methods: We calculated FRI from overnight polysomnography recordings in the Sleep Heart Health Study (SHHS; n = 3,882) and the Osteoporotic Fractures in Men Study (MrOS; n = 1,647). Unlike AHI, FRI assigns a variable weight to each respiratory event based on duration and flow reduction magnitude. Cardiovascular mortality risk was assessed using Cox proportional hazards regression.

Results: In unadjusted analysis (Model 0), when each metric was entered as quintile-based categories, FRI yielded the highest likelihood ratio tests values (SHHS: 54.26; MrOS: 26.93) compared to AHI (SHHS: 42.81; MrOS: 17.31), HB (SHHS: 38.11; MrOS: 23.64), and VB (SHHS: 42.29; MrOS: 10.43). In Model 1, which was adjusted for demographic factors (age, BMI, race, smoking status and sex only in SHHS), time in bed, lipid-lowering medications, and comorbidities (hypertension, stroke, chronic obstructive pulmonary diseases, myocardial infarction, asthma, diabetes and coronary angioplasty only in SHHS), FRI also showed the highest risk estimates among all metrics, with a Q5 hazard ratio (HR) of

1.83 (95% CI: 1.11–3.01) in SHHS and 1.54 (95% CI: 1.13–2.09) in MrOS. By comparison, the Q5 HRs for other metrics were substantially lower: AHI (SHHS: 1.49; MrOS: 1.48), HB (SHHS: 1.64; MrOS: 1.53), and VB (SHHS: 1.35; MrOS: 1.32). FRI also retained statistical significance when modeled as continuous variables in both cohorts (Model 0 and Model 1: $p < 0.05$). Finally, in Model 2 (covariates in Model 1 + AHI, HB, VB, and FRI as continuous predictors), only FRI remained statistically significant in SHHS (HR = 1.02; 95% CI 1.01–1.03).

Conclusions: Our findings suggest that FRI outperforms AHI, HB, and VB in predicting cardiovascular mortality. By integrating both the flow reduction and event duration, the 'FRI', which can be easily derived from flow signals in overnight sleep study, predicts cardiovascular disease mortality across populations.

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From hypoxia to hyperglycemia: the molecular interface of obstructive sleep apnea and type 2 diabetes via *miRNA-181a*, *SIRT1*, and adiponectin

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Introduction: Obstructive sleep apnea (OSA) is an established independent risk factor for type 2 diabetes mellitus (T2DM), with the prevalence of T2DM approximately two times higher among individuals with OSA compared to those without. This study aimed to elucidate the molecular mechanisms linking OSA with T2DM development by investigating oxygen metabolism dysregulation through hypoxia-sensitive *miRNA-181a* expression and associated enzymatic pathways involving sirtuin 1 (SIRT1) and adiponectin. Previous studies have also suggested a positive correlation between adiponectin, metformin intake, and SIRT1 expression.

Materials and methods: All participants underwent standard physical examination and polysomnography. Based on the apnea-hypopnea index (AHI) and T2DM status, participants were categorized into three groups: OSA (AHI >30, $n=26$), OSA+T2DM (AHI >30 and diagnosed T2DM, $n=29$), and control (AHI <5, $n=32$). Blood samples were collected in the evening and morning. An additional morning sample was obtained after at least three months of continuous positive airway pressure (CPAP) therapy ($n=21$). Total RNA was isolated from the buffy coat, and the expression of *SIRT1* and *miRNA-181a* was quantified via RT-qPCR. Protein levels of SIRT1 (intracellular) and adiponectin (serum) were assessed using ELISA. Statistical analyses included the Mann-Whitney U test, Kruskal-Wallis test, and Spearman's rank correlation.

Results: Evening *miRNA-181a* expression differed significantly across the groups: OSA (36.74, IQR: 18.1–108.4), OSA+T2DM (16.78, IQR: 13.5–27.5), and controls (25.61, IQR: 7.1–114.1); $p=0.041$. *SIRT1* expression varied significantly both in the evening (OSA: 44.12×10^{-6} , IQR: 27.9–267.9; OSA+T2DM: 506.60×10^{-6} , IQR: 165.6–1176.8; controls: 323.08×10^{-6} , IQR: 32.5–1136.5; $p=0.012$) and in the morning (OSA: 84.44×10^{-6} , IQR: 48.5–156.5; OSA+T2DM: 553.75×10^{-6} , IQR: 206.2–1254.6; controls: 214.86×10^{-6} , IQR: 46.1–1055.1; $p=0.008$). Adiponectin levels were significantly reduced in OSA and OSA+T2DM groups compared to controls, both in the evening (OSA: 3849.01 ng/ml, IQR: 2812.6–6048.1; OSA+T2DM: 3170.35 ng/ml, IQR: 2658.2–4366.9; controls: 5907.54 ng/ml, IQR: 4142.6–8347.6; $p=0.001$) and in the morning (OSA: 3327.04 ng/ml, IQR: 2678.9–5013.1; OSA+T2DM: 2953.49 ng/ml, IQR: 2296.6–3915.3; controls: 5207.78 ng/ml, IQR: 3604.9–7138.8; $p=0.001$). A weak negative correlation was found between evening *SIRT1* and *miRNA-181a* expression ($r = -0.28$, $p=0.01$). Intracellular SIRT1 protein was undetectable (threshold: 0.31 ng/ml). *SIRT1* expression was significantly higher in OSA patients treated with metformin ($n=23$, $p=0.037$). After CPAP therapy, only *miRNA-181a* showed a significant increase (16.17, IQR: 10.49–32.21 vs. 43.87, IQR: 22.59–86.21; $p=0.047$), while SIRT1 and adiponectin levels remained unchanged.

Conclusions: Elevated *miRNA-181a* expression in OSA patients was associated with reduced *SIRT1* expression, potentially contributing to increased insulin resistance and subsequent T2DM development. Paradoxically, *SIRT1* expression was higher in patients with established T2DM, possibly reflecting metformin use or compensatory mechanisms. Notably, this increase was not accompanied by

elevated adiponectin, suggesting incomplete metabolic adaptation. CPAP therapy was associated with a rise in miRNA-181a expression, with no significant effect on *SIRT1* or adiponectin levels.

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From Resistance to Collapse: Prevalence and 8-Year Progression of UARS to OSA in a Population-Based Cohort

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Introduction: Upper Airway Resistance Syndrome (UARS) is a form of non-hypoxic sleep-disordered breathing characterized by increased inspiratory effort during sleep without overt apneas or oxygen desaturation. Although initially described as distinct from Obstructive Sleep Apnea (OSA), UARS remains controversial due to overlapping clinical features and a lack of consensus in diagnostic standards. Our previous analysis from the São Paulo Epidemiologic Sleep Study (EPISONO) reported a UARS prevalence of 3.1%, predominantly among young, non-obese females. In this longitudinal follow-up, we investigated the long-term trajectory of UARS over eight years and its potential progression to OSA, aiming to clarify whether UARS represents an early manifestation within the OSA spectrum.

Materials and methods: This study utilized a representative subset of adults from the EPISONO cohort who underwent comprehensive evaluations in both 2007 (baseline) and 2015 (follow-up). Inclusion required complete type-I polysomnography and validated symptom questionnaires. UARS was defined using strict criteria: apnea-hypopnea index (AHI) < 5 events/h, minimum SpO₂ ≥ 92%, airflow limitation (AFL) ≥ 5% of total sleep time (TST), and presence of either excessive daytime sleepiness (Epworth Sleepiness Scale (ESS) score > 10) or fatigue (Chalder Fatigue Scale (CFS) score > 3). OSA was classified according to AHI thresholds, with symptom criteria applied to mild cases. Follow-up involved reassessment with identical PSG and survey instruments. Multinomial logistic regression and generalized estimating equations were used to model diagnostic evolution and symptom trajectories over time, with covariates including age, sex, and body mass index (BMI).

Results: Among 571 eligible participants, 18 were diagnosed with UARS at baseline. At follow-up, 6 of these individuals developed OSA (incidence: 33.3%), 7 remained classified as UARS (persistence: 38.9%), and the remainder shifted into other categories. Among the 59 baseline controls, 5 developed OSA (8.5%), and 4 developed UARS (6.8%). UARS diagnosis at baseline conferred a 5.4-fold increased risk of OSA onset ($p = 0.014$), which rose to 11.75-fold after adjusting for sex and age ($p = 0.006$). UARS participants also exhibited significantly higher levels of depressive symptoms (Beck Depression Inventory: 12.89 vs 4.58), anxiety (Beck Anxiety Inventory: 10.5 vs 6.27), daytime sleepiness (ESS: 12.22 vs 7.32), and fatigue (CFS: 5.2 vs 2.42) than controls (all $p < 0.05$). Mean AFL increased markedly in persistent UARS cases, from 10.1% to 33%. Although both groups showed AHI increases over time, the change was more pronounced in the UARS cohort. GEE analyses confirmed UARS status as a significant predictor of worsening mood and fatigue symptoms, independent of age or BMI.

Conclusions: Our findings support the hypothesis that UARS may represent an early, milder phase within the broader spectrum of sleep-disordered breathing. The elevated risk of progression to OSA and persistent burden of sleepiness, fatigue, depression, and anxiety among UARS individuals reinforce the clinical significance of this diagnosis. Early recognition and targeted interventions for UARS may be critical in preventing the emergence of more severe forms of sleep apnea and associated neuropsychiatric morbidity.

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Fusobacterium nucleatum mediates inflammatory effect in pediatric obstructive sleep apnea with adenoid hypertrophy

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Introduction:

Adenoid hypertrophy (AH), a leading risk factor of pediatric obstructive sleep apnea (OSA), is associated with disturbance of oral microbiota, especially the microbial film on adenoids. However, precise microbial characteristics on adenoids and their role in pediatric OSA are unclear.

Materials and methods:

Fifteen polysomnography-confirmed pediatric OSA with AH, and twenty- two controls were enrolled (Approval no.2018-073 and 2019 R061-F01). Metagenomic sequencing was used to identify the microbial characteristics on surface of nasopharyngeal adenoids. Linear discriminant analysis was used to explore differential microbial characteristics and molecular biology techniques were used to assess how such microbial differences may participate in AH.

Results:

Significant differences in β diversity between pediatric OSA and controls indicate close relationships between changes in the bacterial community on adenoids and pediatric OSA. Enrichment of *Prevotella_pleuritidis*, *Porphyromonas_endodontalis*, and *Fusobacterium_nucleatum* were significantly associated with pediatric OSA, among which *Fusobacterium_nucleatum* infection could promote the production of IL1 β in mouse lymphocytes and adenoid primary cells through NLRP3 pathway activation.

Conclusions:

Changes in the microbial structure and function on adenoids may provide an important pathogenic factor for pediatric OSA induced by AH. In particular, *Fusobacterium_nucleatum* may promote inflammatory response that enhances the development of adenoid hypertrophy, thereby serving as potential therapeutic target.

Gender Differences in Changes in Sleep-Related Physical and Mental Symptoms and Quality of Life Following CPAP Treatment in Patients with OSA

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Introduction: Poor sleep quality, memory impairment, emotional disorders, and reduced quality of life (QOL) are prominent symptoms among individuals with obstructive sleep apnea (OSA). Continuous Positive Airway Pressure (CPAP) therapy is widely recognized as the gold standard treatment for OSA. However, the diagnostic criteria and treatment approaches for OSA have historically been based on male-centric models, potentially overlooking gender-specific symptomatology. The objective of this study was to investigate gender differences in changes in sleep-related physical and mental symptoms, as well as QOL, after CPAP treatment among individuals with OSA.

Materials and methods: A prospective study with a repeated measures design was conducted at a sleep outpatient clinic within a medical center. Individuals diagnosed with OSA, defined by an apnea-hypopnea index (AHI) ≥ 5 events per hour as measured by polysomnography, were included. Daytime sleepiness, sleep quality, cognitive function, anxiety and depression, and QOL were assessed using the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Mini-Mental State Examination (MMSE), Hospital Anxiety and Depression Scale (HADS), and the World Health Organization Quality of Life-BREF (WHOQOL-BREF), respectively. Measurements were collected at four time points: baseline (T0, before CPAP initiation), 1 month (T1), 3 months (T2), and 6 months (T3) after CPAP initiation. Repeated measures analyses were conducted to evaluate changes over time.

Results: A total of 121 participants were enrolled, with a mean age of 50.78 years. The male-to-female ratio was approximately 5.4:1 (19 females). Among them, 111 participants initiated CPAP therapy, and 69 completed the 6-month follow-up (T3). CPAP adherence over time did not significantly differ between genders. At baseline, females exhibited significantly poorer sleep quality compared to males ($p = .007$). Following CPAP initiation, improvements were observed in daytime sleepiness, sleep quality, cognitive function, anxiety, and QOL across participants, with notable gender differences. In the fully

adjusted repeated measures model, females consistently demonstrated poorer sleep quality ($\beta = -3.23$, $p < .0001$) and greater improvement in cognitive function ($\beta = 0.70$, $p = .025$) compared to males across all follow-up points. No significant gender differences were observed in changes in daytime sleepiness, anxiety, depression, or QOL.

Conclusions: This study demonstrated that CPAP treatment effectively improved daytime sleepiness, sleep quality, cognitive function, anxiety, and QOL among individuals with OSA. Notable females exhibited persistently poorer sleep quality but greater improvements in cognitive function compared to males following CPAP therapy. No significant gender differences were identified in changes in daytime sleepiness, anxiety, depression, or overall quality of life. These findings highlight the need for gender-sensitive approaches in the evaluation and management of sleep-related symptoms in OSA patients undergoing CPAP treatment.

Gender Effects on Surgical Outcome after Maxillomandibular Advancement for Obstructive Sleep Apnea in the East Asian Patient

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Introduction: Anatomical and physiological differences between genders may influence surgical outcomes in sleep apnoea treatments. Maxillomandibular advancement (MMA) is a common procedure for obstructive sleep apnoea (OSA) patients. Still, the impact of gender on surgical success in the East Asian patient has not been fully explored.

Aim:

This study aims to compare the post-operative outcomes of MMA in East Asian patients, specifically examining gender as an influencing factor.

Materials and methods: A retrospective matched cohort study was conducted on 36 OSA patients (18 males, 18 females) who underwent MMA at Chang Gung Memorial Hospital, Taiwan. Patients were matched by age and body mass index. Pre- and post-operative polysomnographic indices and cephalometric measurements were analysed to assess surgical outcomes. Logistic regression was used to evaluate gender as a predictor of outcomes, adjusted for baseline apnoea-hypopnoea index (AHI).

Results: Surgical success was observed in 83.3% of males and 66.7% of females, with cure rates of 44.4% and 50.0%, respectively. After adjusting for baseline AHI, gender was not a significant predictor of cure (OR 0.99; 95% CI: 0.24–4.17; $p = 0.984$) or success (OR 1.54; 95% CI: 0.28–9.43; $p = 0.619$). Males demonstrated greater improvements in AHI, oxygen desaturation index, arousal index, and wake after sleep onset. Females showed greater gains in rapid eye movement sleep and hyoid elevation.

Conclusions: Gender does not independently predict surgical success or cure following MMA in East Asian OSA patients. However, gender specific responses were noted in certain polysomnographic indices and cephalometric measurements. Further studies are warranted to explore underlying mechanisms influencing these differential responses.

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Genetic Variants of High-density Lipoprotein Cholesterol on Insulin Resistance and Cardiovascular Diseases in Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) and its common comorbidities, including insulin resistance (IR) and cardiovascular diseases (CVD), are frequently manifested as alterations in high-density lipoprotein cholesterol (HDL-C) levels. This study aimed to explore the association between genetic variations of HDL-C and these conditions.

Materials and methods: 4,513 individuals suspected of OSA underwent anthropometric measurements, polysomnography assessments, and serum biochemical testing. Genetic variations of HDL-C were evaluated using 45 single nucleotide polymorphisms (SNPs). IR was assessed via the Triglyceride-Glucose (TyG) index, while CVD risk was determined by the 10-year Framingham CVD risk score (FRS). Inter-relationships among these factors were analyzed through linear regression, with results corrected employing the Benjamini-Hochberg (BH) method.

Results: After BH correction, the rs35950463 and rs10787431 variants positively correlated with the lowest oxygen saturation ($\beta = 0.48$, $P_{BH} = 0.023$; $\beta = 0.046$, $P_{BH} = 0.023$). The variants rs429358, rs328, and rs2980859 were significantly associated with the TyG index ($\beta = 0.056$, $P_{BH} = 0.001$; $\beta = -0.074$, $P_{BH} = 2.3 \times 10^{-6}$; $\beta = -0.084$, $P_{BH} = 1.2 \times 10^{-7}$), while the variants rs651821 and rs75198898 were significantly associated with FRS ($\beta = 0.031$, $P_{BH} = 0.001$; $\beta = -0.039$, $P_{BH} = 8.1 \times 10^{-6}$).

Conclusions: Several HDL-C SNPs significantly correlated with oxygenation status, IR, or CVD risk in OSA patients, suggesting potential targets for preventive and therapeutic interventions.

Higher Ambient Temperatures may Increase Sleep Apnea-Specific Pulse-Rate Response in obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) features repeated sympathetic activation, elevating cardiometabolic and neurocognitive risks. The heart rate response to respiratory events, measured by ΔHR (the difference between the lowest heart rate during the event and the peak following airway reopening), reflects sympathetic activity and correlates with adverse cardiovascular outcomes. Environmental temperature may influence autonomic function: lower temperatures may enhance baseline sympathetic tone and modify ΔHR , while higher temperatures could further elevate the heart rate response. We hypothesize that elevated ambient temperatures are associated with exaggerated post-apneic heart rate elevation in patients with OSA.

Materials and methods: We retrospectively analyzed data from 2,169 Chinese adult participants diagnosed with OSA using in-laboratory polysomnography between January 2017 and December 2024. Ambient temperature data were obtained from official sources. ΔHR was defined as the difference between the maximum and minimum heart rates within an event-related window around each respiratory event, calculated directly from the continuous heart rate recordings. This metric quantitatively reflects sympathetic activation during OSA events and has demonstrated predictive value for adverse cardiovascular outcomes. Associations between ΔHR , OSA severity, and ambient temperature were analyzed.

Results: 1,840 males and 329 females with a median age of 41.0 years (interquartile range [IQR]: 34.0–50.0) and a median body mass index (BMI) of 26.8 kg/m² (IQR: 24.6–29.4) were included in this study. Participants exhibited a median apnea-hypopnea index (AHI) of 32.5 events/hour (IQR: 14.9–59.1). Higher ambient temperatures were significantly associated with greater ΔHR . Specifically, the minimum, mean, and maximum temperatures over 1-day and 7-day periods all demonstrated statistically significant positive correlations with ΔHR ($p < 0.05$ for all comparisons). Stepwise linear regression analysis indicated that each 10°C increase in the 7-day average minimum temperature corresponded to a significant 0.96 bpm increase in ΔHR (95% confidence interval [CI]: 0.48–1.44). During the warmer season (defined as minimum temperature $\geq 4^\circ\text{C}$), ΔHR showed the strongest correlation with the previous 7-day minimum temperature ($\rho = 0.103$, $p < 0.001$). Conversely, no significant correlation was observed during the colder season (minimum temperature $< 4^\circ\text{C}$; with central heating utilized in 617 out of 1,018 days in Beijing) ($\rho = 0.010$, $p = 0.761$). The association between higher temperatures and greater ΔHR was more pronounced among those with BMI ≥ 28 kg/m² ($\beta = 0.109$, 95% CI: 0.024–0.194). No significant associations were observed between ambient temperatures and AHI, SpO₂, sleep latency, or sleep efficiency.

Conclusions: Higher temperature may modulate the compensatory autonomic response to respiratory events in OSA patients, especially among those with higher BMI and during warmer seasonal periods. Ambient factors might be considered as effect modifiers when evaluating OSA-induced pathophysiological consequences.

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Higher Trend of Severe OSA in Normal BMI Patients: Analysis from Western Part of India

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent sleep disorder characterized by repeated episodes of partial or complete obstruction of the upper airway during sleep. This study aims to analyze the demographic, clinical, and comorbidity profiles of patients diagnosed with OSA, and treatment outcomes.

Materials and methods: Data from 42 patients (31 males and 11 females) diagnosed with OSA were analyzed. The patients were categorized based on Body Mass Index (BMI), history of sleep apnea, duration of symptoms, comorbidities, Apnea-Hypopnea Index (AHI), Oxygen Desaturation Index (ODI), and Epworth Sleepiness Score (ESS). Symptom prevalence and treatment outcomes were also recorded.

Results: A total of 42 patients enrolled, with a mean age of 56.1 ± 16 years; 31(73.8%) were males and 11(26.2%) were females. Regarding BMI, 11 (26.2%) patients had a BMI of less than 25, while the majority, 31 (73.8%) patients, had a BMI of 25 or higher. A history of sleep apnea was reported by 37(88.1%), with only 5 (11.9%) having no prior history.

The duration of symptoms varied, with the majority, 39 (92.9%) patients, experiencing symptoms for more than 6 months, and 3 (7.1%) patients for 1 to 6 months. Comorbidities were prevalent, with 11 patients having diabetes (26.2%), 33 patients having hypertension (78.6%), 10 patients having asthma (23.8%), 4 patients having chronic obstructive pulmonary disease (9.5%), 5 patients having ischemic heart disease (11.9%), and 9 patients having dyslipidemia (21.4%). Other comorbidities included post PTCA, chronic rhinosinusitis, severe eosinophilic asthma, asthma-COPD overlap, chronic severe asthma, and asthmatic bronchitis incidence were similar (1,2.4%).

The severity of OSA was categorized as mild for 6 patients (14.3%), moderate for 6 patients (14.3%), severe for 26 patients (61.9%), very severe for 2 patients (4.8%), moderate to severe for 1 patient (2.4%), and mild to moderate for 1 patient (2.4%). Majority of patients were treated with CPAP and outcomes showed that 26 patients experienced improvement (61.9%), while 16 patients remained stable (38.1%).

In current study we observed, out of 42 patients, 11 have **normal BMI** and still have OSA. This represents **26.19%** of the total patients, indicating significant proportion of patients with normal BMI also suffer from OSA.

In group of BMI >25, ODI showed 3% with normal, 16% with mild, 19% with moderate, and 61% with severe scores, compared to 18%, 27%, 18%, and 36% respectively in BMI<25 ($p = 0.262$). For, ESS 29% of the BMI>25 group were classified as normal, 32% mild, 6% moderate, and 32% severe, in BMI<25 group had 45% normal, 36% mild, 9% moderate, and 9% severe scores ($p = 0.48$). Regarding the STOP-BANG score, 77% of individuals with BMI>25 were at high risk and 23% at intermediate risk, compared to 82% and 18% respectively in the BMI<25 group ($p = 1$).

Conclusions: The analysis of the data indicates a high prevalence of severe OSA among the patients. Notable proportion of patients with normal BMI also suffer from OSA, highlighting the importance of considering OSA risk factors beyond BMI. Treatment outcomes showed improvement in more than half of the patients.

High night-to-night variability in OSA severity is associated with prevalent major adverse cardiovascular and cerebrovascular events

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Introduction: High night-to-night variability in obstructive sleep apnoea (OSA) severity is associated with hypertension and increased likelihood of atrial fibrillation events independent of OSA severity.

However, impacts on cardiovascular and cerebrovascular events are unknown. This study aimed to examine the association of OSA severity and its night-to-night variability with cardiovascular disease prevalence.

Materials and methods: Multi-night apnoea-hypopnea index (AHI) data were collected from users of a validated, FDA-cleared under-the-mattress sensor (Withings Sleep Analyzer) who completed six-monthly questionnaires on demographics and physician-diagnosed health conditions including cardiovascular and cerebrovascular diseases. OSA severity (AHI) and OSA variability (root-mean square of successive differences in AHI) were calculated in the 6-months preceding the questionnaire entry. The primary outcome was a composite measure of non-fatal major adverse cardiovascular and cerebrovascular events (MACCE), including myocardial infarction or heart attack, stroke, angina pectoris or coronary artery disease, and congestive heart failure. Logistic models assessed associations between with MACCE prevalence adjusted for age, sex, body mass index, alcohol consumption, smoking status, average OSA severity and physician-diagnosed OSA. The logistic regression results are presented as odds ratios (OR) and 95% confidence intervals (CI), comparing the 75th percentile with the 25th percentile of the continuous exposure variable. Robust covariance was estimated using sandwich estimators by using participants IDs as a cluster variable to account for correlated responses within participants (for those with multiple questionnaire entries).

Results: Among 3,159 participants (mean age: 49±13 years; 19% female; mean BMI: 29±6 kg/m²), 139 (4.4%) instances of MACCE were reported based on the last questionnaire entry. The final dataset included 4,936 questionnaire entries. Among them, 1,982 participants completed a single questionnaire, 725 completed two, and 452 completed more than two entries. Average OSA severity was not associated with MACCE prevalence (moderate-to-severe OSA vs. no OSA: adjusted OR [95%CI]; 1.42 [0.89, 2.24]). However, high night-to-night OSA variability (75th vs. 25th; 11.0 vs. 3.8 events/h) was associated with a 33% increase in the odds of prevalent MACCE, independent of OSA disease severity (adjusted OR [95%CI]; 1.33[1.02, 1.74]). Among participants with mild OSA, high OSA variability (tertile 3 vs. tertile 1) was independently associated with an increased prevalence of myocardial infarction, heart attack and/or stroke events (adjusted OR [95%CI]; 3.93 [1.21, 12.6]). This association was not evidenced in participants with moderate-to-severe OSA, although these results should be interpreted with caution given the reduced number of events once stratified by OSA-severity category.

Conclusions: High night-to-night variability in OSA severity represents a novel clinical OSA phenotype linked to higher cardiovascular and cerebrovascular prevalence, which may be a better marker of risk than OSA severity in individuals with mild OSA. These findings underscore the importance of multi-night OSA assessments to adequately characterise OSA and improve patient management and outcomes.

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Home monitoring of patients under continuous positive pressure by a non intrusive under-mattress sleep analyzer

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Introduction: To determine the performance of the WITHINGS Sleep Analyzer (WSA) in the evaluation of sleep duration and respiratory events, we compared WSA data with CPAP use, residual events and polysomnographic data in patients with CPAP treatment.

Materials and methods: The WSA (CE medical and FDA certified) placed between the bed base and the mattress, records pressure variations and snoring. It was set up in the patient's home after one month of CPAP use. Simultaneous 7-daily reports from CPAP Airsense 11 (Resmed) and WSA were collected. In addition 14 patients had simultaneous recordings of CPAP and WSA under full PSG at home. Patients and home care providers did not receive feedback from the WSA during the protocol.

Results: 75 patients (17F) with a diagnosis of OSAS, mean age 55.1 years (SD 12.1), BMI 30.8 kg/m² (4.7), Epworth Sleepiness Scale 11.2 (5.4), AHI (Apnea-Hypopnea Index) 44.2/hr (20.5) had 480 nights of concurrent WSA and CPAP recordings. Time spent in bed was 8.1 hr (1.2) and sleep time 7.1 hr (1.2) for an average duration of CPAP use of 6.5 hr (1.7) (Wilcoxon test comparison of sleep time WSA vs

CPAP $p < 0.001$). The AHI determined by the WSA was 11.3/hr (12.4) vs 2.0 (1.9) for CPAP ($p < 0.001$). In the 14 patients recorded with PSG, AHI_{psg} was 10.9/hr (8.4) compared to AHI_{wsa} 8.8 (10.9) and AHI_{cpap} 2.9 (2.7) ($p < 0.05$ between PSG and WSA, WSA and CPAP; $p < 0.01$ between PSG and CPAP). **Conclusions:** In this highly adherent patient group, WSA allowed to evaluate Time in bed, Total sleep time and AHI_{wsa}. AHI_{wsa} was higher than AHI_{cpap} and close to AHI_{psg}. In the future WSA could improve CPAP follow-up with better therapy efficacy assessment particularly during the early phase of treatment. WSA may also increase patient empowerment.

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Home Sleep Testing Model In OSA Screening In Patients With Cardiovascular Diseases – Diabetes and Obesity in Vietnam: The First Multi Centre Study

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Introduction: Obstructive Sleep Apnea (OSA) affects approximately 4 million people in Vietnam, with 2.3 million individuals suffering from moderate to severe conditions. Among these, people with existing cardiovascular diseases, hypertension, diabetes, and obesity are at high risk of developing OSA. Therefore, this study aims to assess the prevalence of Obstructive Sleep Apnea in this population group using a Level 3 diagnostic model at home.

Materials and methods: A cross-sectional multicenter survey was conducted from December 2024 to March 2025, involving population with different health problems across Vietnam. Collected data included age, sex, body mass index (BMI), STOP-BANG score, Epworth Sleepiness Scale (ESS), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and comorbid conditions. Selected participants for doing Home Sleep Testing (HST) were for those who had at the moment of study one of the following conditions: Cardiovascular diseases, Hypertension, Diabetes, or Obesity (CHDO). They completed questionnaires (STOP-BANG, ESS) and underwent Type III respiratory polygraphy using self-applied Apnea-Link Air devices at home. Trained technicians at the centers provided remote technical support, reviewed, and standardized these recordings. Statistical analyses included descriptive summaries, correlation assessments, univariate and multivariable linear regression models for AHI, and logistic regression models to identify factors associated with moderate (AHI ≥ 15) and severe OSA (AHI ≥ 30).

Results: Number of included study participants was 340 among 1500 subjects with current health problem across four different regions of Vietnam. Initial screening showed that 268 participants with CHDO problem, 268 subjects had cardiovascular-disease and hypertension, 107 had diabetes mellitus, and 56 were obesity. Participants had a mean age of 59.9 ± 15.1 years, mean BMI of 25.1 ± 3.5 kg/m². A STOP-BANG score ≥ 3 (4.2 ± 1.6) was present in 294 participants (88.0 %), and an mean of ESS: 7.1 ± 5.4 within ESS ≥ 11 was present in 91 participants (27%). Respiratory polygraphy using Apnea-Link Air devices identified OSA in 73% of the participants (28% mild, 24% moderate, and 21% severe). The prevalence of OSA in the Cardiovascular-disease – Hypertension group was 75% (40% mild, 32% moderate, and 28% severe); in the Diabetes mellitus group was 77% (39% mild, 29% moderate, and 32% severe), and in the Obesity group was 76% (23% mild, 37% moderate, and 40% severe). BMI and STOP-BANG scores demonstrated a moderate positive correlation with AHI ($r = 0.33$; $p < 0.001$), whereas ESS had a weak correlation ($r = 0.11$; $p = 0.43$). In multivariable regression, both BMI and STOP-BANG remained significant predictors of AHI, while ESS was not. Logistic models confirmed that both BMI and STOP-BANG significantly predicted the presence of moderate and severe OSA.

Conclusions: Compared to the general population, the prevalence of OSA in the population group with pre-existing cardiovascular diseases, hypertension, diabetes mellitus, and obesity is very high. OSA severity is closely linked with objective measures such as BMI and STOP-BANG scores, but not with subjective daytime sleepiness as assessed by the ESS. These findings underscore the importance of

structured screening tools in those with cardiovascular risk factors. Therefore, a level 3 HST model is effective and suitable for screening OSA in high-risk populations and in emerging countries.

Identification and validation of a novel autophagy-related biomarker in obstructive sleep apnea syndrome

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Introduction: Obstructive sleep apnea syndrome (OSAS) is implicated in tumor progression, with chronic intermittent hypoxia (CIH) driving autophagy and malignancy. This study investigates the role of autophagy in OSAS progression and its implications for colorectal cancer (CRC).

Materials and methods: We analyzed OSAS datasets (GSE135917, GSE38792) from the Gene Expression Omnibus to identify differentially expressed genes (DEGs) and autophagy-related DEGs. Functional enrichment was performed using Gene Ontology, Kyoto Encyclopedia of Genes and Genomes, and gene set enrichment analysis (GSEA). A protein-protein interaction network pinpointed hub genes. CRC datasets from The Cancer Genome Atlas were used for differential expression, survival, GSEA, and immune infiltration analyses. In Sprague-Dawley rats, CIH-induced autophagy and oxidative stress were assessed via reactive oxygen species (ROS) assays. Hub genes were validated in rat models and OSAS patient samples.

Results: GSEA revealed significant enrichment of autophagy-related genes in OSAS. Five hub genes (ATG5, CASP1, MAPK8, EIF4G1, TBK1) were identified, with ATG5 and TBK1 validated. Autophagy-related DEGs were predominantly upregulated in CRC tissues. Elevated TBK1 expression in CRC was associated with improved immunotherapy sensitivity and increased infiltration of CD8+ T cells, macrophages, and regulatory T cells, suggesting modulation of the immune microenvironment. In rats, CIH elevated ROS levels, supporting its role in autophagy activation. TBK1 expression was significantly higher in OSAS patients compared to controls, unaffected by continuous positive airway pressure therapy.

Conclusions: This study pioneers the identification of TBK1 as a key contributor to OSAS progression, highlighting its potential as a novel biomarker and therapeutic target. These findings underscore the interplay between CIH, autophagy, and tumor immunity, offering new avenues for OSAS management and CRC immunotherapy.

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Identification of the prevalence of Obstructive Sleep Apnea in the Cardiology and Neurology Semi-Intensive Units at a private hospital in Brazil

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Introduction: Sleep disorders are three times more prevalent in patients with cardiovascular disease compared to the general population. Obstructive Sleep Apnea (OSA) is the most common type of sleep-disordered breathing and is associated with a 70% relative increase in the risk of cardiovascular morbidity and mortality. OSA is a recognized risk factor for several cardiovascular conditions, including arterial hypertension, heart failure, stroke, coronary artery disease, metabolic syndrome, and cardiac arrhythmias. Polysomnography is considered the gold standard for diagnosing OSA. However, screening questionnaires such as the Berlin Questionnaire (BQ) and STOP-Bang can be utilized as practical tools to identify risk factors for OSA.

Materials and methods: In patients over 18 years of age admitted to the Cardiology and Neurology Semi-Intensive Units with a diagnosis of acute myocardial infarction, atrial fibrillation, systemic arterial

hypertension, stroke, complete atrioventricular block, and heart failure, the Berlin Questionnaire and STOP-Bang screening tools were applied to help identify those at high risk of OSA. After identifying patients at high risk for OSA, they were referred for polysomnography and/or in-hospital or outpatient treatment.

Results: The implementation of this screening allowed the team to effectively identify and manage patients at high risk for OSA, ensuring greater safety throughout hospitalization. Patients could be diagnosed during their stay and promptly begin appropriate treatment for sleep apnea. Furthermore, those scheduled for examinations or procedures involving sedation could be assessed for potential respiratory complications based on their OSA risk profile.

Conclusions: This approach significantly improved understanding and management of OSA risk, enabling the team to provide comprehensive care and reduce potential complications associated with the condition.

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Identifying Obstructive Sleep Apnoea in Headache Clinics: Clinical Clues and Diagnostic Considerations

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Introduction: Encounters with patients experiencing chronic headaches are common occurrences in neurology clinics. However, recognition of underlying obstructive sleep apnoea (OSA) in some of these patients remains limited amongst neurologists, potentially leading to suboptimal treatment with migraine medications and muscle relaxants, resulting in incomplete headache relief. Diagnostic clues from clinical features and ancillary test results are therefore essential to help neurologists identify these patients in a headache clinic and guide appropriate testing and treatment.

Materials and methods: Typical of a consecutive case series, patients who presented to a neurology clinic between June 2024 to June 2025 for the main complaints of chronic headaches (15 days or more, for at least 3 months) and with a STOPBANG score of 3 or more were included into this study. All patients subsequently undergo home sleep apnoea tests (WatchPAT device) or overnight polysomnographies. Clinical features and ancillary test data were retrospectively analyzed, regardless of the presence, absence, or severity of OSA on diagnostic testing.

Results: We studied 26 patients, of which most (73.1%) were women (females to males = 2.7:1). The median age was 54.5 years (inter-quartile range [IQR] 49–63), and the median body mass index (BMI) was 28.3 kg/m² (IQR 23.1–36.6). Over half (53.8%) were obese (BMI >27 kg/m²), 26.9% were overweight (23–27.4 kg/m²), and 19.2% had normal BMI. Nearly all (88.5%) had cardiovascular risk factors—69.2% had hypertension, 30.8% hyperlipidaemia, 30.8% diabetes, 11.5% prior strokes, and 11.5% ischemic heart disease. Half had two or more risk factors. Among those with hypertension, 55.6% (10/18) were diagnosed before age 50, and 27.8% (5/18) before age 40. Chronic bitemporal/bifrontal headaches resembling tension-type headaches were the most common presenting complaint (84.6%), worsening in the morning for most (92.3%). All patients reported snoring and having non-restorative sleep. Other sleep complaints included dry mouth on waking (92.3%), nocturnal micturition (57.7%), choking /coughing during sleep (53.8%), and apnoeic episodes (15.4%). The median STOP-BANG score was 4.5 (IQR 4–5). Less than 1/3 (30.8%) had neck circumferences of >40cm, or BMIs of > 35kg/m² (26.9%). Despite frequent reports of daytime sleepiness (84.6%), their median Epworth Sleepiness Scale score was only 9 (IQR 4–11.5), with half scoring below those of pathologic sleepiness. 23 and 3 patients underwent home sleep apnoea testing and overnight polysomnography respectively. Their median sleep parameters were: sleep latency of 17.5 minutes (IQR 9.5–20), REM latency of 67 minutes (IQR 42.5–90.3), sleep efficiency of 84.6% (IQR 82.5–90.6), overall apnoea–hypopnoea index (AHI) of 24.4 (IQR 16.9–47.7), non-REM sleep of AHI 23.9 (IQR 7.3–45.4), and REM sleep AHI of 34.9 (IQR 28.2–51.6).

Conclusions: Notwithstanding the methodological limitations, our findings highlight the need to consider OSA in patients with chronic tension-type headaches, particularly when they are overweight, or have multiple cardiovascular risk factors. Hypertension before age 50 is an important diagnostic clue, while high Epworth Sleepiness Scale scores appear less reliable. Clinicians should screen for

symptoms of sleep apnoea, and objective sleep assessments are recommended even in those with intermediate STOP-BANG scores.

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Imaging features of upper airway in obstructive sleep apnea patients with epiglottic collapse

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Introduction: The epiglottic location is concealed, and airway collapse and obstruction in OSA patients only occur in sleep. Drug-induced sleep endoscopy (DISE) is a kind of real-time and dynamic laryngoscopy on the upper airway of patients induced to sleep through drugs, which can accurately locate the plane and degree of obstruction. Due to the limited medical resources, it is difficult to apply on a clinical basis and can not be promoted in primary hospitals. Upper airway Computed tomography (CT) It can initially determine the structural factors of nasopharyngeal, oropharyngeal, and glossopharyngeal stenosis during the waking period and has particular clinical guiding value. Therefore, this study aims to screen out OSA patients with epiglottic collapse through DISE examination and compare and analyze the upper airway CT with other OSA patients and people without OSA to summarize the imaging characteristics and rules of patients with epiglottic collapse.

Materials and methods: One hundred and four patients underwent physical examination, polysomnography (PSG), and a three-dimensional CT plain scan of the upper airway. In addition, all patients underwent drug-induced sleep endoscopy (DISE). According to DISE, all patients were divided into the epiglottic and non-epiglottic collapse groups. Eighteen patients with foreign bodies in the esophagus who received treatment in our hospital during the same period completed three-dimensional CT of the upper airway. They denied snoring history and were selected as a standard control group. Collected the relevant data and analyzed the differences among the groups.

Results: A total of 18 patients with foreign bodies in the esophagus were included as normal controls. One hundred four patients with OSA, 27 patients with epiglottic collapse, and 77 patients with non-epiglottic collapse were included. In this study, the incidence of epiglottic collapse was 25.96%. There were statistically significant differences in epiglottic length between patients with epiglottic collapse and the standard control group ($P < 0.05$). In the patients with epiglottic collapse, the epiglottic length ($t=2.162$, $P=0.033$) and the lymph tissue classification of the root of the tongue ($Z=-2.968$, $P=0.003$) were significantly greater than those in the patients with non-epiglottic collapse, and the epiglottis-root of tongue distance ($Z=-2.385$, $P=0.017$) was smaller than the latter. According to Logistic regression analysis, epiglottic collapse and epiglottic width (OR: 1.201; 95%CI: 1.009-1.430, $P=0.039$) were positively correlated, with epiglottic curvature (OR: 0.979; 95%CI: 0.961-0.998, $P=0.030$) was negatively correlated, and with the grade of lymph tissue of tongue root (OR: 1.936; 95%CI: 1.294-2.896, $P=0.001$) was positively correlated.

Conclusions: In patients with epiglottic collapse, the epiglottic length and lymphoid tissue grading of the root of the tongue are significantly greater than those of patients with non-epiglottic collapse, and the epiglottic root of tongue distance is smaller than the latter. CT examination in awake OSA patients with epiglottic collapse can reveal its characteristic indicators. The wider the epiglottic width, the smaller the epiglottic curvature, and the larger the lymph tissue grade of the base of the tongue were effective predictors of epiglottic collapse, and the lymph tissue grade of the base of the tongue was an independent predictor.

Impact of an early follow-up visit on adherence and adherence trajectories after initiation of continuous positive airway pressure therapy for obstructive sleep apnea

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Introduction: Clinical outcomes during continuous positive airway pressure (CPAP) relate to therapy adherence. The impact of different/specific types of patient support on CPAP adherence is rarely

evaluated, meaning there is a lack of knowledge to inform the choice of follow-up strategy for individual patients. The study evaluates the impact of an early home visit on CPAP adherence/adherence trajectories in patients with obstructive sleep apnea, and which factors predict benefit of an early follow-up visit.

Materials and methods: This multicenter cohort study analyzed home service provider data. Participants were adults starting CPAP in 2019–2022 who had >90 days of telemonitoring data. Adherence was compared before and after the early visit, overall and in subgroups based on adherence over the 15 days after starting CPAP (<2 [low], 2–<4 [intermediate] or ≥4 [high] h/night). Adherence trajectories were also determined.

Results: 4,924 patients were included (62.3% male, mean age 59±13 years, apnea-hypopnea index [AHI] 40±17/h). The early follow-up visit took place 16±5 days after CPAP initiation. Change in adherence in the week after versus week before the early visit was 14±3 min/night overall, and -7±2, 60±4, 102±5 min/night in the high, intermediate, and low adherence subgroups, respectively (p<0.01). Adherence gradually decreased after therapy initiation, increased in the 1–2 days before the visit, then declined. Cluster analysis identified two profiles across all early adherence subgroups: responders and non-responders (those with or without better CPAP usage after the early visit, respectively). Responders were slightly older and had higher CPAP motivation than non-responders; higher leak and higher residual AHI predicted improved adherence after the early visit in the intermediate and low adherence subgroups, respectively.

Conclusions: These data highlight the need for deeper understanding of adherence trajectories and the impact of specific follow-up modalities to allow implementation of personalized CPAP therapy management pathways.

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Impact of CPAP Treatment on Inflammatory Markers in Moderate-Severe Obstructive Sleep Apnea Patients: A 12-Month Follow-Up Study

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Introduction: Obstructive Sleep Apnea (OSA) is characterized by intermittent upper airway obstruction, leading to chronic hypoxia and a pro-inflammatory state. The elevation of inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP) and erythrocyte sedimentation rate (ESR), is frequently observed in OSA and is associated with an increased risk of cardiovascular disease. Continuous Positive Airway Pressure (CPAP) is a well-established treatment for OSA; however, its effect on inflammatory biomarkers remains unclear. This study aimed to evaluate the impact of CPAP therapy on hs-CRP and ESR levels in patients with moderate-severe OSA, with good CPAP adherence, over a 12-month period.

Materials and methods: This prospective study was conducted at Chiangrai Prachanukroh Hospital from January 2023 to December 2024. A total of 120 newly diagnosed moderate-to-severe OSA patients were enrolled, all of whom had a minimum CPAP adherence rate of 70%. Participants were predominantly male (86/120, 71.66%) with a mean age of 49.3±15.5 years. The baseline assessment included polysomnography, measurement of hs-CRP, ESR, and metabolic parameters, along with the Epworth Sleepiness Scale (ESS) and STOP-BANG scores. CPAP therapy was initiated after diagnosis, and compliance was monitored through usage data. Follow-up assessments were performed 12 months after initiating CPAP therapy.

Results: At baseline, the mean apnea-hypopnea index (AHI) was 50.88 events/hour, and the mean ESS score was 9.17. After 12 months of CPAP therapy, the mean AHI decreased to 3.67 events/hour. Inflammatory markers, hs-CRP and ESR, showed a trend toward reduction after CPAP therapy, but the changes did not reach statistical significance (hs-CRP: 9.61 to 3.42 mg/L, p = 0.070; ESR: 19.58 to 13.64 mm/hr, p = 0.339). There was a statistically significant decrease in cholesterol levels from 179.17 mg/dL to 148.41 mg/dL (p = 0.036), but no significant changes were observed in blood pressure,

fasting blood sugar (FBS), or HbA1c levels. CPAP usage was adequate, with a mean daily usage of 5.77 ± 1.39 hours and an overall adherence rate of 87.5%.

Conclusions: This study indicates that while CPAP therapy in patients with moderate-severe OSA led to a reduction in inflammatory markers such as hs-CRP and ESR, these changes did not reach statistical significance. However, the reduction observed suggests a potential benefit of CPAP therapy in decreasing systemic inflammation. Despite the lack of statistical significance, these findings contribute to the ongoing debate regarding the role of CPAP in reducing inflammation and improving cardiovascular outcomes in OSA patients. Further studies with larger sample sizes and longer follow-up are needed to fully understand the effects of CPAP on inflammation in OSA patients.

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Impact of Insomnia and Periodic limb movements of sleep on Mortality in OSA: A High-Risk Phenotype Identified by A Cluster Analysis

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Introduction: Obstructive sleep apnea (OSA) is a heterogeneous syndrome, which makes the Apnea-Hypopnea Index (AHI) insufficient in predicting clinical outcomes, including mortality. This study sought to identify novel OSA phenotypes through a cluster analysis of polysomnographic (PSG) data and to determine their association with all-cause and specific-cause mortality.

Materials and methods: We retrospectively analyzed the records of 3,380 patients with an AHI ≥ 15 /h who underwent PSG between January 1994 and December 2020 at the Center for Sleep and Chronobiology at Seoul National University Hospital, a tertiary medical center in the Republic of Korea. Seven principal components, which are the result of a principal component analysis (PCA) to reduce dimensionality, were associated with oxygen desaturation, sleep fragmentation, deep sleep, periodic limb movements of sleep (PLMS), REM sleep, hypopnea, and shallow sleep, respectively. Then, a K-means cluster analysis was performed to identify distinct OSA phenotypes. Mortality was ascertained from national death records provided by Statistics Korea through December 31, 2022. Using Kaplan-Meier survival analysis, we compared all-cause mortality and specific-cause mortality comprised of cardiovascular and cerebrovascular diseases. A Cox proportional hazards model was used for adjusting age, sex, BMI and comorbidities. The mortality risk of the identified phenotypes was then compared with that of typical AHI-based severity groups (moderate vs. severe OSA).

Results: Four distinct phenotypes were identified. Cluster 1 (n=1,956, 57.8%) was characterized as 'Severe OSA' (median AHI 31.3/h). Cluster 2 (n=674, 19.9%), termed 'Moderate OSA with stable sleep', had a moderate AHI (median 26.6/h) and preserved sleep architecture (median sleep efficiency [SE] 87.1%). Cluster 3 (n=427, 12.6%), termed 'Very severe OSA with hypoxemia', comprised the youngest (median age 49) and predominantly male (92.7%) patients, exhibiting a very severe AHI (median 69.4/h) and the most severe hypoxic burden (median time with $\text{SpO}_2 < 90\%$ 29.6%). Cluster 4 (n=323, 9.6%), described as 'Comorbid insomnia and sleep apnea with PLMS', included the oldest patients (median age 62) with the shortest sleep time (median total sleep time 399.5 min) and the highest PLMS (median 44.5/h). While moderate OSA and severe OSA showed no significant difference in all-cause (Log-rank $p=0.29$) or specific-cause mortality (Log-rank $p=0.09$), mortality rates showed a significant difference

among the cluster. For all-cause mortality (Log-rank $p < 0.001$), Cluster 4 showed the highest and Cluster 2 the lowest rates. After adjusting covariates, Cluster 3 (Hazard Ratio [HR] 1.95, 95% Confidence Interval [CI] 1.13–3.36, $p = 0.017$) and Cluster 4 (HR 2.10, 95% CI 1.43–3.08, $p < 0.001$) had significantly higher mortality risk than Cluster 1. For specific-cause mortality (Log-rank $p < 0.001$), only Cluster 4 showed a significantly higher adjusted risk compared to Cluster 1 (HR 3.19, 95% CI 1.36–7.50, $p = 0.008$).

Conclusions: This study identified distinct obstructive sleep apnea (OSA) phenotypes by cluster analysis using multiple polysomnography (PSG) variables that reflect underlying pathophysiology, which demonstrated superior prognostic value for both all-cause and specific-cause mortality compared to the typical AHI-based classification. Our findings suggest that for predicting the mortality of OSA, it is crucial to consider not only the severity of respiratory disturbance but also co-existing features such as sleep time and PLMS.

Impact of Obstructive Sleep Apnea on Daily Life by Disease Severity Level: Analysis from the SHINE Survey

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Introduction: Obstructive sleep apnea (OSA) is a serious, chronic, sleep-related breathing disease characterized by intermittent airway blockage during sleep, leading to disrupted breathing, fragmented sleep, and reduced oxygenation. OSA is often underdiagnosed particularly in mild cases, despite its significant negative impact on daily functioning and quality of life. This analysis aimed to evaluate the impact of OSA on daily life of people living with OSA, based on self-reported OSA severity levels.

Materials and methods: The SHINE online patient survey, developed in consultation with patient advocates and OSA experts, was administered to 1,500 OSA patients in the United States. Data were analyzed using generalized linear models with a binomial distribution and logit link function, adjusted for age group, BMI category, race, region, income level, comorbidities, and time since diagnosis. Model outcomes included: (1) whether OSA limited patients' ability to engage in regular, non-work activities (rated 3, 4 or 5 on a 5-point scale), (2) whether OSA affected work productivity (rated 3, 4 or 5 on a 5-point scale), and (3) experienced ≥ 2 negative OSA symptoms in the past 30 days.

Results: Among respondents, 13% reported mild, 54% moderate, and 30% severe OSA. Results showed that patients at all levels of severity experienced symptoms and negative impact to daily activities and work productivity. The percentage of patients who reported ≥ 2 symptoms in the past 30 days was 84%, 91% and 86% ($p = 0.003$) among mild, moderate and severe patients, respectively. Mild (48%), moderate (64%) and severe (62%) patients also reported that OSA affected their non-work activities ($p < 0.01$). Among employed patients, 39%, 51%, and 48% of mild, moderate and severe patients, respectively, reported that OSA negatively impacted work productivity ($p = 0.002$). Comorbidities, including COPD, diabetes, and insomnia, were significantly associated with increased odds of OSA affecting work and non-work activities ($p < 0.05$).

Conclusions: Patients with OSA across the severity spectrum experienced daily life challenges, with severity generally correlating with greater impact. Surprisingly, even those with mild OSA experienced significant negative impact on their daily work and non-work activities. These findings emphasize the importance of early screening, diagnosis and treatment to delay the progression to severe OSA.

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Impact of Obstructive Sleep Apnea on Nocturnal Ketone Metabolism: A Breath Acetone Analysis Study

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Introduction: In recent years, ketogenic diets have gained popularity as effective strategies for weight loss and metabolic improvement. A key aspect of these approaches lies in the body's transition into a state of ketosis—shifting from glucose to fat as the primary fuel source, thereby promoting ketone

body production. However, poor sleep quality or sleep disturbances may impair ketogenesis, potentially reducing the expected metabolic benefits.

Obstructive sleep apnea (OSA) refers to sleep-disordered breathing caused by partial or complete airway obstruction. Despite its potential impact, empirical evidence on whether OSA disrupts overnight changes in ketone levels remains limited. Therefore, this study aims to investigate whether OSA influences overnight breath acetone fluctuations by comparing pre-sleep and post-sleep ketone levels, and to develop a predictive model based on sleep-related parameters.

Materials and methods: We conducted a cross-sectional study at Shuang-Ho Hospital to investigate the impact of obstructive sleep apnea (OSA) on overnight ketone metabolism. A total of 66 adult participants underwent overnight Polysomnography (PSG) and were categorized into two groups based on their Apnea-Hypopnea Index (AHI): the non-severe OSA group (AHI < 30, n = 42) and the severe OSA group (AHI ≥ 30, n = 24). Breath acetone levels were measured before and after sleep using a portable breath ketone meter. The change in breath acetone ($\Delta\text{Acetone} = \text{post-sleep} - \text{pre-sleep}$) was used as a marker of nocturnal ketogenesis. We performed Student's t-tests and Chi-Square tests to compare demographic and PSG variables between the groups. Spearman correlation analyses were used to assess associations between $\Delta\text{Acetone}$ and OSA-related variables. Finally, a logistic regression model was constructed to identify predictors of a negative overnight acetone change ($\Delta\text{Acetone} < 0$), using $\Delta\text{Acetone} > 0$ as the reference group.

Results: Among the 66 participants, those in the severe OSA group (n = 24) exhibited significantly higher age, weight, BMI, neck circumference, and waist circumference than the non-severe group (n = 42) ($p < 0.05$). PSG results showed that severe OSA patients had significantly lower mean SaO_2 , higher AHI, ODI, Arousal Index (Arl), and greater proportions of light sleep stages (N1 and Wake) ($p < 0.05$). The overnight change in breath acetone ($\Delta\text{Acetone}$) was significantly lower in the severe group (-0.52 ± 0.60) than in the non-severe group (-0.12 ± 0.57 ; $p = 0.01$). Spearman correlation revealed that AHI and ArI were negatively correlated with $\Delta\text{Acetone}$ ($r = -0.453$ and -0.454 , respectively; $p < 0.01$). Logistic regression analysis further identified AHI as a significant predictor of negative overnight acetone change (OR = 1.058, 95% CI: 1.003–1.117, $p = 0.04$), after adjusting for ArI, weight, and neck circumference.

Conclusions: This study provides preliminary evidence that obstructive sleep apnea (OSA), particularly with higher AHI levels, may impair overnight ketone metabolism. AHI was identified as a significant predictor for a negative overnight change in breath acetone. These findings highlight the potential metabolic consequences of untreated OSA and suggest a novel physiological link between sleep-disordered breathing and impaired lipid metabolism.

Impaired Cardiovascular Autonomic Regulation in Patients with Obstructive Sleep Apnea: A Heart Rate Variability-Based Analysis

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Introduction: Obstructive sleep apnea (OSA) is characterized by repeated airway obstruction during sleep, leading to hypoxia and sympathetic activation. These physiological changes may impair autonomic regulation, increasing cardiovascular risk. Heart rate variability (HRV) is a useful marker of autonomic function, but few studies have examined how OSA severity affects HRV before and after sleep. This study aimed to investigate the impact of OSA severity on heart rate variability (HRV), a marker of autonomic function, before and after sleep.

Materials and methods: We conducted a retrospective study of 34 adult patients (mean age 55.7 ± 13.5 years; 64.7% male) who underwent overnight polysomnography (PSG) between January and December 2021. Patients with previous cardiovascular, pulmonary, neurological, psychiatric diseases, or those on medications affecting HR were excluded. HRV was assessed using time- and frequency-domain indices from electrocardiography (ECG) recorded 1 hour after sleep onset and 1 hour before awakening. Participants were classified into mild, moderate, and severe OSA groups based on apnea-hypopnea index (AHI).

Results: The mean AHI was 29.9 ± 17.2 . Severe OSA patients showed significantly higher AHI (50.6 ± 13.1) and lower minimum oxygen saturation ($73.5 \pm 13.9\%$) compared to moderate and mild groups ($p < 0.05$). While time-domain HRV indices did not differ significantly among groups, a non-significant trend toward increased morning LF power (indicative of sympathetic activation) was observed in the severe

OSA group compared to others. A higher AHI was significantly associated with parasympathetic tone (HF power) in the morning, suggesting impaired recovery of autonomic balance.

Conclusions: No previous studies have directly compared heart rate variability complexity before and after sleep to investigate whether sleep apnea itself influences HRV complexity. OSA severity correlates with autonomic dysregulation, particularly reduced parasympathetic activity and sustained sympathetic activation during sleep. These findings underscore the importance of evaluating HRV in OSA patients as a potential marker for cardiovascular risk.

Implantable respiratory state detection in stimulation target-IPG ECG lead

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Introduction: Hypoglossal Nerve Stimulation (HNS) has been developed as an effective treatment for moderate to severe Obstructive Sleep Apnea (OSA). Closed-loop stimulation is expected to significantly improve the efficacy of HNS by detecting the respiratory status of the patient, such as inspiration, expiration, hypoventilation and apnea. To realize implantable closed-loop HNS for OSA, a sensing system suitable for implantable application is required to collect physiological signals to detect the respiratory status.

Materials and methods: In this study, the standard lead ECG signals were first acquired by PSG for analysis, and the respiratory state information was obtained by parsing based on the principles of the QRS complex wave amplitude modulation effect caused by the oscillation of the electrocardiographic axis with respiration and respiratory sinus arrhythmia. Further based on the now widely used platforms of Vagus Nerve Stimulator (VNS) and Polysomnography (PSG), the ECG signals are collected and analyzed to obtain the respiratory status through its built-in implantable acquisition system. The VNS has a built-in ECG acquisition module to detect the onset of epilepsy and other patients, because the stimulation target of the VNS, the vagus nerve, is located in a similar position to the hypoglossal nerve, and its IPG is generally implanted 1-2 cm below the clavicle, which is the same as that of the IPG implantation of the HNS. The acquisition of stimulation target-IPG lead ECG signals by VNS can simulate the ECG signals acquired by HNS and detect the respiratory status based on the relationship between respiration and ECG. Similarly, in this study, the ECG signals of VNS stimulation target-IPG lead were collected by PSG in vitro and analyzed to obtain the respiratory status.

Results: By analyzing the standard-lead ECG signals acquired by PSG with the respiratory signals, the peak value of the electrocardiographic R-peak and the heart rate decreased during inspiration and increased during expiration; the rate of change of the peak value of the R-peak and the rate of change of the heart rate were significantly reduced in hypoventilation as well as in apnea, and the peak change of the R-peak and the change of the heart rate were strongly correlated with respiratory status. The peak R-peak changes in the stimulation target-IPG leads captured by VNS were also highly positively correlated and periodic with the heart rate variability, and the period was consistent with the respiratory cycle, which was the same as the characteristics of the changes in the standard PSG leads, and enabled the estimation of respiratory status.

Conclusions: The through-VNS neurostimulation target-IPG lead ECG signals enable effective detection of respiratory status, which in turn enables closed-loop HNS for OSA.

Improving Treatment Outcomes in Obstructive Sleep Apnea By Personalized Optimization of Mandibular Advancement Devices: Clinical Outcomes from a Prospective Cohort Study

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Introduction: Mandibular advancement devices (MADs) are an established treatment for obstructive sleep apnea (OSA), often titrated subjectively based on symptom relief. However, this subjective

approach may result in suboptimal outcomes and premature titration termination. This study evaluates whether objective polygraphy (PG)-guided optimization in combination with individualized clinical evaluation improves treatment efficacy.

Materials and methods: This sub-analysis of the First Line OSA Therapy (FLOSAT) study included moderate to severe OSA patients with apnea/hypopnea index (AHI) between 15 and 65/hour sleep. Other inclusion criteria were BMI <35 kg/m², obstructive AHI 15–65/h, central AHI <30% of total AHI, no prior MAD or CPAP. All patients initiated MAD therapy (ProSomnus EVO) at maximum comfortable protrusion minus 3 mm, followed by self-titration based on symptom relief. Post-titration efficacy was assessed via polysomnography (PSG). Responders were defined as AHI <10/h. Non-responders underwent additional PG-guided titration. Differences in respiratory parameters (AHI, and oxygen desaturation index (ODI)) between responders and non-responders were evaluated.

Results: Of 86 patients, 73 (85%) responded to subjective titration, while 13 (15%) required further PG-guided optimization. In the responder group, AHI and ODI improved significantly under MAD therapy: AHI from 23.9 (17.3; 31.3)/h to 6.7 (4.7; 10.2)/h and ODI from 18.7 (13.6; 26.5)/h to 8.8 (5.6; 12.5)/h. In the non-responders who needed additional titration, both respiratory parameters improved following optimization: AHI reduced from 29.8 (21.6; 40.6)/h at baseline to 15.9 (13.9; 19.6)/h after subjective titration to 12.8 (8.4; 20.9)/h after PG-guided titration, while ODI reduced from 26.3 (16.2; 32.0)/h at baseline to 15.4 (10.7; 17.8)/h after subjective titration to 9.6 (7.3; 14.2)/h after PG-guided titration. While personalized optimization enhanced outcomes overall, not all patients achieved similar therapeutic benefits. Moreover, the degree of improvement, varied depending on the respiratory index used.

Conclusions: Subjective titration alone may be insufficient for MAD therapy, at least in “non-responders”. Objective optimization improves efficacy but must be tailored to individual response variability. Standardized yet adaptable protocols may enhance outcomes. Furthermore, the degree of improvement can vary, depending on the respiratory index used. The results of this study are specific for the MAD used, and may not be generalizable to all MADs

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Increased urinary IgM excretion in patients with obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is characterized by intermittent hypoxia which results in systemic inflammation and oxidative stress. OSA is associated with albuminuria and chronic kidney disease. Elevated urinary immunoglobulin M (IgM-uria) levels are associated with a high rate of renal cardiovascular death. There is limited information regarding IgM-uria and albuminuria in patients with OSA. This study aims to assess the association between various OSA severity markers and the biomarkers IgM-uria and albuminuria

Materials and methods: This is a cross-sectional study in which 124 patients were enrolled and underwent overnight polysomnography. Patients' urine samples were collected in the morning, and urinary IgM and albumin levels were measured, along with other demographic and clinical characteristics.

Results: Multiple linear regression analysis, adjusting for age, sex, smoking status, body mass index and hypertension, revealed a significant association between IgM-uria and albuminuria and various OSA severity markers including mean SpO₂, ODI, and AHI. Among patients without diabetes, a one standard deviation (SD) decrease in mean SpO₂ was associated with a significant 0.65 SD increase in IgM-uria (p < 0.001) and a 0.5 SD increase in Albuminuria (p < 0.000). An increase in ODI by one SD was associated with an increase in IgM-uria by 0.29 SD (p = 0.014) and an increase in Albuminuria by 0.33 SD (p = 0.006). An increase in AHI by one SD was associated with an increase in IgM-uria by 0.24 SD (p = 0.034) and an increase in Albuminuria by 0.22 SD (p = 0.043). However, these associations were not found to be statistically significant among patients with diabetes.

Conclusions: Urinary IgM and albumin levels were associated with OSA severity and hypoxemia levels in non-diabetic patients, indicating that IgM-uria and Albuminuria are a potential biomarker for renal and cardiovascular complication in OSA.

Independent and dose-dependent effect of sleep apnea-specific hypoxic burden on hypertension in obstructive sleep apnea: results from Shanghai Sleep Health Study cohort

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Introduction: Obstructive sleep apnea (OSA)-specific hypoxic burden (HB) was recognized as a novel metric for quantifying OSA and its physiological consequences. This study aimed to evaluate the association between HB and incidence of hypertension among OSA in Chinese population.

Materials and methods: Suspected OSA subjects were examined in the sleep laboratory with standard polysomnography between February 2008 and January 2022. After identifying and adjusting potential confounders and covariates, the logistic regression model evaluated odds ratios (ORs) for hypertension incidence based on HB metric in three models. Furthermore, a stratified analysis was performed according to OSA severity.

Results: A total of 5108 subjects (4287 OSA and 821 simple snoring [PS] subjects) were included in the analysis. The incidence of hypertension in $32.4 < HB \leq 100.31$, $100.31 < HB \leq 251.02$, and $HB > 251.02$ was increased by 40.4%, 95.0%, and 115.6% compared to $HB \leq 32.40$, respectively (OR[95% confidence interval (CI)], 1.404[1.138,1.731], 1.950[1.586,2.397], and 2.156[1.748,2.659], all $p < 0.01$; linear trend, $p < 0.001$). In PS group, the hypertension incidence in $HB > 14.21$ was 1.201 times higher than that in $HB \leq 3.07$ (OR[95%CI], 2.201[1.111,4.358], $p < 0.05$; linear trend, $p = 0.03$). Compared to PS, the association between HB and hypertension incidence was significant in OSA, especially in moderate to severe OSA (linear trends, all $p \leq 0.001$).

Conclusions: HB in OSA is independently and dose-dependently associated with hypertension incidence. The study expounds on the advantages and clinical significance of HB in assessing hypertension incidence. HB may be a better predictor for hypertension in a hypoxia-affected population.

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Independent association between sleep apnea-specific hypoxic burden and dyslipidemia in obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is associated with and contributes to lipid metabolism. Current researches assess hypoxic indicators and lipid metabolism without AHI stratifying based on the primary criteria. Our study aims to explore the advantages and threshold of sleep apnea-specific hypoxic burden (HB) in evaluation for OSA and lipid metabolism.

Materials and methods: This is a large-scale cross-sectional study enrolled subjects examined with standard polysomnography (PSG) from Jan 2011 to Jan 2022. Demographic, clinical, and sleep characteristics were collected. Confounders were adjusted by collinearity diagnosis before assessment. Multiple linear regression analyses were used to assess the association between HB and lipid profile. Furthermore, logistic regressions were used to evaluate the odds ratio (OR) of prevalent dyslipidemia among the HB quartiles stratified by apnea-hypopnea index (AHI).

Results: A total of 4312 subjects were included within 498 primary snoring (PS) and 3814 OSA (696 in mild, 747 in moderate, and 2371 in severe). The dyslipidemia prevalence was evidently increased with HB quartile both in the whole cohort and OSA group (p -value for trends, both $p < 0.001$). After stratified by AHI, compared with PS group, the dyslipidemia prevalence across the HB quartile in severe OSA

was increased from 58.0% to 98.6% (OR[95% confidence interval (CI)], 1.580[1.205,2.072], 1.664[1.263,2.193], 1.712[1.287,2.276], and 1.986[1.481,2.663], all $p < 0.01$; linear trend, $p < 0.001$). The hyper-low-density-lipoprotein cholesterolemia remained significance across the HB quartile in moderate OSA (linear trend, $p = 0.001$). Furthermore, positive increasing linear trends were presented among triglyceride (TG) level in severe OSA ($p < 0.001$), among total cholesterol (TC) level in moderate to severe OSA (both $p < 0.001$), and among low-density-lipoprotein cholesterol (LDL-C) level when AHI $\geq 5/h$ ($p = 0.021$ in mild OSA, $p < 0.001$ in moderate and severe OSA).

Conclusions: In this cross-sectional study, higher HB was associated with male, older, heavier individuals with worse PSG indexes and greater dyslipidemia prevalence, which appeared more sensitive in severe OSA. Furthermore, the HB performed as an independent factor for early warning of LDL-C level when OSA was diagnosed.

Inflammatory Biomarkers and Symptom Severity: The Role of Cytokines in Paediatric OSA

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Introduction: Obstructive sleep apnoea (OSA) affects 1-5% of primary school-aged children. While polysomnography (PSG) is the gold standard for OSA diagnosis, it has limitations in capturing the full spectrum of OSA symptoms. Therefore, parent-reported symptoms are also valuable. Snoring, the main symptom of OSA, is closely related to upper airway inflammation putatively driven by soft tissue vibrations within the upper airway. This study investigated the relationship between OSA symptoms and nasal inflammatory profiles.

Materials and methods: Children aged 5 to 11 years were recruited for clinical evaluation and underwent overnight PSG. OSA was diagnosed with an obstructive apnoea-hypopnoea index (OAHI) ≥ 1 . The Paediatric Sleep Questionnaire (PSQ) was used to measure OSA symptoms. Nasal epithelial lining fluid (NELF), sampled by three-day nasal strip tests in both morning and evening, was collected for each participant. Cytokine concentrations in NELF were measured by Cytometric Bead Array (CBA). The cytokine concentrations were averaged for each participant and natural log-transformed before being taken into a Generalised Linear Model (GLM). Potential confounders, including sex, age, body mass index (BMI) z-score, and the presence of allergic rhinitis, were adjusted for in the GLMs.

Results: Eighty children (31.2% girls) with a mean age of 8.76 years (SD = 1.65) were studied. Among them, 41 (51.3%) children had OSA. Seventeen (21.3%) children were overweight or obese with a BMI z-score larger than 1.036, and 58 (72.5%) children had allergic rhinitis. In adjusted GLMs, a higher PSQ score was significantly associated with a higher level of TNF- α [$\beta = 3.20$, 95% CI: (1.03, 5.37), $p = .004$]. It was also associated with a higher IL-10 despite not reaching statistical significance [$\beta = 3.02$, 95% CI: (-0.16, 6.21), $p = .067$]. Within the subgroup of children with OSA, both TNF- α [$\beta = 4.74$, 95% CI: (1.31, 8.16), $p = .01$] and IL-10 [$\beta = 5.12$, 95% CI: (1.51, 8.73), $p = .0086$] were significantly associated with the PSQ score, showing greater coefficients compared to the overall sample after being adjusted for confounders.

Conclusions: This study reveals a significant association between PSQ scores and nasal cytokine levels, highlighting the role of upper airway inflammation in the symptomatology of paediatric OSA. This potentially indicates a bi-directional interplay between OSA symptoms and upper airway inflammation. Combining PSG results, parent-reported symptoms and nasal inflammatory biomarkers may allow the identification of children with OSA in need of early attention.

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Influence of Respiratory Event Characteristics on Event-Specific Hypoxic Burden

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Introduction: Obstructive sleep apnea (OSA) is a medical condition, characterized by repeated pauses and reductions in airflow during sleep. The prevalence of OSA is rising notably in high-income nations, a trend that is closely associated with increasing rates of obesity. Diagnosis and severity grading of OSA are predominantly based on the apnea-hypopnea index (AHI), which quantifies the frequency of apneic and hypopneic events per hour of sleep. Despite its widespread use, the AHI is limited in that it fails to capture the temporal characteristics and physiological impact of respiratory disturbances, such as the duration, depth, and corresponding oxygen desaturation burden. Recent studies have demonstrated that the OSA-specific hypoxic burden (HB)—which integrates the frequency, depth, and duration of desaturation events—shows strong associations with multiple adverse clinical outcomes. Calculating the HB for each respiratory event may serve as a tool for quantitatively analyzing the physiological characteristics and pathophysiological impact of apneas and hypopneas. Therefore, this study was designed to investigate how event-specific HB varies with the type and duration of respiratory events.

Materials and methods: Twenty-eight adult male subjects with complaints of snoring and suspected sleep apnea underwent polysomnography (PSG). PSG data were manually scored by a certified sleep technician in accordance with the 2012 American Academy of Sleep Medicine (AASM) scoring criteria. The pre-event baseline SpO₂ was defined as the maximum SpO₂ recorded within the 100 seconds preceding the termination of the event. The area between the baseline and the oxygen desaturation curve corresponding to each respiratory event is defined as event-specific HB. Violin plot, linear regression analysis, one-way ANOVA and subsequent pairwise comparisons were used for statistical analysis.

Results: A statistically significant difference in HB was observed between the two groups ($p < 0.001$), with apnea events demonstrating a higher HB compared to hypopnea events. A strong positive correlation was observed between HB and apnea duration ($R = 0.75$), indicating that longer apnea events are associated with greater HB. In contrast, the correlation between HB and hypopnea duration was minimal, suggesting that variations in hypopnea duration have limited influence on HB. An overall trend of increasing HB with longer event duration is observed, particularly in apnea events. Apneas accompanied by arousal (A-AR) exhibited a significantly higher HB compared to those without arousal ($p < 0.001$). In contrast, no significant difference in HB was observed between hypopnea events with and without arousal ($p > 0.05$).

Conclusions: Event-specific HB was higher in apneas than in hypopneas. In particular, within apneas, longer event duration and the presence of arousal were associated with a significantly greater HB.

Infrared Optical Gas Imaging for Sleep Apnea Diagnosis

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Introduction: Polysomnography (PSG) is the standard method for diagnosing obstructive sleep apnea (OSA), but its use of multiple contact sensors can disrupt sleep and reduce test accuracy. Recent non-contact methods, such as audio and radar-based devices, offer convenience but cannot directly measure respiratory airflow. Infrared optical gas imaging, which visualizes exhaled carbon dioxide, may overcome these limitations by enabling direct, contactless monitoring of respiration during sleep. This study aimed to evaluate its feasibility as an alternative tool for OSA diagnosis.

Materials and methods:

We recruited 50 participants from Ajou University Hospital between June and August 2018. All participants underwent overnight polysomnography (PSG) and were simultaneously recorded using infrared optical gas imaging (FLIR GF343) to visualize exhaled CO₂. Standard sensors (oronasal thermistor and nasal cannula) were used during the first half of sleep and removed during the second half. Respiratory events were also measured using chest and abdominal belts. Infrared-derived airflow signals were extracted using a face-tracking and temperature-differential algorithm, allowing calculation of respiratory parameters such as AHI, RDI, and apnea/hypopnea indices. Data were scored based on AASM 2012 criteria.

Results: Respiratory parameters derived from infrared optical gas imaging showed strong positive correlations with those from standard PSG, both in the presence and absence of nasal cannula. Apnea-hypopnea index (AHI) values were particularly well-aligned ($p > 0.85$ with sensors, $p > 0.72$ without). Receiver operating characteristic (ROC) analysis confirmed the diagnostic validity of infrared imaging, with area under the curve (AUC) values exceeding 0.8. Although infrared imaging tended to slightly overestimate AHI, it reliably detected sleep-related respiratory events, even without contact-based sensors.

Conclusions: Infrared optical gas imaging accurately detected respiratory events during sleep; therefore, it may be employed as a screening tool for OSA.

"INNOVATING SLEEP APNEA SCREENING: TELE-OSA QUESTIONNAIRE- A NOVEL TELEPHONIC SCREENING TOOL FOR MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA"

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Introduction:

- Prevalence of obstructive sleep apnea (OSA) varies between 6-17% in general adult population. Untreated severe OSA has 2-3-fold increased risk of all-cause mortality. Despite high prevalence, OSA often remains undiagnosed.
- Access to polysomnography (PSG), gold standard for diagnosis, can be limited in LMICs like India due to several factors like availability of sleep centers, geographical distribution (often concentrated in urban areas), cost of services, referral processes, awareness and workforce shortages.
- Consequently, sleep clinics often experience overwhelming patient loads and prolonged waiting times, underscoring urgent need to streamline screening and triage pathways.
- Drawbacks of existing screening questionnaires are usage of objective parameters (anthropometric measurements) and reliance on age, gender, and BMI which can introduce biases.

Materials and methods:

- This was a retrospective, single centre, observational study. 522 patients who underwent level 1 PSG during 2022-2024 in our sleep laboratory were included. All patients filled a self-administered 12-item questionnaire tool in vernacular language (Hindi) during time of admission.
- Eligibility
 - Inclusion:- Adult patients aged >18 years and have completely filled 12-item questionnaire during time of admission.
 - Exclusion :- Patients who have not filled the questionnaire, already on treatment for OSA, pregnant women and those with technically inadequate polysomnography studies.
- Statistical analysis was done in IBM-SPSS-version-26.0 statistical software. Exploratory factory analysis was done and 7 questions were selected. Sample was randomly divided into two parts:

development (80%, n=421) and testing subsample (20%, n=101). Multi-variate logistic regression analysis was done on development subsample to construct the model. Finally, we assessed the discriminative performance of this score in both development and test subsamples and determined cross-validation and diagnostic accuracy.

Results:

- TELE-OSA questionnaire includes five items (snoring, stops breathing while sleeping, wake up from sleep due to gasping/choking, nocturia and nocturnal GER).
- Cutoff score of 6 was identified, demonstrating high specificity (83%) and moderate sensitivity (55%).
- TELE-OSA had high specificity compared with existing screening questionnaires [STOP-BANG (59%), STOP (66%), GOAL (45%), NOSAS (78%) No-apnea (53%)] and highest diagnostic accuracy [AUC: TELE-OSA-0.77, STOP-BANG-0.76, STOP-0.71, GOAL-0.77, NOSAS-0.77, No-apnea-0.68].

Conclusions:

- This study introduces the Tele-OSA Questionnaire, a novel telephonic screening tool designed to facilitate the identification of individuals at risk for moderate to severe OSA.
- It includes only the construct of the disease (OSA) and does not include risk factors associated with the disease.
- It can be used via telephonic interview or surveys, even by proxy informants viz., bedpartners.
- The developed questionnaire has acceptable psychometric properties at the cutoff score of 6. Further, properties across different cut-offs and prevalence are also provided so that users may choose a specific cut-off according to the population in which they intend to use the questionnaire.
- Existing screening questionnaires have high sensitivity but less specific which increases the burden on sleep labs. Tele-OSA is a highly specific questionnaire and can reduce the burden on sleep centres, making diagnostic processes more accessible in resource-constrained settings.

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Insomnia as a Symptom of REM-related OSA: A Retrospective Cross-Sectional Study in 1736 OSA Patients

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Introduction: REM-related obstructive sleep apnea (REM-OSA) is a *polysomnographic phenotype* of OSA characterized by respiratory events predominantly occurring during REM sleep, affecting approximately 12–36% of all OSA patients.

Several studies have suggested that REM-OSA may be more prevalent in females, particularly in those presenting with depressive symptoms.

In our previous study of 3,234 OSA patients, we found that the main symptom of REM-OSA was not excessive daytime sleepiness.

Given the well-established bidirectional relationship between insomnia and depression, this raises important clinical questions.

Insomnia is frequently observed in patients with OSA, yet the specific relationship between REM-OSA and insomnia remains unclear.

We hypothesized that insomnia, rather than excessive daytime sleepiness, may be a primary complaint among patients with REM-OSA.

To test this hypothesis, we examined whether REM-OSA is independently associated with insomnia-related sleep disturbance as measured by the Pittsburgh Sleep Quality Index (PSQI).

Materials and methods:

We retrospectively analyzed 1736 adults with OSA ($AHI \geq 5$) who underwent overnight polysomnography and completed the PSQI at a sleep center in Japan. REM-OSA was defined using three stringent criteria:

- **REM-OSA 1:** overall $AHI \geq 5$ and AHI during REM ($AHI-REM$) / AHI during NREM ($AHI-NREM$) ≥ 2
- **REM-OSA 2:** overall $AHI \geq 5$, $AHI-REM/AHI-NREM \geq 2$, and $AHI-NREM < 15$
- **REM-OSA 3:** overall $AHI \geq 5$, $AHI-REM/AHI-NREM \geq 2$, $AHI-NREM < 8$, and REM sleep duration > 10.5 minutes

Patients who did not meet REM-OSA 1 criteria were categorized as having NREM-OSA. Multiple linear regression models were used to evaluate the association between REM-OSA and PSQI, adjusting for age, sex, BMI, and REM/NREM-AHI. Subgroup analyses were performed by sex.

Results: REM-OSA accounted for 24.4%, 16.8%, and 8.9% of patients according to definitions 1, 2, and 3, respectively. Across all definitions, patients with REM-OSA had significantly higher PSQI scores compared to those with NREM-OSA ($p < 0.001$). In multivariate analyses, REM-OSA was independently associated with higher PSQI scores, with the strongest effect observed for REM-OSA 3 ($\beta = 1.26$, 95% CI 0.54–1.98, $p = 0.001$). Subgroup analyses showed that this association was more evident in female patients, who consistently had higher PSQI scores than males.

Conclusions: REM-OSA is significantly associated with insomnia-related sleep disturbance, especially among female patients and when defined as REM-OSA 3. These findings suggest that insomnia, rather than excessive daytime sleepiness, may be a predominant complaint in REM-OSA. Clinicians should consider incorporating insomnia assessments such as the PSQI into the routine diagnostic evaluation and phenotyping of OSA patients, particularly those with REM-predominant respiratory events.

Integrative Prognostic Framework Linking Sleep-Disordered Breathing-Associated Genes to Tumor Hypoxia and Immune Evasion Across Cancers

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Introduction: Sleep-Disordered Breathing (SDB), characterized by intermittent hypoxia and sleep fragmentation, is increasingly recognized as a systemic physiological stressor influencing tumor progression and immune modulation. However, its molecular footprint across cancer types remains underexplored.

Materials and methods: We curated 164 genes associated with SDB from literature and sleep-related databases. Using transcriptomic data from 32 cancer types in The Cancer Genome Atlas (TCGA), we developed an SDB-related prognostic model via LASSO-Cox regression. This model generated a risk score used to stratify patients into high- and low-risk groups. Kaplan-Meier survival analyses, multivariate Cox regression, and time-dependent ROC curves evaluated model performance. Functional enrichment and immune deconvolution were performed to explore underlying biology.

Results: The SDB gene signature significantly predicted overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) across multiple cancer types. High-risk groups were enriched in hypoxia, epithelial–mesenchymal transition, IL-17 signaling, and angiogenesis pathways. The SDB score correlated positively with immune checkpoint expression, stromal activity, and proliferative indices. Integration into a nomogram with clinical variables enhanced survival prediction accuracy (C-index > 0.70). External validation in independent datasets confirmed model robustness, especially in hypoxia-sensitive tumors such as lung adenocarcinoma, glioblastoma, and clear cell renal carcinoma.

Conclusions: This study is the first to establish a pan-cancer SDB-associated transcriptomic signature. Our findings suggest that SDB-induced molecular alterations may contribute to tumor aggressiveness

and immune evasion. This integrative framework bridges sleep medicine and oncology, supporting future investigations into SDB management as an adjunct cancer therapy strategy.

Inter-Gender Differences in Obstructive Sleep Apnoea Severity Across Age Groups

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Introduction: Attended overnight polysomnography (PSG) is generally considered the diagnostic gold standard for sleep disorders. However, long waiting times have adversely affected patients' access to diagnostic and therapeutic tests. With the increasing demand for obstructive sleep apnea (OSA) diagnosis, level 3 tests have been used to expedite the diagnosis of patients with a high likelihood of OSA.

Materials and methods: Between 30 October 2023 and 31 March 2025, 2192 patients underwent level 3 sleep tests. 1093 patients were tested with NOX T3S device while 1099 patients were tested with Embletta MPR device. For those tested with NOX T3S, sleep stages were estimated using a combination of respiratory data and actigraphy. The Chi-square test was performed to assess the relationship between age groups, gender, and OSA severity. Apart from mild (Apnoea Hypopnoea Index AHI 5 to <15), moderate (AHI 15-30), and severe (AHI >30) OSA, patients with low total AHI (<5) but position- or REM-AHI > 5 and snoring > 10 % of sleep time were classified as borderline.

Results: Among the 1,489 males and 703 females in this review, mean age was 53±9.55 years (range 18 to 78 years). Patients were further divided into four age groups (AG 18-30, AG 31-45, AG 46-60, and AG 61-78). Both age group and gender showed statistically significant relationships with OSA severity in the AG 31-45 ($p \leq 0.05$) and AG 46-60 ($p \leq 0.05$) groups. [Chart 1: OSA Severity by Age Group and Sex](#)

A higher percentage of severe OSA was found in males compared to females, particularly in the AG 31-45 and AG 46-60 groups. There were statistically significant differences in AHI and Oxygen Desaturation Index (ODI) between males and females, with males having more severe disease. In the subgroup with sleep efficiency results ($n=1093$), sleep efficiency was similar between the two genders (male 82.6% versus female 83.89%). [Chart 2: Gender Analysis of Sleep Metrics](#)

As total AHI increased from normal to high, there was a corresponding increase in REM AHI, supine AHI and Snoring %. Patients with severe OSA exhibited significantly higher REM AHI (55.88) and supine AHI (61.02) compared to other severity levels. Snoring % was also highest in this group (39.92%). As expected, individuals with normal OSA had the lowest REM AHI (3.18), supine AHI (2.24), and Snoring % (8.15). However, in the borderline group, the snoring percentage, REM AHI, and supine AHI values were all significantly higher than those in the normal group ($p \leq 0.05$). [Table 3: Severity of OSA](#)

Conclusions: Severe OSA was more often present in males than females, particularly in the age range of 31 to 60 years old. In this population of symptomatic patients who underwent level III testing, the diagnosis of a group with snoring percentage, REM AHI and supine AHI that were higher than the normal group remained undefined. Further testing with PSG and longitudinal follow-up of this borderline group would help to elucidate the nature and course of disease.

Intermittent Hypoxia Accelerates Full-Thickness Cutaneous Wound Healing in Sprague-Dawley Rats: The Role of Upregulated TGF- β and YAP Expression

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Introduction: Re-epithelialization is a critical step in the complex processes of cutaneous wound healing. Tissue oxygenation is a key microenvironmental determinant for wound healing involving re-epithelialization. This study investigated the effects of intermittent hypoxia (IH) on full-thickness skin wound healing in Sprague Dawley rats, focusing on transforming growth factor-beta signaling and Yes-associated protein expression dynamics.

Materials and methods: Eight male rats were equally randomized to receive either daily 8-hour cyclic hypoxia (10-21% oxygen) or normoxic conditions until complete re-epithelialization. Consistent round full-thickness skin wounds with a diameter of 1cm were made on the dorsum of both groups of rats. From the second day after wound surgery. The re-epithelialization processes were monitored, and blood and healed tissue samples were obtained until the wounds closed completely.

Results: Intermittent hypoxia reduced healing time by 21% compared to controls (20.0 ± 1.8 vs 24.3 ± 2.5 days, $P < 0.05$), with elevated serum transforming growth factor-beta levels (184.9 ± 10.9 vs 120.6 ± 8.7 , $P < 0.05$) but unchanged vascular endothelial growth factor and epidermal growth factor concentrations. Sustained upregulation of Yes-associated protein isoforms 1 and 2 ($P < 0.05$ for both) persisted throughout healing in hypoxic-exposed regenerating epithelium, correlating temporally with accelerated wound closure. The histological findings of the healed epithelium in NC group rats were closer to normal than in IH group rats.

Conclusions: These findings reveal that controlled hypoxic stimulation enhances cutaneous re-epithelialization through coordinated activation of TGF- β signaling pathways and concomitantly enhancing the expression of YAP protein. This finding suggests novel therapeutic targets in re-epithelialization remodeling and tissue regeneration in the wound healing progress.

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International expert consensus statement: surgical failure in obstructive sleep apnea

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Introduction: Upper airway (UA) surgery is commonly employed in the treatment of patients with obstructive sleep apnea (OSA). The intricate pathophysiology of OSA, variability in sites and patterns of UA collapse, and the interaction between anatomical and non-anatomical factors in individual patients may contribute to possible surgical failures. This clinical consensus statement aims to identify areas of agreement among a development group comprising international experts in OSA surgery, regarding the appropriate definition, predictive factors in patients, and management of surgical failure in OSA treatment.

Materials and methods: A clinical consensus statement (CCS) was developed using the Delphi method by a panel of 35 contributors from various countries. A systematic literature review adhering to PRISMA guidelines was conducted. A survey consisting of 60 statements was then formulated and presented to the experts.

Results: Following two rounds of the Delphi process, consensus or strong consensus was achieved on 36 items, while 24 items remained without consensus. Specifically, 5 out of 10 statements reached consensus regarding on the 'Definition of Surgical Success/Failure after OSA Surgery'. Regarding the 'Predictive Factors of Surgical Failure in OSA Surgery', consensus was reached on 10 out of 13 statements. In the context of the 'Diagnostic Workup in OSA Surgery', consensus was achieved on 9 out of 13 statements. Lastly, in 'Treatment in Surgical Failure Cases', consensus was reached on 12 out of 24 statements.

Conclusions: The management of OSA after surgical failure presents a significant clinical challenge for sleep specialists. This CCS provides valuable guidance for defining, preventing, and addressing surgical failures in the treatment of OSA syndrome.

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Interceptive Dysfunction During Wakefulness in Obstructive Sleep Apnea: An Analysis of Heartbeat-Evoked Potentials

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent sleep disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent hypoxia, fragmented sleep, and excessive daytime sleepiness. While much research has focused on the nocturnal consequences of OSA, its effects during wakefulness remain underexplored. Emerging evidence suggests that OSA may disrupt interoceptive processing—the brain’s ability to perceive and integrate internal bodily signals such as heartbeats. Interoception plays a crucial role in self-awareness, emotional regulation, and decision-making. Impairments in this domain have been linked to mood disorders, cognitive decline, and reduced quality of life. However, how OSA affects cortical responses to cardiac activity during wakefulness remains poorly understood. Heartbeat-Evoked Potentials (HEP), derived from EEG recordings time-locked to R-peaks in the ECG signal, offer a non-invasive method to assess cortical sensitivity to cardiac activity and serve as a reliable biomarker of interoceptive processing. Prior studies have shown altered HEP amplitudes in populations with impaired interoception, such as those with depression and anxiety disorders. However, no study has yet systematically investigated HEP modulation in individuals with OSA during wakefulness.

Materials and methods: Data from 366 participants were analyzed using 5-minute EEG and ECG recordings from a pre-sleep wakeful period. EEG was recorded from six channels and ECG via Lead I and II. Signals were filtered, re-referenced, and eye-blink artifacts removed. Time-locked EEG epochs around R-peaks were averaged to compute HEP waveforms. Analysis focused on the 300–700 ms post-R-peak window to minimize cardiac field artifact contamination. Group comparisons between Normal and Apnea groups were performed using non-parametric cluster-based permutation tests, revealing significant differences in central and frontal regions. Mean HEP amplitudes were compared using t-tests, with effect sizes (Cohen’s d) and confidence intervals reported.

Results: Cluster-based permutation analysis revealed significant differences in HEP amplitudes between Normal and Apnea groups during wakefulness, particularly in central (320–480 ms) and frontal (540–680 ms) electrode regions. The Jonckheere-Terpstra test confirmed monotonic trends across OSA severity levels. Cohen’s d showed moderate-to-small effect sizes, especially at C3. Confidence intervals reflected distinct amplitude shifts with increasing severity. No differences were found in occipital electrodes, suggesting that OSA-related changes are localized to brain areas involved in interoceptive processing.

Conclusions: Our findings show that individuals with OSA exhibit altered cortical processing of cardiac signals during wakefulness, reflected in changes in HEP amplitudes. These changes correlate with apnea severity and suggest impaired interoceptive processing—an essential mechanism for emotional regulation, self-awareness, and autonomic balance. Clinically, this indicates that OSA is not just a sleep-related breathing disorder but also involves neuro-cardiac dysfunction during wakefulness, potentially contributing to daytime symptoms such as fatigue, mood disturbances, and cognitive deficits. HEP emerges as a promising non-invasive biomarker for the early detection of neurophysiological impairments in OSA, even before sleep onset. Its integration into routine EEG-based assessments could enhance diagnostic precision and monitoring of OSA-related brain-body interactions. In summary, this study identifies OSA as a systemic condition affecting brain-heart communication beyond sleep, offering new insights for more integrated and effective patient management.

Interpretable Machine Learning Using Questionnaire Data: A Scalable Approach for Sleep Apnea Screening

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Introduction: Early detection of sleep apnea is critical to preventing long-term cardiovascular and metabolic complications. However, traditional screening methods often rely on costly bio-signal measurements or symptom-dependent questionnaires that may miss at-risk individuals. This study presents a clinically applicable machine learning framework that leverages easily obtainable questionnaire data to support large-scale, low-cost early screening of sleep apnea while providing clear, interpretable insights for clinical decision-making.

Materials and methods: We developed an XGBoost model to classify individuals into normal/mild and moderate/severe sleep apnea groups using only demographic and lifestyle-related variables. Data were drawn from the Sleep Heart Health Study (SHHS), with relevant features selected from 12 questionnaires, during the first (SHHS1) and second (SHHS2) visits. These features cover physiological, behavioral, medical history, and treatments information. For interpretability, we applied SHapley Additive exPlanations (SHAP) and TreeExplainer2Rule (Te2Rule) to generate rule-based explanations aligned with clinical reasoning. These methods enable clear visualization of the model's decision-making process, making the results easier to interpret and more convincing. They also offer valuable insights into which features most influence the predictions.

Results: The model achieved an AUC of 0.793, with 64.88% accuracy, 60.84% precision, 55.59% sensitivity, 72.11% specificity, and F1-score of 0.581 in identifying moderate to severe cases using questionnaire data from the first visit. When combined with follow-up visit data—reflecting physiological and behavioral changes over a 5-year period—the additional information improved model performance. Specifically, the model achieved an AUC of 0.753, with 68.45% accuracy, 65.90% precision, 63.13% sensitivity, 72.88% specificity and F1-score of 0.645. Key clinical predictors included neck circumference (with a common decision threshold of 35-38 cm), age, waist circumference, and BMI (common decision threshold of 25.5). Male sex and a history of hypertension were linked to increased risk, while coffee consumption showed a surprising negative association with sleep apnea severity. Most of these insights align with known clinical risk factors and offer practical decision rules that can be easily applied in clinical settings. Additionally, SHAP values have an additive property, allowing for transparent breakdowns of how predictions are calculated for each patient—providing useful insights that may support personalized behavioral interventions.

Conclusions: Despite the inherent limitations of self-reported data, our model achieved significant improvement in AUC and specificity compared to existing sleep apnea screening questionnaires (e.g., STOP-BANG). The enhanced model's performance—particularly the improved class balance when incorporating both first-visit and follow-up information—highlights the value of long-term monitoring and data collection. This study demonstrates the potential of explainable AI to support cost-effective, scalable, and interpretable sleep apnea screening. The SHAP method explains the impact of each feature on the model's output, while Te2Rule illustrates how the model combines high-impact features to arrive at a final decision.

Investigation of nasal obstruction as a risk factor for SDB: prevalence of SDB in patients who underwent endoscopic nasal sinus surgery

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Introduction: To investigate the prevalence of sleep-disordered breathing (SDB) in patients with nasal diseases who underwent endoscopic nasal sinus surgery (ESS) compared with control patients without nasal disease who underwent tonsillectomy.

Materials and methods: An observational retrospective case-control study was conducted of 150 adults with nasal diseases who underwent ESS (ESS group) as well as 94 adults with no nasal symptoms or diseases who underwent tonsillectomy due to infection of the tonsils (tonsillectomy group). Patients with obstructive sleep apnea, patients with a chief complaint of snoring or excessive daytime sleepiness, or patients having large tonsils were excluded from the study. Home sleep apnea testing was performed prior to admission for surgery.

Results: The prevalence in normal, mild, moderate, and severe SDB was respectively 30.0%, 38.0%, 22.7%, and 9.3% in the ESS group and 50.0%, 39.4%, 10.6%, and 0% in the tonsillectomy group. There were significant differences in the mean 3% oxygen desaturation index (3%ODI) score between the ESS and tonsillectomy groups in men but not in women. Obese men in the ESS group were much more susceptible to having moderate or severe SDB when they were aged ≥ 40 years. Regression analysis revealed that the preoperative 3%ODI score had two significant determinants in the ESS group—BMI and male sex—whereas age, nasal resistance, and CRS with nasal polyps were not significant predictors.

Conclusions: Among patients who underwent ESS, 32.0% had moderate to severe SDB, including 9.3% with severe SDB. Nasal obstruction could be a potential risk factor for SDB in male patients.

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Ischemic Preconditioning as a Potential Cardioprotective Mechanism of Obstructive Sleep Apnea in Patients with Acute Coronary Syndrome

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Introduction: Obstructive sleep apnea (OSA) is associated with intermittent hypoxemia, which may induce myocardial ischemic preconditioning - a mechanism potentially attenuating ischemic injury. This effect could influence the clinical presentation of acute coronary syndromes by favoring non-ST-elevation myocardial infarction (NSTEMI) over ST-elevation myocardial infarction (STEMI). We prospectively examined the relationship between OSA severity and the type of myocardial infarction (MI).

Materials and methods: We prospectively enrolled 607 consecutive patients hospitalized with a diagnosis of acute myocardial infarction (NSTEMI or STEMI). The study was conducted at two tertiary care centers where primary percutaneous coronary intervention (PCI) is the standard treatment for acute MI. Sleep evaluations were performed using a portable diagnostic device in all patients who remained clinically stable for at least 48 hours following admission.

Results: OSA was present in 65.7% of patients; NSTEMI was diagnosed in 30%. NSTEMI prevalence increased with OSA severity ($p < 0.001$). In patients without or with mild OSA, the NSTEMI-to-STEMI ratio was 59.4% vs. 70.1% ($p = 0.01$); in those with moderate to severe OSA (apnea-hypopnea index ≥ 15 events/hour), this ratio reversed to 40.6% vs. 29.9% ($p = 0.01$). Moderate to severe OSA independently predicted NSTEMI ($p = 0.021$). Patients with NSTEMI and moderate to severe OSA had significantly lower peak troponin T levels than those with STEMI ($1.538 \pm 2.771 \mu\text{g/L}$ vs. $3.085 \pm 3.127 \mu\text{g/L}$; $p < 0.001$).

Conclusions: Greater OSA severity is associated with higher NSTEMI prevalence and less myocardial injury, supporting a potential cardioprotective role via ischemic preconditioning. This mechanism may partly explain reduced cardiovascular mortality in some OSA populations and the limited efficacy of CPAP in secondary prevention. Personalized CPAP strategies considering ischemic preconditioning may improve patient outcomes.

Is CPAP enough? Real-life burden of residual events in treated OSA patients

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Introduction: Continuous positive airway pressure (CPAP) is the first-line treatment for patients with moderate to severe Obstructive sleep Apnea (OSA) and is highly effective when used consistently. However, optimal adherence to CPAP therapy remains a major challenge, often limited by discomfort and adverse effects. As a result, patients on CPAP may still experience residual obstructive events, particularly during periods of non-use, a phenomenon we here refer to as "hidden Apnea Hypopnea Index" (hAHI). Our objective was to estimate the residual burden, based on hAHI, during a relative long period of time in a cohort of patients on CPAP treatment.

Materials and methods: This analysis is based on the *MetaSleep* project (NCT05986487), a prospective, observational, multicenter study conducted across 10 regions in Spain. The *MetaSleep* study included adult patients with hypertension and OSA who had been prescribed CPAP therapy based on routine clinical criteria. The hAHI was evaluated by the *Withings Sleep Analyzer*, an FDA-cleared, under-the-mattress contactless device. Simultaneously, objective daily CPAP usage data were collected to assess adherence.

Results: A total of 116 patients were recruited, leading to 5909 monitored nights. The median (Q1; Q3) monitoring duration was 14 (5; 20.25) days before and 46 (14; 76) days after CPAP initiation. The median age of participants was 58.0 (51.0; 64.0) years, 30.2% were female. Patients had a median CPAP adherence of 5.4 (3.9; 6.7) hours per night. According to home monitoring data, patients exhibited a mean (SD) pre-CPAP AHI of 39.6 (26.6) events/hour. Following the initiation of CPAP therapy, a significant reduction in hAHI was observed, with a mean change (95% CI) of -13.25 (-18.4 to 8.01) events/hour. Despite this improvement, patients still showed a substantial OSA burden while on CPAP, with a mean (95% CI) hAHI of 22.36 (18.27 to 25.45) events/hour. Additionally, 51.1% of patients experienced more than half of their nights with an hAHI ≥ 15 events/hour. A significant inverse and non-linear association between hAHI and the number of hours of CPAP use was observed.

Conclusions: Despite a good CPAP compliance, patients treated with CPAP continue to experience a considerable burden of residual obstructive events. The hAHI remains elevated in a substantial proportion of patients. These findings highlight the importance of personalized monitoring to better understand the true effectiveness of CPAP therapy and to identify patients with insufficient control of obstructive events.

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Jaw Corrective Surgery in patients with jaw deformities having Obstructive Sleep Apnea

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Introduction: The study aims to assess the prevalence of obstructive sleep apnea (OSA) among patients with jaw deformities and to study the outcome of jaw corrective surgery on these patients.

Materials and methods: This prospective study was conducted among patients previously not diagnosed with OSA who were scheduled for jaw corrective surgery between 2021 and 2022. Home Sleep Apnea testing (HSAT) was used in addition to the Epworth Sleepiness Scale (ESS) and STOP-BANG questionnaire. Consented patients did HSAT preoperatively and postoperatively. Experienced surgeons performed jaw corrective surgery at Oman's foremost oral and maxillofacial surgery center.

Results: A total of 64 patients (24 males and 40 females; mean age of 28.23 years) were included in the study. The study indicated that 43.75% of patients with jaw deformities have OSA. The effect of jaw corrective surgery on the severity of OSA was also evaluated in 39 patients only. There was an improvement in the clinical OSA symptoms postoperatively (p-value < 0.05). However, no significant difference was observed in the Apnea-Hypopnea Index (AHI) (p-value > 0.05).

Conclusions: Silent OSA is common among patients with jaw deformity. However, jaw corrective surgery does not significantly improve it and does not improve substantially mild sleep apnea.

Lactylation-Related Gene Signatures Define Molecular Subtypes and Therapeutic Targets in Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a widespread sleep disorder driven by chronic intermittent hypoxia (CIH), contributing to serious complications such as cardiovascular and metabolic diseases. Recent studies suggest that epigenetic modifications, particularly lactylation, play a pivotal role in OSA pathogenesis by interacting with CIH. Despite this, the specific contributions of lactylation-related genes to OSA remain largely unexplored. Our study aims to elucidate the expression patterns and functional significance of lactylation-related genes in OSA, with a focus on identifying molecular subtypes and their associated immune signatures. Through advanced computational analyses, we aim to reveal novel epigenetic insights that could drive the development of precision therapies for OSA.

Materials and methods: A total of 332 lactylation-related genes were obtained from the Molecular Signatures Database. Adipose tissue expression data were sourced from GEO datasets GSE135917 (8 controls, 34 OSA cases) and GSE38792 (8 controls, 10 OSA cases) on the GPL6244 platform. Differential genes (adjusted $P < 0.01$) were identified using limma in R. Functional enrichment and co-expression analyses were performed via clusterProfiler and GeneMANIA. Key genes were selected by LASSO and SVM-RFE, ranked by SHAP, and validated in GSE38792. A nomogram was evaluated by decision curve analysis. Subtypes were identified by consensus clustering using PCA-derived lactylation scores. Immune infiltration was analyzed via ssGSEA, with regulatory networks constructed in NetworkAnalyst. Validation included ELISA and qPCR in OSA patient and CIH mouse models.

Results: In the GSE135917 dataset, 79 lactylation-related genes were differentially expressed in OSA patients. Consensus clustering defined two subtypes. Group B showed higher lactylation scores and increased immune infiltration. LASSO and SVM-RFE identified four key genes, with TMSB4X upregulated and PRAM1 downregulated in OSA. Their expression patterns were validated in GSE38792 and CIH mouse adipose tissue via qPCR. SHAP confirmed their discriminative value. A nomogram incorporating TMSB4X and PRAM1 showed strong clinical utility. ELISA revealed elevated lactate in OSA patients and CIH mice. Serum IL-6 and TNF- α levels correlated positively with TMSB4X and negatively with PRAM1, supporting links between lactylation and immune dysregulation.

Conclusions: This study identifies distinct molecular subtypes of OSA based on lactylation-related gene expression, highlighting their roles in disease heterogeneity. TMSB4X and PRAM1 were identified as potential diagnostic and therapeutic targets, with consistent trends across human and mouse models. A nomogram incorporating these genes showed strong clinical utility. Elevated lactate and inflammatory cytokines further support the association between lactylation and immune dysregulation. These findings provide new epigenetic insights into OSA and suggest potential for lactylation-based precision therapies.

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Links of sleep-disordered breathing with dementia risk and healthcare utilization

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Introduction: In this study, potential associations of sleep-disordered breathing (SDB) with incident mild cognitive impairment (MCI), dementia, and healthcare utilisation will be examined using Kaiser Permanente (KP) Mid-Atlantic States electronic health record (EHR) data. Additionally, how these associations differ by race, sex, and adherence to continuous positive airway pressure (CPAP) therapy will be examined. Moreover, finding relevant influences of these associations, such as race/ethnicity, sex, and adherence to CPAP treatment, is one of the goals. Another is to verify the relationship between SDB diagnosis in KP EHR and the later development of MCI and dementia, as well as subsequent health service utilization.

Materials and methods: To investigate the relationship between OSA diagnosis and MCI and dementia diagnosis in the KP EHR, we will use an observational study design. ICD-10 codes for SDB and a variety of cognitive outcomes (such as moderate impairment and dementias) will be used to determine our key indicator, SDB diagnostic status, and cognitive outcomes. KP's vast database, which contains data on hospitalised patients, outpatients, and pharmacies, will be one of the data sources for our mixed effects models. Under the guidance of frameworks, cost-utility analysis will assess outcomes using information such as QALYs and medical costs. This approach can be put into practice in less than a year by focusing on direct and indirect cost comparisons and using the data that is now available.

Results: Our findings are supported by initial outcomes from previously published investigations. Over a five-year period, older women with sleep-disordered breathing had a 1.85-fold higher risk of mild cognitive impairment or dementia (Yaffe et al., 2011). Similarly, older persons with untreated obstructive sleep apnoea showed a noticeably higher rate of cognitive decline than those without SDB (Gosselin et al., 2019). Our preliminary data shows SDB may be a significant risk factor for neurocognitive impairment, especially for MCI.

Furthermore, even after treatment, individuals with OSA used healthcare resources and related expenses significantly more than controls (Sterling et al., 2024). Our study also highlights the financial cost of OSA and the importance of determining the factors that affect results, such as adherence to treatment and population inequalities.

Conclusions: This study provides important knowledge gaps about the relationship between SDB and healthcare burden and cognitive impairment, as well as how these relationships may differ among demographic groups. The information gathered will help develop accessible methods of diagnosing, treating, and controlling OSA, which could enhance healthcare and cognitive outcomes for a variety of demographics. The results will also help guide future research to see whether treatments, including the use of CPAP, and comprehensive sleep surgical procedures, can lower the risk of dementia.

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Long-term effects on blood pressure of soft tissue surgery for obstructive sleep apnea treatment in adults: a systematic review and meta-analysis

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Introduction: We conduct a systematic review and meta-analysis to evaluate long term effect of soft tissue surgery on blood pressure (BP) in adults with obstructive sleep apnea (OSA).

Materials and methods: PubMed, Scopus, the Cochrane library, and Ovid Medline databases were searched through January 2024. Manual searches were also obtained. This review included studies assessing impact of soft tissue surgery for the treatment of OSA in adults on long-term BP.

Results: A total of five studies (299 patients) met our inclusion criteria. Pooled random effects analysis demonstrated a statistically significant long-term postoperative reduction of BP, with average systolic BP reduction of 14.04 mmHg [95%CI (-21.97, -6.11); P=0.0005]. Pooled random effects analysis of data from four studies (277 patients) also demonstrated statistically significant long-term postoperative reduction of diastolic BP by 6.88 mmHg compared with preoperative baseline [95%CI (-13.31, -0.45); P=0.04].

Conclusions: Soft tissue surgery for OSA treatment in adults significantly resulted in long-term blood pressure reduction.

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Long-Term Outcomes of Combined Sleep Surgery for Obstructive Sleep Apnea: A 14-Year Retrospective Study in Hong Kong Patients

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Introduction: This is the first retrospective study to evaluate long-term outcomes of combined sleep surgery for OSA patients in Hong Kong over a 14-year period (2010-2024). The study aims to assess postoperative outcomes during early (<2 years), intermediate (2-4 years), long-term (4-8 years), and very long-term (>8 years) follow-ups for patients who underwent sleep surgery at the Department of Dentistry and Maxillofacial Surgery, United Christian Hospital, Hospital Authority.

Materials and methods: All subjects underwent maxillomandibular advancement surgery and advancement genioplasty as primary treatments. Simultaneous intra-pharyngeal surgery and/or staged transverse expansion surgery were performed based on individual clinical needs. Inclusion criteria included pre-operative Apnea-Hypopnea Index (AHI) ≥ 5 and age at surgery ≥ 16 . Objective outcomes were evaluated at various post-operative time points using polysomnography including Apnea-hypopnea index (AHI), Respiratory Disturbance Index (RDI), Oxygen Desaturation Index (ODI) and Lowest Oxygen Saturation (LSAT). Subjective outcomes were assessed using Epworth Sleepiness Scale (ESS).

Results: A total of 44 OSA subjects (male: 38, female: 6; age: 43.61 $\pm$ 13.15 [mean $\pm$ SD], range: 22-67; BMI: 24.11 $\pm$ 3.85) underwent sleep surgery. Significant improvement in AHI was observed with reduction from 44.64 $\pm$ 18.59 to 9.64 $\pm$ 8.10 events per hour in the early post-operative stage (<2 years, $p < 0.001$), to 16.80 $\pm$ 11.06 events per hour in the intermediate term (2-4 years, $p < 0.001$), 18.48 $\pm$ 9.45 events per hour in the long term (4-8 years, $p < 0.001$) and to 20.35 $\pm$ 10.33 events per hour in the very long term (>8 years, $p < 0.01$).

However, partial relapse was observed with AHI increasing significantly between the early postoperative stage (<2 years) and the intermediate term (2-4 years) ($p = 0.02$) and between the early postoperative stage and the long term (4-8 years) ($p < 0.001$) and the very long term (>8 years) though it was not statistically significant ($p = 0.15$). A similar trend was observed in RDI and ODI values. LSAT significantly improved from preop 75.30 $\pm$ 10.76 to 85.72 $\pm$ 5.91 (<2years, $p < 0.001$), then dropped to 85.36 $\pm$ 2.74 (2-4years, $p = 0.001$) and 81.46 $\pm$ 5.87 (4-8years, $p < 0.001$) and 80.88 $\pm$ 6.47 (>8years, $p = 0.480$). Nonetheless, improvement in ESS score was reported post-operatively after combined sleep surgery. Possible reasons for AHI increase in long term & very long term could be due to laxity of upper airway soft tissue with time, skeletal relapse, normal aging and weight gain.

Conclusions: This retrospective study highlights the short-and long-term effectiveness of combined sleep surgeries for OSA patients in Hong Kong. There was significant reduction in AHI and was sustained even in the very long term (>8 years), although partial relapse in AHI was observed during long term follow-ups. These findings emphasize the importance of continued monitoring and adjunct therapies to sustain the benefits of MMA-based OSA surgery.

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Low Arousal Threshold as a Predictor of Hypoglossal Nerve Stimulation Therapy Adherence

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Introduction: Obstructive sleep apnea (OSA) entails a complex interplay between anatomic vulnerability and pathophysiologic endotypes such as low arousal threshold (ArTH). Low ArTH is present in >33% of OSA patients and causes frequent arousals from sleep in response to small changes in airflow. Low ArTH has been linked to poor sleep quality, increased daytime symptoms, and poor long-term CPAP adherence. We evaluate the importance of ArTH on outcomes following Hypoglossal Nerve Stimulation (HGNS).

Materials and methods: Patients who underwent HGNS placement between 2020-2023 at two academic institutions were included. ArTH was determined using the following formula: $[AHI < 30 \text{ events/h}] + [SpO_2 \text{ nadir} > 82.5\%] + [\text{Hypopnea}\% > 58.3\%]$. A score of 1 was added for each criterion (low ArTH ≥ 2). Hypopneas were defined as a 30% reduction in airflow associated with a $\geq 4\%$ oxygen desaturation. HGNS adherence was defined as $\geq 4\text{h/night}$ for $>70\%$ of nights. Wilcoxon-rank-sum and Chi-squared tests were performed in R studio.

Results: Of 160 patients, 65 (40.6%) patients had low ArTH preoperatively. 88% and 76% of all patients were adherent to HGNS therapy at 3 and 6 months, respectively. Patients with low ArTH had lower average AHI at baseline (22.2 vs 39.0 events/h, $p < 0.001$), experienced smaller reductions in AHI following therapy, and were more likely to shift from adherence (at 3 months) to non-adherence (at 6 months) (26% vs. 5.3%, $p < 0.001$). Low ArTH patients had decreased % of nights used (82.6% vs 88.8%, $p = 0.037$) and % of nights used ≥ 4 hours (72.6% vs 81.6%, $p = 0.014$) but there was no statistical difference in hours/night (6.8 vs 7.2, $p = 0.11$) or pauses/night (0.68 vs 0.48, $p = 0.2$).

Conclusions: Low ArTH was associated with an unfavorable shift from HGNS adherence to nonadherence over time. Identifying patients with low ArTH preoperatively may improve precision care for OSA patients.

Machine learning-based prediction of sleep apnea and insomnia using objective sleep data from a contactless smartphone application

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Introduction: Rates of underdiagnosis for obstructive sleep apnea (OSA) and insomnia remain unacceptably high. We developed machine learning models leveraging ecologically valid, objective sleep data from contactless consumer sleep technology to predict insomnia and OSA risk, supporting early diagnosis and treatment.

Materials and methods: Objective sleep metrics from the PSG-validated SleepScore mobile application were linked to OSA and insomnia labels in two cohorts. Dataset 1, the survey-threshold-labelled set, comprised 2,813 users (423,085 nights) with Athens Insomnia Scale scores ≥ 6 (indicating insomnia; 74.4 %) or NoSAS scores ≥ 8 (high risk for OSA; 54.9 %). Dataset 2, the self-reported-diagnosis set, contained 68,230 users (2.27 million nights) who self-reported insomnia (6.2 %) or OSA (9.1 %) diagnosis; users with comorbidities (Insomnia or Apnea and RLS or Narcolepsy or Bruxism) or ongoing treatment were excluded. Dataset 1 inclusion criteria was based on objective sleep; insomnia = sleep-onset latency > 30 min, wake after sleep onset > 30 min, and total sleep time < 6.5 h with sleep efficiency $< 80\%$ or sleep-maintenance index $< 85\%$; OSA = ≥ 12 awakenings on ≥ 3 consecutive nights or ≥ 7 on ≥ 3 nights/week for ≥ 4 of the past 8 weeks. Identical preprocessing generated 262 per-user features capturing nightly distributions, weekday-weekend contrasts, temporal trends and frequency metrics. Automated Machine Learning (PyCaret) compared classifiers using 10-fold cross-validation with 20 % holdout, optimising kappa and retaining the ten most informative features. Models were evaluated with AUROC, confusion matrices and standard metrics. Generalizability was tested by

training on the self-reported cohort and validating on the survey-threshold cohort, using user-level 80/20 splits to prevent target leakage.

Results: In Dataset 1, OSA was best predicted by a user-level logistic regression model (accuracy 68 %, AUC 0.74, recall 67 %, precision 72 %, F1-score 0.69). In Dataset 2, a different logistic regression model performed best (accuracy 71 %, AUC 0.77, recall 69 %, precision 27 %, F1-score 0.38). Among users who completed the NoSAS questionnaire, the logistic model achieved 63 % accuracy, 0.73 AUC, 74 % recall, 15 % precision, and 0.24 F1-score, outperforming the questionnaire itself (accuracy 51 %, AUC 0.72, recall 82 %, precision 12 %, F1-score 0.21). For insomnia, the top-performing model in Dataset 1 was a user-level LDA (accuracy 59 %, AUC 0.62, recall 61 %, precision 80 %, F1-score 0.70), while a different LDA model led in Dataset 2 (accuracy 70 %, AUC 0.68, recall 53 %, precision 14 %, F1-score 0.23).

Conclusions: The developed models demonstrate promising capability in predicting insomnia and OSA risks using exclusively app-derived sleep stage data. App-based screening outperformed the AUC of well-established screeners such as NoSAS and approximated the Athens Insomnia Scale. This research demonstrates the promise of consumer sleep technologies to flag potential sleep disorders for users in order to motivate diagnosis and treatment to improve sleep health.

Management of Sleep Apnoea and Insomnia in Primary Care: effectiveness of pilot feasibility study

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Introduction: Obstructive sleep apnoea (OSA) and insomnia are the two most common sleep disorders in Australia but remain under-recognised. Access to timely care is limited by over-reliance on specialist-led models. A mixed-methods pilot study evaluated the effectiveness and feasibility of a guideline-based approach to general practitioner (GP) and practice nurse-led OSA and insomnia management in primary care. This poster presents findings from the quantitative analysis only.

Materials and methods: Adults at a single primary care facility were screened for chronic insomnia and OSA using the Epworth Sleepiness Scale (ESS), OSA-50, and Sleep Condition Indicator (SCI). Patients were eligible if they screened positive for chronic insomnia (SCI $\leq$ 16 with symptoms $>$ 3 months) or were at high risk for symptomatic OSA (ESS $\geq$ 8 and OSA-50 $\geq$ 5). Participants at high risk of OSA underwent home-based diagnostic testing using a limited channel sleep study (ApneaLink, ResMed). Moderate-severe OSA was defined as 3% oxygen desaturation index (ODI) $\geq$ 16/hour, these participants were offered continuous positive airway pressure (CPAP) therapy as first-line therapy. Participants with chronic insomnia were offered cognitive behavioural therapy for insomnia (CBTi), delivered by a trained nurse or sleep psychologist, or via Sleepio (Big Health), an evidence-based digital CBTi platform. Mood and psychological health were assessed using the Generalised Anxiety Disorder 7 (GAD-7), Patient Health Questionnaire 9 (PHQ-9), and Kessler Psychological Distress Scale (K10). Primary effectiveness outcomes were change in ESS for the OSA group and SCI for the insomnia group at 3, 6, and 12 months. Secondary outcomes included mood measures (GAD-7, PHQ-9, K10), CPAP adherence, and residual apnoea-hypopnoea index (AHI).

Results: Nineteen patients at high risk for OSA (68% male, age 50.2 $\pm$ 15.2 [mean $\pm$ SD]years, BMI 33.3 $\pm$ 7.8kg/m²) were recruited. Of these, nine (47%) were diagnosed with moderate-severe OSA (3%ODI 29.6 $\pm$ 5.8/hr). Mean ESS significantly improved from baseline (11.2 $\pm$ 0.5[mean $\pm$ SE]) at 3, 6 and 12 months (5.2 $\pm$ 0.5, 4.2 $\pm$ 0.6 and 4.5 $\pm$ 0.5, respectively; F=45.51, p<0.001). At 12 months CPAP was used by 7 of the 9 (78%) patients, with mean usage 4.3 $\pm$ 3.1[SD]hrs/night and a residual AHI of 1.5 $\pm$ 0.8/hr. Fifteen patients with chronic insomnia (53% male, age 55.2 $\pm$ 15.9[mean $\pm$ SD]years, BMI 28.2 $\pm$ 4.4kg/m²) were recruited. Eight (53%) patients opted for nurse-led CBTi, four (27%) used Sleepio, one (7%) saw a sleep psychologist and two (13%) opted for no treatment. Mean SCI at 3, 6 and 12 months (20.9 $\pm$ 1.2[mean $\pm$ SE], 18.9 $\pm$ 1.3 and 21.1 $\pm$ 1.2 respectively) was significantly improved compared to baseline (11.9 $\pm$ 1.1, F=14.42, p<0.001). Significant improvements in GAD-7, PHQ-9 and K10 were observed at 6 and 12 months for both OSA and insomnia groups (p<0.05).

Conclusions: Sustained improvements in sleepiness, insomnia and mood suggest early evidence of clinical benefit from primary care-led management of OSA and chronic insomnia. These findings

suggest that structured, guideline-based care for OSA and chronic insomnia can be effectively delivered by general practice staff.

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Mandibular advancement device versus CPAP on cardiovascular health and quality of life in OSA — a pre-specified 12 months follow up of outcome

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Introduction: Obstructive sleep apnoea (OSA) is a significant cause of hypertension. Guidelines recommended screening and treatment of hypertension in OSA; however, evidence comparing mandibular advancement devices (MAD) to continuous positive airway pressure (CPAP) on cardiovascular health is lacking. We presented the relative effectiveness of MAD versus CPAP in long-term sleep and heart health.

Materials and methods: In a, randomized, non-inferiority trial (margin 1.5 mmHg), 321 participants, aged over 40, with hypertension and high cardiovascular risk were recruited. Of these, 220 participants with OSA (apnoea-hypopnea index ≥ 15 events/h) were randomized to either MAD or CPAP (1:1). This report presents the secondary outcomes at 12-month follow-up on the relative effectiveness of MAD versus CPAP in ambulatory BP reduction, quality of life (QoL) (sleep-specific: ESS, SAQLI, FOSQ; general: SF-36, EQ-5D), cardiac arrhythmia, and myocardial remodelling.

Results: A total of 89 (80.9% of 110) participants from MAD, and 91 (82.7% of 110) participants from CPAP completed 12-month follow-up. The median daily usage was 5.5 hours for MAD and 4.9 hours for CPAP. The between-group difference in 24h mean BP from baseline to 12-month was - 0.57 mmHg (95% confidence interval: -2.53 to 1.39, non-inferiority $P < 0.001$). Compared with the CPAP group, MAD group demonstrated a larger reduction in all the 24h with the most pronounced differences observed in the asleep BP parameters [between group difference in asleep mean BP: -2.33 mmHg (95% confidence interval: -5.08 to 0.42, $P = 0.003$); asleep systolic BP: -2.54mmHg (95% confidence interval: -6.19 to 1.11, $P = 0.015$); asleep diastolic BP: -2.26mmHg (95% confidence interval: -4.73 to 0.22, $P = 0.002$)]. Both the MAD and CPAP improved QoL, and the improvement is more pronounced in sleep-specific questionnaires ($P < 0.001$ for all sleep-specific questionnaires). CPAP had greater improvement in FOSQ from sleep-specific questionnaires ($P=0.038$), and social QoL in SF-36 from general questionnaires ($P=0.013$). The ambulatory ECG monitoring showed no between-group differences in % atrial fibrillation($P=0.209$), % ventricular ectopic isolated count ($P=0.790$) and % supraventricular ectopic isolated count ($P= 0.333$). The cardiac MRI sub-study (101 participants : MAD= 45, CPAP= 56) showed CPAP had greater improvement in right ventricular stroke volume ($P=0.023$) and MAD had greater improvement in circumferential strain favours the MAD group ($P=0.015$).

Conclusions: At 12 months , MAD was non-inferior to CPAP for reducing 24h mean arterial BP. MAD showed greater reduction in 24h BPs, especially during asleep. Our findings show that MAD treatment is a viable alternative to CPAP in the treatment of OSA, with non-inferior effects across many important cardiac and health outcomes.

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Measures of OSA by baseline BMI classification in participants from SURMOUNT-OSA trials: post-hoc analyses

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Introduction: In SURMOUNT-OSA, tirzepatide reduced apnoea-hypopnoea index (AHI), sleep apnea specific hypoxic burden (SASHB), and body weight (BW). Here we evaluated weight reduction (WR) and measures of OSA based on baseline body mass index (BMI) category.

Materials and methods: SURMOUNT-OSA (NCT05412004) evaluated tirzepatide versus placebo for 52 weeks in participants with moderate-to-severe obstructive sleep apnoea (OSA) with obesity. Study 1 (N=234) and 2 (N=233) included participants not using, or using positive airway pressure (PAP) therapy, respectively. These post-hoc analyses analyzed WR and measures of OSA by baseline BMI categories (<35, ≥35 and <40, and ≥40 kg/m²) using on-treatment data. Mixed-model repeated measures were applied for continuous variables, and logistic regression for binary outcomes.

Results: Study 1 included 77, 74, and 83 participants; and Study 2 had 66, 88, and 79 participants in the baseline BMI categories <35, ≥35 and <40, and ≥40 kg/m², respectively. Baseline demographics, AHI, and Epworth sleepiness scale (ESS) were generally similar across subgroups, with higher BMI categories tending to have more female participants, be slightly younger, and have higher AHI and ESS. In Study 1, at Week 52, the placebo-corrected decrease associated with tirzepatide across BMI categories was 19.0-26.4 events/hour or 46.7-54.4% for AHI, 53.5-67.5% for SASHB, and 16.0-17.8% for BW. The odds ratio for a ≥50% reduction in AHI associated with tirzepatide compared to placebo was 6.92-11.91; and it was 3.10-18.84 for AHI<5, or AHI 5-14 with ESS≤10. In Study 2, at Week 52, the placebo-corrected decrease associated with tirzepatide across BMI categories was 21.8-27.8 events/hour or 47.1-62.4% for AHI, 58.4-73.4% for SASHB, and 17.3-18.6% for BW. The odds ratio for a ≥50% reduction in AHI associated with tirzepatide compared to placebo was 6.94-11.06; and it was 6.35-9.97 for AHI<5, or AHI 5-14 with ESS≤10. All results were statistically significant versus placebo (p<0.01), except for the odds ratio for AHI<5, or AHI 5-14 with ESS≤10 in Study 1 with baseline BMI≥40 kg/m² subgroup. There was no consistent trend in WR or OSA measures between baseline BMI categories across both studies.

Conclusions: These post-hoc analyses suggested that OSA measures associated with tirzepatide treatment were generally improved compared to placebo, regardless of baseline BMI.

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Measures related to obstructive sleep apnea after tirzepatide treatment by baseline OSA severity: post-hoc analyses of SURMOUNT-OSA

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Introduction: In the SURMOUNT-OSA clinical studies, tirzepatide improved measures of obstructive sleep apnea (OSA) and cardiometabolic parameters in participants with moderate-to-severe OSA and obesity, including apnea hypopnea index (AHI), sleep apnea specific hypoxic burden (SASHB), systolic blood pressure (SBP), C-reactive protein (CRP), and body weight (BW). Here we evaluate the associations between tirzepatide treatment and changes in these parameters versus placebo by baseline OSA severity.

Materials and methods: SURMOUNT-OSA (NCT05412004) comprised two Phase 3 studies comparing the effects of tirzepatide maximum tolerated dose (10 mg or 15 mg once weekly) versus placebo in adults with moderate-to-severe OSA and obesity over 52 weeks. Study 1 participants were not on positive airway pressure (PAP) therapy; Study 2 participants were on PAP. These post-hoc analyses classified on-treatment participants with non-missing baseline AHI measurements into approximately evenly weighted OSA severity subgroups by baseline AHI (moderate, AHI ≥15 to <30; severe, AHI ≥30 to <70; very severe, AHI ≥70). Measures related to OSA were analyzed by logistic regression for binary outcomes and mixed-model repeated measures for continuous variables.

Results: In our analyses, we did not observe consistent associations between baseline OSA severity and changes in measures of OSA or cardiometabolic parameters across both studies. Significant differences between severity subgroups were observed for change difference in AHI ($p=0.032$) and percent body weight reductions ($p=0.042$) among participants not on PAP in Study 1. In Study 1 and 2, tirzepatide was associated with significant reductions versus placebo in AHI, SASHB, SBP, and BW across all severity subgroups. In both studies, the odds of achieving $\geq 50\%$ AHI reduction with tirzepatide were significantly higher than with placebo in all severity groups. The odds of achieving AHI < 5 or AHI 5-14 with Epworth Sleepiness Scale ≤ 10 were also significantly higher with tirzepatide than placebo in all subgroups except the Study 1 very severe subgroup. Greater reductions were observed in high-sensitivity CRP with tirzepatide than placebo across all severity groups, though significant differences were only associated with the severe subgroup in both studies.

Conclusions: In these post-hoc analyses of the SURMOUNT-OSA studies, tirzepatide was associated with significant improvements versus placebo in measures of OSA and cardiometabolic parameters irrespective of participants' OSA severity at baseline or PAP therapy use.

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Mechanism Analysis of the REM-Related Oxygen Desaturation in Patients with Moderate to Severe OSA

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Introduction: This study aimed to determine the factors underlying rapid eye movement (REM) sleep-related oxygen desaturation (OD) in patients with obstructive sleep apnea (OSA).

Materials and methods: All subjects underwent overnight polysomnography with synchronous genioglossus electromyography (GGEMG) using intraoral electrodes. For those subjects diagnosed with moderate or severe OSA (AHI > 15 events/h), we respectively calculated the average OD during rapid eye movement (REM-OD) and non-rapid eye movement sleep (NREM-OD). The ratio of REM-OD/NREM-OD ≥ 1.5 was defined as patients with REM-related OD. The upper airway anatomy was measured by three-dimensional computed tomography (3D-CT) in all subjects.

Results: Comparing the REM-related OD group ($n=15$, AHI 68.01 ± 18.35 events/h) to the NREM-related OD group ($n=18$, AHI 57.48 ± 28.81 events/h), the former had a more severe lowest oxygen saturation overnight (56.14 ± 7.06 vs. 70.92 ± 14.49 , $p=0.009$). GGEMG variables were similar between the two groups, except for apnea time in the REM period ($p<0.001$). Parameters measured by 3D-CT of the UA showed that the REM-related OD group had a narrower glossopharyngeal airway, with a smaller minimal anteroposterior airway dimension (12.41 ± 2.99 vs. 17.58 ± 4.78 , $p=0.020$) and smaller minimal cross-sectional airway area (119.81 ± 30.94 vs. 199.78 ± 75.02 , $p=0.005$).

Conclusions: REM-related OD in OSA patients is closely associated with glossopharyngeal airway narrowing, which is the leading factor in the prolongation of apnea events during REM sleep, while the contribution of genioglossus myoelectric activity to this mechanism is not obvious.

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Mechanism analysis of the site, pattern, and degree of upper airway obstruction during drug-induced sleep endoscopy in patients with obstructive sleep apnea

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Introduction: Drug-induced sleep endoscopy (DISE) is an effective way to locate the pattern of upper airway obstruction; however, it is unclear how anatomical and functional factors affect DISE findings in patients with obstructive sleep apnea. To assess the anatomical and genioglossus electromyography (ggEMG) indicators in obstruction patterns classified by the VOTE system.

Materials and methods: This cross-sectional prospective study was conducted at the Beijing Tsinghua Chang Gung Hospital between September 2019–April 2023. obstructive sleep apnea patients, aged 20–60 years with an AHI $\geq$ 15 without treatment, were included. The anatomical factors were measured by UACT and the ratio of unit phasic ggEMG / inspiratory negative pressure was used to evaluate genioglossus function. Based on VOTE system, the complete velum (V) obstruction was divided into anterior-posterior, lateral and concentric groups, and the oropharynx lateral walls (O) or tongue base (T) collapse were divided into six types (O₁₋₂T₀₋₂) for comparison. The epiglottic (E) patterns were grouped by the score of collapse.

Results: The study included 107 participants aged 38.8 $\pm$ 8.0 years with an AHI of 48.2 $\pm$ 19.6 events/h. The V pattern groups showed no statistical ggEMG differences; however, the lateral group exhibited the highest BMI (H=11.467, P=0.003), narrowest velopharynx mLAT (H=6.405, P=0.041), and largest glossopharynx mAP (H=8,395, P=0.015). In the O/T groups, we found that O₂T₁ tended to have a higher BMI (t=-2.833, P=0.007), longer glossopharynx length (t=-2.595, P=0.014), narrower glossopharynx mLAT (t=2.585, P=0.017), and were more likely to combine genioglossus dysfunction against the negative inspiratory pressure (χ^2 =7.502, P=0.023). In the E groups, E₂ exhibited the narrowest mAP (velopharynx: H=11.007, P=0.004; glossopharynx: H=7.057, P=0.029) and the longest glossopharynx length (H=9.653, P=0.008), whereas E₀ showed the lowest ggEMG activation while awake (R1, H=8.591, P=0.014) and during sleep-onset (R2, H=9.792, P=0.007).

Conclusions: In obstructive sleep apnea, various anatomical and functional factors affect the upper airway obstructive site, pattern, and degree. O₂T₁ had a high tendency for genioglossus dysfunction that needed a comprehensive etiological treatment.

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Medullary Transcriptome and Proteomics Converge on Energy Homeostasis in the Pause-Prone C57BL/6J Mouse

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Introduction: GWAS reports on sleep apnea have been unsuccessful in linking gene polymorphisms to obstructive sleep apnea using AHI (Salman, Shulman et al. 2020, Trzepizur, Blanchard et al. 2022). When this happens one can turn to animal models to uncover traits that underpin the appearance of sleep disordered breathing. Ventilatory instability- burst irregularity and post-hypoxic pauses- occurs in the C57BL/6J (B6) and not in the A/J in-bred mouse strain in wakefulness and sleep, is linked to brainstem presence of apolipoprotein A2 (apoA2), and is absent in the chromosomal substitution strain B6a1, and both *in vivo* and *in vitro* in apoA2 homozygote knock out (KO) mice (Gillombardo et al. 2017). The purpose was to uncover biologic functions linked to the *in vivo* pause physiology affected by the B6 apoA2 polymorphism.

Materials and methods: Part 1: medulla and pons mRNA extracted from B6, A/J and B6a1 mice were comparatively profiled using mouse Gene Expression Array 1.0 array (Affymetrix).

Part 2: Complete brainstem samples from *apoa2* KO and B6 (wild type) mice underwent comparative proteomic profiling using Rosetta Elucidator quantitative software. Network analyses were conducted using the Ingenuity Pathway Analysis (IPA).

Results: Part 1: Genes consistently downregulated in the brainstem of stable breathing strains were *apoa2* (as expected), but also *Tnni1*, *Arl4c*, *CDH20*, and *DARC*; the genes upregulated in both the medulla and pons were *SDHC* (the fourth protein of Complex II) and *Wdfy1* (one of other genes associated with RETT syndrome).

Part 2: a total of 6307 peptides were identified and quantified, with 1150 peptides mapping to 298 unique proteins differentially expressed based on three cutoff criteria (P-value ≤ 0.05 , two or more peptides per protein, and fold change of 2 or greater). IPA analysis identified oxidative phosphorylation, citric acid cycle and respiratory electron transport as the top canonical pathways. Differences in ATP-citrate synthase, V-type proton ATPase subunit C1, cytochrome c oxidase subunit 5A, and cytochrome b-c1 complex subunit 2 were confirmed by SRM analysis.

Conclusions: Brainstem *apoa2* presence requires homozygotic B6 SNPs and will affect biological expression in genes and proteins other than *apoa2*. Pathways identified in cellular bioenergetics and mitochondrial function converge in both Part 1 and Part 2 datasets, uncovering a novel mechanism that may produce repetition of obstructive and non-obstructive apneas during sleep.

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Mineralocorticoid Receptor Blockade Attenuates Cardiovascular Dysfunction in Obese Mice Subjected to Intermittent Hypoxia

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Introduction: Obstructive sleep apnea (OSA), particularly prevalent in obesity, is marked by cycles of intermittent hypoxia (IH) and substantially increases cardiovascular disease (CVD) risk and mortality. Mineralocorticoid receptor antagonists (MRAs) improve outcomes across CVD spectra. We evaluated whether spironolactone (SPL) and the next-generation MRA finerenone (FIN) preserve coronary and cardiac function in mice subjected to chronic IH

Materials and methods: Male and female C57BL/6J mice received a high-fat diet (HFD) or low-fat diet (LFD) for 10 weeks, then underwent daily 16-week exposures to IH (90 s at 21% O₂ alternating with 90 s at 6% O₂) or room air. Cohorts were treated with SPL, FIN, or placebo. We measured mean arterial pressure (MAP), echocardiographic ejection fraction (EF) and E/A ratio (diastolic function), and coronary flow velocity reserve (CFVR). In vitro vascular reactivity of left anterior descending coronary and renal arteries was assessed using acetylcholine (ACh)-induced dilation and U46619-mediated constriction.

Results: Both SPL and FIN normalized IH- and HFD-elevated MAP in male mice. In LFD-IH males, SPL and FIN improved EF, whereas HFD and HFD-IH groups did not benefit. Diastolic dysfunction (E/A ratio) persisted post-MRA in HFD-IH mice. FIN—but not SPL—restored CFVR in HFD-IH males, indicating superior coronary protection. In coronary rings, both MRAs reduced U46619-induced constriction under LFD-IH, but only FIN rescued ACh-mediated relaxation in both LFD-IH and HFD-IH males. Female mice showed no improvement in vasoconstriction or vasodilation after either MRA in HFD-IH

Conclusions: Chronic IH compounded by diet-induced obesity impairs cardiac and coronary function in a sex- and diet-dependent manner. MRA therapy, particularly with the selective FIN, reverses key aspects of IH- and obesity-induced cardiovascular dysfunction in male mice. These findings support FIN's potential as a targeted adjunct to mitigate CVD risk in OSA patients.

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More Than Muscle: Revealing the Cortical Effects of Myofunctional Therapy in OSA

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Introduction: Obstructive Sleep Apnea (OSA) is a major health concern characterized by repeated upper airway collapse during sleep, resulting in fragmented sleep and increased cardiovascular risk (1). Continuous Positive Airway Pressure (CPAP) remains the standard treatment but suffers from poor long-term adherence due to poor compliance/bulkiness, noise, and discomfort (2). Mandibular advancement device (MAD) offers a better-tolerated mechanical alternative; however, MAD efficacy is variable, and they can cause dental side effects, such as occlusal changes (3). Both therapies primarily address the mechanical aspect of airway patency without targeting the underlying neuromuscular dysfunction. Myofunctional Therapy (MFT), consisting of targeted oropharyngeal exercises, has emerged as a promising non-invasive alternative/intervention. Our previous studies demonstrated that both MAD and brief MFT sessions can induce corticomotor neuroplasticity, assessed via Transcranial Magnetic Stimulation (TMS) (4-7). However, the long-term neurophysiological and clinical effects of MFT remain to be fully elucidated.

The primary aim of this project is to determine whether a structured MFT program induces corticomotor neuroplasticity in oropharyngeal muscles, and sleep outcomes in OSA patients. Secondary aims include, 1) comparing baseline corticomotor control between OSA patients and healthy controls, 2) assessing the sustained effects of MFT over 12 weeks, and 3) evaluating whether combining MFT with MAD results in superior neurophysiological and clinical outcomes compared to MAD alone.

Materials and methods: The project consists of three integrated studies. **Study 1** (cross-sectional) evaluates baseline corticomotor control and immediate neuroplastic responses to a single MFT session in OSA patients versus healthy controls. **Study 2** (randomized controlled trial) assesses the effects of a 12-week MFT program on corticomotor excitability, and sleep outcomes. **Study 3** (prospective nested cohort) tests whether the combination of MFT and MAD provides greater benefits than MAD therapy alone. Participants will undergo home sleep-apnea testing, patient-reported outcomes (ESS, PSQI, EQ-5D-5L, MoCA), and TMS-based neurophysiological assessments. Statistical analyses include t-tests, Mann-Whitney U tests, repeated measures ANOVA.

Results: Expected Results: Study 1 will clarify whether OSA patients exhibit baseline corticomotor impairments and immediate neuroplastic responses to MFT. Study 2 will evaluate whether daily MFT over 12 weeks enhances corticomotor control and clinical sleep outcomes. Study 3 will investigate the potential synergistic effects of combining MFT with MAD therapy on corticomotor control and clinical sleep outcomes. We hypothesize that MFT will induce measurable neuroplastic adaptations associated with improved airway function and sleep quality.

Conclusions: Demonstrating that MFT drives corticomotor neuroplasticity and sleep outcomes would establish it as a clinically valuable, patient-centered therapy for OSA. Beyond functioning as a standalone intervention, MFT may also enhance the effects of traditional treatments such as MAD, offering a more comprehensive, functionally oriented approach to OSA management. This integrated strategy could reduce reliance on mechanical therapies alone, lower healthcare costs, and may contribute to improve patients' quality of life.

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Morphological phenotypes of the oral cavity and hard palate in Thai adults with obstructive sleep apnea: A case-control study

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Introduction: Obstructive sleep apnea (OSA) is a prevalent condition influenced by a range of anatomical and functional factors. Among these, morphological variations in the oral cavity, hard palate, and tongue significantly contribute to OSA pathogenesis and severity. While craniofacial morphology differs across ethnicities, data specific to the Thai population remain limited. Understanding these structural characteristics is essential for guiding individualized diagnostic and therapeutic strategies. This study aimed to characterize and compare the anatomical characteristics of the oral cavity, including the hard palate and tongue, between Thai patients with OSA and individuals at low risk for OSA.

Materials and methods:

This prospective case-control study was conducted at Rajavithi Hospital. Sixty participants were enrolled: 30 patients with OSA confirmed by polysomnography and 30 low-risk control subjects identified via the STOP-BANG questionnaire. Anatomical evaluation comprised: (1) hard palate morphology (palatal width and height measured at specific dental landmarks using intraoral scanning), (2) palatal roof-to-tongue width ratio, and (3) ankyloglossia-related measures, including mouth opening with tongue tip to incisive papilla (MOTTIP), maximal interincisal mouth opening (MIO), and Kotlow's free-tongue length. Statistical analysis was performed with a significance threshold of $p < 0.05$.

Results: Patients with OSA had significantly narrower palatal roof width compared to controls (mean 18.85 mm vs. 22.41 mm; $p < 0.001$), and significantly greater palatal height at the inter-canine ($p = 0.038$) and inter-first premolar ($p = 0.017$) positions. Although the overall palatal roof-to-tongue width ratio did not significantly differ between groups ($p = 0.147$), patients with severe OSA showed a strong association between narrow palates and increased tongue width (ratio 1:3, $p = 0.049$). No statistically significant differences were observed in ankyloglossia-related measurements: MOTTIP ($p = 0.268$), MIO ($p = 0.572$), or Kotlow's measurement ($p = 0.102$).

Conclusions: Thai patients with OSA exhibit a narrow, high-arched palatal vault and a proportionately wider tongue, especially in cases of severe disease. Integrating comprehensive evaluations of oral cavity morphology into standard clinical assessments may improve diagnostic accuracy and facilitate the selection of targeted interventions, such as palatal expansion or localized surgical therapies, intended to alleviate airway obstruction and enhance outcomes in OSA.

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Multidisciplinary Speciality Sleep Clinic: a novel approach to sleep medicine in India

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Introduction: Sleep disorders are complex conditions and require the involvement of multiple providers; however, sleep care globally is fragmented and compartmentalised. A comprehensive sleep centre should house specialities like pulmonology, otolaryngology, dentistry, psychiatry, neurology and weight management under one roof. This paper presents a novel approach implemented in a outpatient chest and sleep centre in Bengaluru, India.

Materials and methods: The sleep disorders clinic was envisaged as a multidisciplinary team (MDT) that sees each patient, followed by a multidisciplinary discussion (MDD) culminating in a comprehensive treatment plan. Patients underwent a level 1 or 3 PSG before or after the first consultation. Each patient first consulted a pulmonologist where an initial plan was proposed; followed by ENT and dental consultations. This was followed by an MDD and involvement of dieticians, psychologists, and physical therapists as indicated. A detailed management protocol was generated with priority-based therapy options. This study compares the initial treatment plan with the final plan and evaluates the impact of the MDT and MDD on therapeutic recommendations.

Results: From April 2024 to July 2025, 149 patients presented with sleep related complaints. Of these, 121 completed the full diagnostic workflow and underwent MDD.

Among them, 106 of 121 (87.60%) were diagnosed with OSA, 10 (8.26%) with COMISA, and 2 (1.65%) each with insomnia and UARS, and 1 (0.83%) no conclusive diagnosis.

Following the initial pulmonary consult, 113 (93.38%) patients were advised CPAP, 5 (4.13%)

Mandibular Advancement Device (MAD), and 12 (9.92%) behavioural intervention.

After the MDD, management options were optimised: 90 (74.38%) patients were recommended PAP therapy, 12 (9.92%) ENT surgery, 21 (17.36%) MAD and 28 (23.14%) behavioural intervention, among other adjunctive management.

Of the 21 patients recommended MAD, 8 were intolerant to PAP, 2 were diagnosed with UARS and were ineligible for PAP and 11 were offered MAD as first-line therapy.

ENT surgery was recommended to 12 patients to optimize PAP therapy or manage OSA; of which it was first line therapy for 7 patients. Adjunctive therapies and further investigations post MDD included DISE for 31, repeat PSG for 10, myofunctional therapy for 37 and weight management for 79 patients. PAP therapy before ENT intervention was advised for 23 and drug therapy to improve nasal airflow for 71 patients.

Of the 28 patients advised behavioural intervention, 12 received it as primary treatment for insomnia/COMISA while 16 for secondary care of anxiety, depression, and for reducing barriers to healthcare and CPAP.

Following MDD, PAP recommendations decreased by 20.35%, MAD increased by 320%, and behavioural therapy increased by 133%. ENT interventions (DISE/ surgery/ pharmacological therapy), myofunctional therapy and weight management were recommended only after MDD.

Conclusions: The integration of multiple fields in a single centre minimises redundancy and is time and cost efficient for patients. It alters the default initiation of PAP therapy for patients with sleep-disordered breathing. Major challenges revealed in the study were reluctance for invasive therapeutic/ diagnostic procedures and patients lost to follow up after PSG. In conclusion, this model allows for individualised strategies and a multi-pronged approach for managing sleep disorders.

Multifactorial Relationships among the Waist-to-hip Ratio, Insulin Resistance, and Obstructive Sleep Apnea: A Large-scale Cohort Study

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Introduction: Metabolic comorbidities related to obstructive sleep apnoea (OSA) are a major concern in regarding OSA prognosis and complexity. However, few studies have investigated the interrelationships among these metabolic comorbidities. We explored the associations among insulin resistance (IR), the waist-to-hip ratio (WHR), and OSA using innovative and rigorous statistical methods.

Materials and methods: We enrolled 5,326 subjects after meticulous recording anthropometric, biochemical, and standard polysomnographic parameters. The relationships among IR, WHR, and OSA were analyzed using confirmatory factor analysis (CFA) as well as moderation and mediation analyses.

Results: CFA showed that IR and obesity were strongly correlated (loading = 0.73, $p < 0.001$). OSA was associated with both obesity and IR (loading = 0.57, $p < 0.001$; loading = 0.46, $p < 0.001$, respectively). Obesity was strongly associated with both the body mass index (BMI) and the WHR (loading = 0.82, $p < 0.001$; loading = 0.67, $p < 0.001$, respectively). WHR served as a moderator; the interaction effect between WHR and IR on the apnoea-hypopnea index (AHI) was significant (coefficient = -2.451; $p = 0.023$). Mediation analyses showed that WHR explained 14.93%, 14.02%, and 13.10% of the associations between IR and AHI, the oxygen desaturation index, and the micro-arousal index, respectively.

Conclusions: Multifactorial relationships are apparent among IR, WHR, and OSA. The complex interrelationships highlight the intricate clinical interactions among metabolic dysfunction, central obesity, and sleep-disordered breathing, emphasizing the multifaceted nature of OSA and its related health implications.

Multi-night monitoring of variability in OSA severity and associated impacts on daytime impairment and quality of life

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Introduction: Night-to-night variability in obstructive sleep apnoea (OSA) severity limits the utility of single-night polysomnography (PSG) for both diagnostic accuracy and ability to accurately detect associated clinical outcomes. This study investigated if longitudinal assessment of variability in OSA severity with under-mattress multi-night monitoring of the apnoea-hypopnea index (AHI) or other baseline disease characteristics are associated with key daytime clinical outcomes.

Materials and methods: A total of 100 participants with suspected OSA were recruited to the Simplified Assessment and Monitoring of OSA (SAMOSA) observational cohort study. Each participant underwent a clinical interview and physical examination. Validated questionnaires were administered, including the Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and EuroQol 5-dimension health-related quality of life scale (EQ-5D-5L). Participants were prospectively observed for 30 days using an FDA-cleared under-mattress device (Withings Sleep Analyser, Withings, France). All underwent single-night PSG prior to or during the monitoring period. Night-to-night variability in the AHI (hereafter referred to as “AHI variability”) was determined using the root-mean-squared of successive differences in nightly AHI estimates from the under-mattress device. Multiple regression analyses were performed to identify PSG and under-mattress device measurements associated with symptom severity and quality of life (visual analogue scale).

Results: There were 81 participants included in the final analysis, after exclusion of 14 due to OSA treatment prior to or during baseline monitoring, and 5 due to failure to obtain nightly AHI measurements during the baseline period. The remaining participants (51% female) had a mean±SD age of 52±16 years and BMI of 31±8 kg/m². At baseline, participants were, on average, normotensive (blood pressure 126/83±15/10 mmHg), reported daytime sleepiness within the normal range (ESS 7±5), subthreshold insomnia (ISI 12±6.1) and had moderate OSA on PSG (AHI 22±27 events/hr). High AHI variability was associated with high OSA severity (by one-way ANOVA, $F [3, 77] = 34.5, p < 0.001$). High average in-home AHI was associated with increased ESS ($B[95\%CI] = 0.071[0.009 - 0.13], p = 0.024$), whereas single-night PSG AHI was not ($B[95\%CI] = 0.027[-0.014 - 0.069], p = 0.19$). AHI variability was not associated with ESS or quality of life. High AHI variability was associated with lower ISI ($B[95\%CI] = -0.23[-0.46 - -0.006], p = 0.044$), adjusting for age, sex, BMI and OSA severity.

Conclusions: This study is the first to prospectively evaluate multi-night under-mattress monitoring in OSA and links with key daytime outcomes. These data demonstrate that multi-night AHI estimates are more closely associated with severity of daytime sleepiness than single night PSG, a finding which could help clinical decision making for OSA management. Improved reported insomnia with higher AHI variability represents a hypothesis generating finding, and further evaluation of the effects of sleep timing and architecture on variability are needed.

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Multi-night phenotypes of sleep-disordered breathing are associated with increased arterial stiffness

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Introduction: Arterial stiffness is a robust predictor of end-organ damage and cardiovascular mortality, beyond traditional risk factors. Pulse-wave velocity (PWV) is a well-established, non-invasive measure of arterial stiffness, serving as a proxy of vascular aging and cardiovascular risk. Prior studies examining the relationship between obstructive sleep apnea (OSA) and PWV, based on single-timepoint assessments, have yielded inconsistent results. Emerging multi-night sleep-disordered breathing (SDB) phenotypes, including high night-to-night variability in OSA severity and regular snoring, are

independent predictors of adverse cardiovascular outcomes (e.g. hypertension). However, the role of multi-night SDB metrics on arterial stiffness remains unexplored. This study investigates the associations between multi-night OSA severity, OSA variability, and snoring with repeated multi-year measurements of arterial stiffness.

Materials and methods: Longitudinal data (January 2021–November 2024) were collected from adult users of two FDA-cleared consumer health tracking devices: an under-mattress sleep sensor and a smart scale. Nightly apnea-hypopnea index (AHI) and snoring metrics were derived from the sleep sensor using ballistography and sound analysis (validated against gold-standard polysomnography). Aortic-leg PWV measurements were derived from the scale using impedance plethysmography and ballistocardiography (validated against gold-standard applanation tonometry). Participants with <52 sleep or <12 PWV readings per year were excluded. OSA severity was categorized by average AHI: <5 (no OSA), 5–15 (mild), 15–30 (moderate), and 30+ events/h (severe). OSA variability was calculated using the root mean square of successive nightly AHI differences. Snoring was quantified as the average percentage of total sleep time spent snoring. Multivariable linear regression models examined the associations between multi-night sleep metrics and average PWV, adjusting for age, sex, and BMI. Models for OSA variability and snoring further accounted for OSA severity and each other. Associations of age with PWV were also analysed for context. Results are reported as β coefficient and 95%CI.

Results: The study included 29,653 participants from 20 countries (mean age 52 ± 12 years; 84% male; BMI 27.3 ± 4.9 kg/m²). Participants had a median [IQR] of 252 [103] sleep and 38 [64] PWV measurements per year. OSA prevalence was 34% mild, 17% moderate, and 8% severe. Mean PWV was 7.56 ± 1.02 m/s. Compared to participants without OSA, higher OSA severity was significantly associated with increased PWV: mild OSA ($+0.17$ [0.15–0.19] m/s), moderate OSA ($+0.27$ [0.24–0.30] m/s), and severe OSA ($+0.24$ [0.20–0.29] m/s). Among those with mild OSA, greater OSA variability (75th vs. 25th; 12.0 vs. 6.8 events/h) was significantly associated with a further $+0.11$ [0.07–0.15] m/s PWV increase. High snoring burden (75th vs. 25th; 16.5% vs 1.9%) was significantly associated with a $+0.19$ [0.16–0.21] m/s PWV increase. For reference, a 16-year age difference (75th vs. 25th; 61 vs. 45 years) was associated with a $+0.68$ (0.67 to 0.70) m/s PWV increase.

Conclusions: In this large, real-world study, multi-night OSA severity, night-to-night OSA variability, and regular snoring were each independently associated with a clinically meaningful increase in arterial stiffness. These novel findings underscore the value of multi-night sleep monitoring for improved cardiovascular risk stratification and suggest that arterial stiffness may be a key mechanistic pathway linking SDB with cardiovascular pathology.

Multi-Omics Sequencing and Mendelian Randomization Analysis Identifies Corticotropin-Releasing Hormone Receptors (GRHR) as a Potential Therapeutic Target for Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a multifactorial sleep-related breathing disorder characterized by recurrent upper airway obstruction during sleep, resulting in intermittent hypoxia, sleep fragmentation, and excessive daytime sleepiness. Although mechanical interventions such as positive airway pressure and surgery are effective, pharmacological options remain lacking. This is partly due to limited knowledge of the neurobiological circuits and molecular pathways regulating upper airway motor control. The hypoglossal motor nucleus (HMN), which innervates the genioglossus muscle, plays a central role in maintaining upper airway patency. Here, we aimed to identify novel therapeutic targets for OSA through a combination of brainstem and peripheral tissue multi-omics profiling, and human genetic analyses.

Materials and methods: A rat model of OSA was established via chronic intermittent hypoxia (CIH) exposure. We performed single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics on the HMN and genioglossus muscle to characterize cellular heterogeneity and spatial gene expression dynamics under hypoxic stress. Targeted neurotransmitter-focused metabolomic profiling was conducted on serum samples of human and rat model to evaluate systemic and local neuroendocrine alterations.

To translate these findings to human populations, we integrated data from the UK Biobank Pharma

Proteomics Project and conducted two-sample Mendelian randomization (MR) analysis using cis-acting protein quantitative trait loci (pQTLs) to test for causal associations between circulating proteins and OSA risk. Sensitivity analyses included reverse MR and Bayesian colocalization to validate causal direction and genetic co-regulation.

Results: Multi-omics profiling revealed significant upregulation of corticotropin-releasing hormone receptor (CRHR) in the HMN and genioglossus muscle following CIH exposure. Spatial transcriptomics confirmed localized CRHR expression enrichment in motor regulatory nuclei. Metabolomic analyses indicated CRHR-linked dysregulation of neuroendocrine and energy metabolism pathways, potentially impairing upper airway neuromuscular responsiveness.

Mendelian randomization analysis identified a significant causal relationship between genetically predicted circulating CRHR levels and increased OSA susceptibility (inverse variance weighted odds ratio > 1.0, $p < 0.001$). Reverse MR analysis excluded reverse causality, and Bayesian colocalization supported a shared genomic architecture between CRHR-regulating variants and OSA-associated loci. Ongoing functional validation using central and peripheral CRHR agonists/antagonists in CIH-exposed rats further suggests a modulatory role of CRHR in genioglossus excitability and upper airway stability during sleep.

Conclusions: This study provides convergent evidence from central and peripheral transcriptomics, metabolomics, and human genetic analyses identifying CRHR as a mechanistically relevant and pharmacologically actionable target in OSA. By implicating CRHR in the regulation of hypoglossal motor outflow and upper airway dilator muscle tone, our findings lay the groundwork for future therapeutic strategies aimed at restoring neuromuscular control in sleep-disordered breathing.

Multi-Tier Evaluation for Obstructive Sleep Apneics undergoing Maxillomandibular Advancement

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Introduction: Maxillomandibular advancement (MMA) has been the most effective surgical option in reducing AHI (apnea-hypopnea index). Despite the high success rate, the long-term and cure rates remain low. Pre-surgical evaluations of craniofacial anatomy, cephalometry, and nasopharyngoscopy may provide information on craniofacial structures and airway dimensions. Polysomnographic indices show the physiological presentation. However, the correlation between structure and physiological indices is scarce. In this study, we tried to find a clinically feasible model to conduct sophisticated and comprehensive pre-surgical evaluation by organizing a multi-tier pre-surgical evaluation for adult OSA patients. In addition to the gold standard of polysomnography, commonly used tools include clinical craniofacial evaluation, 2D/3D photo analysis, 2D/3D cephalometry and airway dimension measurements, computational fluid dynamics study, and drug-induced sleep (sedative) endoscopy. The purpose of this study was to identify the feasibility of multi-tier pre-surgical evaluation and its correlation to surgical simulation of MMA and the polysomnographic outcomes.

Materials and methods: A retrospective review was conducted on 30 OSA patients undergoing multi-tier pre-surgical evaluation, computer-aided surgical simulation and MMA. Craniofacial anatomical evaluation, cephalometric measurements from 2D/3D radiographs, and nasopharyngoscopic evaluation under local and general anesthesia were reviewed. Combining with polysomnographic indices, the correlation between the evaluation and surgical outcomes was tested.

Results: On average, the maxilla(at A point) and the mandible(at B point) were advanced 4.0 ± 2.9 mm and 13.2 ± 3.7 mm, respectively. After surgery, generally, SNA and SNB increased $3.7 \pm 3.2^\circ$ and $6.3 \pm 2.0^\circ$, respectively. Apnea-Hypopnea Index (AHI) was significantly reduced from $39.6 \pm 24.7/\text{hr}$ to $4.0 \pm 7.0/\text{hr}$. Surgical success was 100% for females and 93.2% for males. Intra-luminal obstruction leads to the priority of obstruction removal by intra- or extra-pharyngeal obstructive soft tissue resection. Pharyngeal airway dimensions observed during awake/sedative/anesthesia and sitting/supine were correlated with polysomnographic indices before and after surgery.

Conclusions: Through multi-tier pre-surgical evaluations, we may obtain a comprehensive assessment to connect anatomy to sleep physiology and build a rational treatment plan for individual patients.

Next-Generation Hypoglossal Nerve Stimulation Therapy for the Treatment of Obstructive Sleep Apnea

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Introduction: Hypoglossal nerve stimulation (HGNS) is a proven therapy for moderate to severe OSA patients who struggle with CPAP. The next-generation Inspire HGNS System (Inspire V) is designed to simplify the procedure by including sensing technology within the IPG and eliminating the sense lead. It is also designed to provide enhanced patient comfort and more efficient patient management with new features including therapy ramp duration and smaller amplitude step sizes. This study includes implant and follow-up of the first worldwide implants of this new-generation HGNS technology.

Materials and methods: First implants and activations of this new technology occurred in a prospective, multicenter study of 44 patients in Singapore, who are being followed to 6 months post-therapy activation. Baseline and medical history were collected for all participants. Implant information including duration of implant (from first incision to last closure) was reported and compared to implant times from the previous generation (which included implantation of a sense lead). Inspiration Phase Overlap Percent (IPOP) was measured by in-lab PSG. The objective of this measure is to demonstrate non-inferiority of inspiratory overlap with Inspire V compared to previous generations of the Inspire system. Therapy use after activation of the therapy was reported at 3 months post-implant. Adverse events were also collected.

Results: A total of 44 participants (88.6% male; mean age: 55.68±10.24 yrs; baseline AHI: 36.97±15.23; baseline BMI: 26.91±2.75) were implanted with the Inspire V system between September 2024 and February 2025. No unexpected adverse effects have been reported at or after implant of the systems. Implant times decreased by 20.4% compared to implant of the previous HGNS system. At the 3 months' visit, ramp duration (5/10/15 min) was reportedly utilized in 25% of patients to provide support for comfort and/or insomnia. The smaller amplitude step size was reportedly utilized in 12% of patients, specifically to support comfort while the patient is acclimating to therapy. Results of IPOP are pending and will be available at the time of presentation. Mean therapy use at 3 months post-activation (n=30) is 6.0±1.67 h/nt.

Conclusions: The next-generation HGNS technology provides more efficient implantation as well as features that can be employed to increase patient comfort and utilization.

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Niacin infusion suppresses free fatty acids in individuals with obstructive sleep apnea and prediabetes: Insights from an ongoing mechanistic study

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Introduction: Obstructive Sleep Apnea (OSA) has been strongly linked with impaired glucose metabolism independently of obesity, but underlying mechanisms remain to be elucidated. It is well recognized that increased adipose tissue lipolysis, i.e., excess free fatty acids (FFAs), can lead to insulin resistance and glucose intolerance. In OSA, FFAs have been reported to be elevated. We hypothesize that excess FFAs induced by OSA lead to insulin resistance and glucose intolerance. Here, we present findings from an ongoing mechanistic study in individuals with prediabetes and moderate-to-severe OSA studied under experimental sleep conditions. We use continuous niacin (i.e. vitamin B3) infusion as a tool to suppress lipolysis to interrogate the role of excess FFAs and downstream metabolic impairments in OSA.

Materials and methods: Individuals with OSA and prediabetes were studied under three in-lab conditions in random order using a within-subject crossover design with a 4-week washout period between study conditions: (a) untreated OSA (i.e., Baseline), (b) 5 nights of continuous positive airway pressure (i.e., CPAP) treatment of OSA, (c) continuous niacin infusion (i.e., Niacin) overnight through the end of metabolic testing on the following day. On the final day of each condition, all subjects underwent an isotope tracer-based oral glucose challenge with frequent blood sampling to assess insulin sensitivity and glucose dynamics. Post-challenge FFA suppression was calculated from the area-under-the-curve (AUC; trapezoidal rule) from glucose ingestion until the nadir FFA values. Plasma FFA

concentrations were measured via enzyme-based colorimetric Wako non-esterified fatty acid kits. Comparison across conditions was performed using linear mixed effect models with a Kenward-Roger small sample adjustment. In this preliminary analysis, no adjustment for multiple comparisons was made.

Results: Findings are reported from all available data in a total of 16 subjects (age: 48 ± 11 years, BMI: 34 ± 6 kg/m²). Mean fasting FFA levels (overall $p < 0.0001$) were suppressed with Niacin ($n = 11$) by ~58% compared to Baseline ($n = 13$) and by 54% compared to CPAP ($n = 14$) ($p < 0.0001$ for both), but CPAP did not differ from Baseline ($p = 0.298$). Post-challenge AUC FFA (overall $p < 0.0001$) was suppressed with Niacin by ~51% compared to Baseline ($p < 0.0001$) and by ~42% CPAP ($p = 0.001$). CPAP treatment reduced post-challenge AUC FFA by ~18% compared to Baseline ($p = 0.051$). Additional data analysis on glucose metabolism (e.g., insulin sensitivity) derived from isotope-tracer based minimal models is ongoing.

Conclusions: Niacin suppressed both fasting and post-challenge FFA levels in individuals with OSA and prediabetes. For the first time in OSA patients, these findings show that Niacin can be an effective tool to suppress lipolysis to interrogate the mechanistic role of FFAs in impaired glucose metabolism in OSA. The complete dataset from this study will provide mechanistic insights into how OSA can directly impair glucose metabolism and inform future treatment strategies.

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Nicotine Use and Sleep Architecture in Postmenopausal Women with Obstructive Sleep Apnea

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Introduction: Previous literature suggests that nicotine use and postmenopausal status contribute to decreased sleep quality and increased risk of sleep disorders, particularly obstructive sleep apnea (OSA). Hormonal changes during menopause are believed to influence fat distribution and respiratory stability during sleep, increasing susceptibility to obstructive sleep apnea (OSA). In addition to hormonal factors, lifestyle and physiological variables such as smoking and body mass index (BMI) have been identified as critical contributors to the onset and severity of sleep apnea in this population. However, there is little research on the combined effects of nicotine use and postmenopausal status on sleep architecture. This study seeks to explore whether nicotine affects sleep architecture among postmenopausal women with OSA. It also explores whether there is an interaction between nicotine exposure and body mass index (BMI) in influencing sleep.

Materials and methods: A retrospective cohort study was conducted on 32 postmenopausal women diagnosed with OSA with and without a history of smoking from a community clinic. Body mass index (BMI), history of diabetes, and smoking status and history were collected. Comprehensive sleep metrics were recorded for each participant through an overnight polysomnography, including time spent in bed, percentage of wakefulness, light sleep (% N1 and % N2), deep sleep (% N3), REM sleep, and total sleep time (TST).

A student t-test was used to compare sleep parameters between postmenopausal women with and without a history of smoking. Multiple linear regression analyses were performed to assess whether BMI modified the relationship between smoking and sleep outcomes.

Results: Although there were no statistically significant differences (all $p > 0.05$), there was a trend in which postmenopausal women with a history of smoking had shorter TST compared to those without a history of smoking. The smoking group had a mean TST of 6.38 ± 1.51 hours, whereas the non-smoking group averaged 7.11 ± 0.69 hours ($t(29) = -1.86$, $p = 0.0725$). The multiple linear regression analyses examining the effect of BMI and nicotine use on sleep parameters failed to demonstrate significance (all $p > 0.05$).

Conclusions: In this study, nicotine use and BMI was not significantly associated with changes in sleep architecture in postmenopausal women. There was a trend in which postmenopausal women with a history of smoking had a shorter TST, suggesting that there may be a subtle effect that could not be detected due to the small sample size which limited statistical power. Further research is warranted to

explore the association between nicotine use and sleep architecture in postmenopausal women across multiple geographic and clinical settings to increase generalizability.

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Nighttime Light Exposure Predicts Higher Sleep Apnea Risk: A Prospective Study with Explainable Machine Learning

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Introduction: Nighttime artificial light is an increasingly prevalent environmental exposure that may affect sleep health. However, its role in the development of sleep apnea remains underexplored. We investigated the longitudinal association between objective nighttime light exposure and incident sleep apnea, and evaluated its relative contribution and independence using explainable machine learning.

Materials and methods: A total of 84,774 adults (62.43 ± 7.82 years; 55.0% female) without sleep apnea at baseline were included. Nighttime light exposure was derived from seven-day wrist-worn actigraphy recordings and categorized into quartiles. Incident sleep apnea was identified from hospital and primary care records. Cox proportional hazards models were used to estimate hazard ratios (HRs) with sequential adjustment for demographic, behavioral, and clinical covariates. An XGBoost-based survival model with SHapley Additive exPlanations (SHAP) was further used to assess the relative importance and interaction profile of each predictor.

Results: Over a median of 9.3 years (total 773,025 person-years), 802 participants were diagnosed with sleep apnea. Participants exposed to ≥ 32.5 lux at night (upper quartile) had a 36% higher risk of developing sleep apnea compared to those exposed to ≤ 1.4 lux (lowest quartile) (HR=1.36; 95% CI: 1.07–1.73; $p_{\text{adj}} = 0.032$). SHAP-based interpretation demonstrated that nighttime light exposure was among the predictors included in the cumulative 90% of total model importance, based on mean absolute SHAP values across all 23 covariates. Compared to other top predictors such as BMI category and physical activity, which exhibited stronger interaction patterns (maximum SHAP interaction strength = 0.05), nighttime light showed minimal interaction with other covariates (maximum = 0.02). Along with non-significant results from likelihood ratio tests for interaction terms with age, sex, chronotype, diet, and physical activity (all $p_{\text{adj}} > 0.05$, respectively), these findings support the independent and robust role of nighttime light exposure in predicting sleep apnea risk.

Conclusions: Nighttime light exposure is a robust and novel predictor of sleep apnea risk. Further studies are needed to determine whether nighttime light exposure can serve as a modifiable environmental target for sleep apnea prevention.

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Non-contact On-device Detection of Obstructive Sleep Apnea from Infrared Video

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Introduction: Despite growing demand for accessible sleep monitoring, traditional polysomnography (PSG) remains limited by high cost, discomfort, and poor feasibility for long-term use. Alternative sensor-based and wearable solutions often suffer from compliance issues, noise sensitivity, and limited generalizability. In contrast, video-based methods offer a non-contact, user-friendly approach for assessing respiratory patterns and sleep position. However, existing methods require high computational resources, strict recording conditions, and lack validation on large-scale datasets. We propose **SIAction**, a non-contact, on-device system for continuous obstructive sleep apnea (OSA) monitoring using infrared video.

Materials and methods: *SIAction* captures the full sleep environment via a wall-mounted infrared camera and processes data locally to ensure privacy. The system was developed and evaluated using the **Korea Video Sleep Study (KVSS)** dataset, comprising 936 overnight recordings (over 5,000 hours) from three institutions. Each video is synchronized with PSG annotations, and facial regions are anonymized. Through analysis, we identified respiratory arousals (RAs)-brief cortical arousals following apnea or hypopnea episodes, typically accompanied by distinctive movements-as reliable visual markers of disordered breathing. *SIAction* detects RA events and sleep positions every 30 seconds using a unified four-class deep learning model. A regression model then estimates the apnea-hypopnea index (AHI), which is used to classify OSA severity (normal, mild, moderate, severe) and determine positional OSA (POSA) by comparing supine and non-supine AHI values.

Results: *SIAction* was trained on 70% of 475 recordings from Hospital A, with 15% used for validation and 15% for testing. It outperformed both video- and signal-based baselines across all tasks. For AHI estimation, it achieved a Spearman correlation of 0.91, mean absolute error of 9.31, and R^2 of 0.76. Based on the estimated AHI, the system achieved a macro F1 of 87.93 for OSA screening ($AHI > 15$) and 61.67 for severity classification. It reached 100% relaxed accuracy, where predictions within one adjacent severity level are considered correct. For POSA classification, macro F1 was 70.87. All processing is performed on-device. The system runs in real time on a \$120 Jetson Nano using only the CPU, processing each 30-second epoch in 16 seconds. Raw video is discarded after processing, retaining only diagnostic results to preserve privacy. The model trained on Hospital A generalized well to external test sets from Hospitals B (205 recordings) and C (110 recordings), confirming strong cross-institutional robustness.

Conclusions: *SIAction* demonstrates that RA-driven, position-aware video analysis enables accurate and efficient OSA monitoring without physical contact or cloud-based processing. Running in real time on a low-cost, on-device system, it ensures both privacy and scalability for home and clinical use. Trained on a large, diverse dataset and validated across institutions, *SIAction* offers a practical, generalizable alternative to PSG for long-term, non-intrusive sleep apnea assessment.

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Nonlinear Associations Between AHI, Hypoxemia, and Cardiometabolic Risk: The Xiangya SDB Cohort study from mainland China

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Introduction: Sleep-disordered breathing (SDB) has been associated with cardiovascular and metabolic diseases; however, limited research has explored the relationship between the severity of sleep apnea and comorbidities in individuals with a high apnea-hypopnea index (AHI), particularly when oxygen saturation-related parameters are considered.

Materials and methods: We include individuals from The Xiangya SDB Cohort Study(I) who completed sleep monitor at the Sleep Medicine Center of Xiangya Hospital of Central South University from January 1, 2016 to December 31, 2023. Also, related electronic medical records of demographic characteristics and relevant comorbidity diagnoses were extracted. The severity of OSA was evaluated

using the AHI and the percentage of total sleep time spent with oxygen saturation <90% (T90). Restricted cubic spline (RCS) analysis, logistic regression models, and k-means clustering were employed to assess the association between OSA severity and the prevalence of cardiometabolic comorbidities, including hypertension (HTN), coronary heart disease (CHD), heart failure (HF), atrial fibrillation (AF), cerebrovascular disease (CeVD), and diabetes mellitus (DM).

Results: A total of 7,631 individuals aged 18 years or older with suspected sleep apnea were selected from The Xiangya SDB Cohort Study, among whom 4,383 were suspected to have obstructive sleep apnea (including 3,816 with confirmed OSA and 567 without SDB). After adjusting for confounding factors, a nonlinear association was observed between AHI and the prevalence of HTN, CHD, and CeVD. Further analysis showed that when AHI <40, there was a positive association between AHI and HTN (OR: 1.012; 95% CI: 1.002–1.021). However, when AHI ≥40, AHI was negatively associated with HTN (OR: 0.992; 95% CI: 0.985–0.999), CHD (OR: 0.988; 95% CI: 0.979–0.997), AF (OR: 0.978; 95% CI: 0.963–0.993), and CeVD (OR: 0.989; 95% CI: 0.979–0.999). K-means clustering of suspected OSA patients using AHI and T90 identified three clusters: low-AHI, high-AHI/low-T90, and high-AHI/high-T90. In the high-AHI/low-T90 group, AHI remained negatively associated with HTN (OR: 0.987; 95% CI: 0.979–0.996), CHD (OR: 0.986; 95% CI: 0.976–0.997), AF (OR: 0.968; 95% CI: 0.951–0.984), and CeVD (OR: 0.989; 95% CI: 0.978–1.000). In contrast, within the high-AHI/high-T90 group, T90 showed a negative effect on comorbidities: HTN (OR: 0.988; 95% CI: 0.976–0.999), CHD (OR: 0.968; 95% CI: 0.949–0.988), and HF (OR: 0.966; 95% CI: 0.941–0.992). When using AHI of 40 and T90 of 25 as cutoff values to classify suspected OSA patients into low-AHI, high-AHI/low-T90, and high-AHI/high-T90 groups, the results were consistent with the cluster-based approach.

Conclusions: Our findings suggest a nonlinear association between AHI and the prevalence of OSA-related comorbidities. Among individuals with severe OSA (AHI ≥40), the severity of OSA exhibited a paradoxical inverse association with several comorbid conditions, and T90 of 25 may serve as a useful threshold for subgroup classification in this population. These results highlight the need for a more nuanced classification of patients with high AHI, beyond the conventional AHI-based stratification, to better identify those at elevated risk for cardiovascular and metabolic comorbidities in clinical settings.

Nrf2 Pathway Activation: A Neuroprotective Strategy Against ER Stress-Mediated Apoptosis in Obstructive Sleep Apnea

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Introduction: Chronic intermittent hypoxia (CIH), a hallmark of obstructive sleep apnea (OSA), is a major contributor to pediatric cognitive impairment, partly through endoplasmic reticulum stress (ERS)-mediated apoptotic pathways. While Nrf2 signaling is renowned for conferring neuroprotection in models of neurological disease, the involvement of this pathway in mitigating ERS-associated apoptosis and modulating antioxidant responses specifically in CIH-challenged prefrontal neurons requires further elucidation.

Materials and methods: This research examined the influence of Nrf2 on cognitive impairment and mechanistic pathways triggered by CIH, employing both cellular (PC12) and animal (4-week-old male C57BL/6 mice) models. Nrf2 signaling was modulated via specific activation and inhibition protocols to evaluate its function in CIH-mediated neuropathology. Y-maze testing assessed cognitive function. Morphological alterations indicative of damage were visualized by light and electron microscopy. Protein abundance was determined using Western blotting (WB) and immunofluorescence assays.

Results: In PC12 cells modeling OSA-related neuronal injury, chronic intermittent hypoxia (CIH) exposure significantly induced endoplasmic reticulum stress (ERS) and subsequent apoptosis. This was demonstrated by upregulation of ERS markers (p-PERK, ATF4, CHOP) and apoptotic markers (cleaved Caspase-3). Concurrently, CIH activated the antioxidant system via elevated expression of Nrf2, HO-1, and Gclc. Pharmacological activation of Nrf2 by sulforaphane (SFN) attenuated CIH-induced apoptosis through suppression of ERS signaling and enhanced HO-1 expression. Conversely, the Nrf2 inhibitor ML385 exacerbated these effects.

In a murine CIH model, 4-week exposure impaired spatial learning and memory in Y-maze tests. Histological analysis revealed increased neuronal apoptosis in the prefrontal cortex, marked by elevated cleaved Caspase-3 and Nrf2 pathway activation. SFN treatment mitigated cognitive deficits

and neuronal apoptosis by inhibiting ERS signaling and upregulating HO-1. In contrast, Nrf2 inhibition produced opposing outcomes.

Conclusions: Collectively, our data indicate that Nrf2 activation attenuates CIH-induced cognitive impairment by suppressing neuronal apoptosis through inhibition of the PERK-ATF4-CHOP pathway and upregulation of HO-1 expression.

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Obstructive Sleep Apnea and Medical Comorbidities in the Asian Population: Evidence From a Nationwide Healthcare System Data in South Korea

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Introduction: Obstructive sleep apnea (OSA) is a breathing disorder characterized by recurrent airway obstruction during sleep. Previous western studies have investigated the link between medical disorders and the pathophysiology of OSA. The prevalence and comorbidity rates of OSA; however, vary across different countries and racial groups. This study aimed to delve into medical comorbidities in patients with OSA using a large nationwide healthcare database in Korea.

Materials and methods: This nationwide study used the Korean National Health Insurance claims database (2010-2019). The effect of OSA on the incidence of medical disorders was estimated using the Cox proportional hazard ratio (HR) model. The results were reported as crude and adjusted HRs with 95% confidence intervals (CI). Subgroup analysis was conducted by sex and age.

Results: In total, 103,785 patients with OSA and 207,570 patients without OSA were included. OSA group had significantly higher HRs for ischemic heart disease and stroke even after adjusting for hypertension, dyslipidemia, and diabetes. The OSA group also showed an increased risk of metabolic syndrome-related diseases, chronic kidney disease, and gastroesophageal reflux disease. Female patients with OSA exhibited notably higher rates of comorbid liver cirrhosis, chronic obstructive pulmonary disease, and asthma. The cardiovascular burden of patients increased in accordance with the patients' age.

Conclusions: Korean patients with OSA have a significantly increased risk of cardio-cerebrovascular diseases, which aligns with the previous studies conducted in the western countries. This result holds particular significance as it represents the first nationwide, population-based study conducted in Asia.

Obstructive Sleep Apnea and α -Synucleinopathies: Nationwide Analysis from South Korea's Healthcare Database

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Introduction: Obstructive sleep apnea (OSA) is increasingly acknowledged for its correlation with systemic health issues, notably neurodegenerative diseases. This study assesses the association between OSA and α -synucleinopathies, focusing on Parkinson's disease (PD), Parkinson's disease dementia (PDD), and Dementia with Lewy Bodies (DLB), and highlights the influence of demographic factors.

Materials and methods: A retrospective cohort study on 103,785 OSA patients and matched controls was conducted using data from South Korea's National Health Insurance claims database from 2010 to 2019. We investigated the incidence of PD, PDD and DLB in OSA patients, applying chi-square tests, t-tests, and a multivariable logistic regression model to calculate adjusted odds ratios (AOR), with further subgroup analysis by sex and age.

Results: Analysis showed that OSA patients had significantly higher odds ratio for PD (AOR of 2.166, 95% CI: 1.84-2.549, $p < .0001$) and DLB (AOR of 4.001, 95% CI: 1.501-10.66, $p = 0.0056$). Subgroup analysis revealed a stronger association of PD and DLB with OSA in males, with an increased risk in those over 60 years of age.

Conclusions: The study indicates a significant association between OSA and an increased risk of PD and DLB, underscoring the critical role of demographic factors. These insights advocate for enhanced monitoring and tailored management of OSA, especially in patients at higher risk of neurodegenerative diseases, and pave the way for future research into the progression and therapeutic management of these conditions.

Obstructive sleep apnea in the general population - A very common, serious, but treatable chronic condition

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent and multifactorial disorder, strongly associated with other chronic conditions. However, whether population-level screening and treatment of OSA is feasible remains uncertain. This study aimed to estimate the prevalence of moderate to severe OSA in a well-defined, middle-aged general population and to evaluate the feasibility of identifying and treating OSA through population-based screening.

Materials and methods: Icelandic participants in the multinational Burden of Obstructive Lung Disease (BOLD) study were invited to undergo home sleep apnea testing (HSAT). Participants with an apnea-hypopnea index (AHI) ≥ 15 events/hour were offered clinical evaluation. Those who were symptomatic and interested in treatment were referred for positive airway pressure (PAP) treatment.

Results: Of the 378 individuals invited to screening, only 18 declined. Another 26 had a prior OSA diagnosis. A total of 334 (55% male) completed a technically adequate HSAT. Among them, 132 (39.5%) had an AHI ≥ 15 events/hour. Of these, 126 underwent clinical evaluation, and 96 were referred for PAP treatment. Compared to the 30 individuals not referred, the PAP-treated group was younger, had higher mean AHI (30.2 vs. 20.2 events/hour), and a greater prevalence of cardiometabolic comorbidities. PAP initiation and follow-up adhered to standard clinical protocols, although some procedures were modified due to the COVID-19 pandemic. Eleven individuals discontinued PAP within the first three months, and according to hospital records, another 24 had quit by two years. At the two-year follow-up, all 96 were re-invited; 43 were no longer using PAP, while 53 remained long-term users. Among them, 24 had used PAP for more than four hours per night on average in the previous 30 days. Long-term PAP users were more likely to be male and had a higher mean BMI at baseline (32 vs. 30 kg/m²).

Conclusions: Undiagnosed OSA affects approximately one-third of the general middle-aged population. Most individuals identified through screening accepted clinical evaluation and found PAP treatment a feasible option. Long-term adherence to PAP therapy was comparable to routine clinical settings. These findings suggest that population-based OSA detection, clinical management and PAP treatment are achievable goals, with approximately half of those identified with OSA becoming long-term PAP users – corresponding to 15% of the general population.

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Obstructive sleep apnea is associated with sympathetic overactivation in non-elderly but not elderly

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Introduction: Obstructive sleep apnea (OSA) has been noted to associate with sympathetic overactivation. Our previous studies have shown that OSA predicted increased risk of incident hypertension, but the strength of their association significantly decreases with age. We hypothesized that OSA was associated with sympathetic overactivation in non-elderly but not elderly.

Materials and methods: We consecutively recruited adults with OSA from the Sleep Disorders Clinic of Shantou University Mental Health Center. The elderly were defined as age>50 years. The sympathetic activity was assessed by 24-hour urinary norepinephrine. Blood pressure was measured manually in the evening prior to PSG and in the morning right after PSG, with their mean values used for statistical analyses. Interaction terms of age*Time under 90% of SpO₂ [T90], and subgroup of age were introduced to determine the different association between OSA and sympathetic overactivation among patients with different ages. Mediation effect models were used to explore the association between OSA, sympathetic overactivation, and blood pressure in patients with different ages.

Results: A total of 166 OSA patients were included with a mean age of 45.51±10.33 years. Each 1-hour increase in T90 was significantly associated with 4.76-μg increase in 24-hour urinary norepinephrine ($\beta=0.29$, 95%CI=2.30~1.21, $p<0.001$) with adjustment of age, sex, body mass index, hypertensive medication, and REM%. Interestingly, the interaction terms of T90*age and T90*elderly were significant ($p=0.002$ and 0.017). Among the non-elderly, each 1-hour increase in T90 was associated with 6.36-μg increase in 24-hour urinary norepinephrine ($\beta=0.37$, 95%CI=3.41~9.31 $p<0.001$), 3.43-mmHg increase in SBP ($\beta=0.39$, 95%CI=1.84~5.03, $p<0.001$) and 2.99-mmHg increase in DBP ($\beta=0.44$, 95%CI=1.80~4.20, $p<0.001$), whereas such associations were not evident among elderly (all $p\geq0.667$). Mediation effect models showed that the 24-hour urinary norepinephrine significantly mediated the association between T90 and SBP with mediation effect of 13.41%, as well as DBP with mediation effect of 7.67% among non-elderly but not elderly. Consistent findings were also observed in the sensitivity analyses with AHI as independent variable replacing T90.

Conclusions: OSA is associated with sympathetic overactivation in non-elderly but not elderly. Early assessment and intervention should be especially warranted in non-elderly OSA patients.

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Obstructive Sleep Apnea (OSA): Do symptoms correlate with severity?

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Introduction: Obstructive Sleep Apnea (OSA) is a common sleep disorder characterized by recurrent partial or complete airway obstruction during sleep. The gold standard method for diagnosis of OSA remains polysomnography (PSG). Cost, limited certified personnel and availability of sleep labs necessitate alternate measures to diagnose OSA. Previous studies have shown a poor correlation between OSA severity and its classic symptoms, such as snoring, witnessed apneas (WA) excessive daytime sleepiness (EDS) and daytime fatigue (DF). This study aims to compare these symptoms across different OSA severities and examine any potential correlation in Indian ethnicity.

Materials and methods: This is a retrospective study involving patients diagnosed with OSA from a tertiary sleep center during the years 2023 and 2024. Data including demographic details, Apnea hypopnea index (AHI), and Epworth Sleepiness Scale (ESS) were collected. These patients were questioned regarding symptoms they experienced which included snoring, WA, EDS, DF. Responses to symptoms were recorded as "Yes", "No", or "Not recorded". Correlations between AHI severity and clinical parameters were done.

Results: Of the 1142 patients diagnosed with OSA, 888 were males (77.7%) and 254 were females (22.3%). There were 274 patients with Mild OSA, 299 patients with Moderate OSA, 569 patients with severe OSA. Snoring was reported by all patients regardless of OSA severity. Assessment of correlation of demographic features with severity of OSA revealed that age was significantly different between the groups except for moderate versus severe. BMI also showed significant correlation with severity of OSA, though there was no difference between mild and moderate OSA. Using logistic regression, EDS, DF, WA had a sensitivity of 90.6% and precision of 0.524 to predict the presence of Mild or Moderate OSA, a 99.8% sensitivity and 65.7% precision for predicting Moderate or Severe OSA, and 100%

sensitivity and 67.7% precision for predicting Mild or Severe OSA. However, ordinal regression showed that a model including all the four symptoms was not a good fit. ESS and WA were the only symptoms which remained significant when expecting likelihood of severity of OSA.

Conclusions: The study indicates that while there is not a uniform correlation between the severity of OSA and reported symptoms such as EDS, DF, and WA, there is a noticeable trend of increased symptom reporting amongst the severe OSA cohort. The findings suggest that older individuals and those with a higher body mass index (BMI) are more likely to experience more severe forms of OSA. The study also highlights the limited precision in the current methods used to assess OSA severity, re-emphasizing the need for more objective diagnostic tools, such as PSG, to provide more accurate and comprehensive diagnosis.

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Obstructive sleep apnea (OSA) –The Iceberg In The Sea Of Comorbidities

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Introduction: Obstructive Sleep Apnea (OSA) is the second most common sleep disorder, affecting nearly 1 billion adults worldwide.³ The AASM's recent campaign rightly emphasizes that *OSA is more than a snore!*⁴ OSA is often the hidden contributor to diabetes, hypertension, dyslipidemia, stroke, AF, insomnia, depression, GERD, asthma, cognitive decline, and RLS.

Materials and methods: Five life-changing OSA cases transformed by PAP therapy

- **Case 1 (ComOSAR; OSA + RLS/PLMS):** A 73-year-old overweight female with hypertension, Bronchial asthma, pulmonary hypertension, and depression exhibited persistent symptoms despite PAP therapy. Repeat PSG showed severe OSA (AHI 33.9/hr), poor sleep efficiency, PLM index 128/hr, and labs showed iron deficiency. This presentation aligns with *ComOSAR*⁵, observed in ~24% of OSA patients.
- **Case 2 (MS + OSA):** A 66-year-old obese female with stable multiple sclerosis and incidental MCA aneurysm presented with dyspnea; PSG revealed moderate OSA (AHI 21.7/hr). OSA commonly worsens MS symptomatology—including fatigue, cognition, and quality of life.
- **Case 3 (UARS):** A 35-year-old obese female with daytime somnolence, tachycardia, idiopathic intracranial hypertension, and empty-sella syndrome showed mild OSA on Level 1 PSG (AHI 13.3/hr) but a Level 3 study revealed 1,575 flow-limited breaths, diagnostic of *Upper Airway Resistance Syndrome (UARS)*—a condition producing significant sleep fragmentation and daytime dysfunction despite low AHI .
- **Case 4 (Fibromyalgia + Parasomnias):** A 60-year-old obese female with fibromyalgia, rhinitis, and parasomnias exhibited severe OSA (AHI 53/hr). BiPAP titration (IPAP 14/EPAP 10 cm H₂O) resolved sleep paralysis, hypnopompic hallucinations, and significantly reduced fibromyalgia fatigue within a month.
- **Case 5 (OSA-related AF):** A 41-year-old obese hypertensive surgeon with paroxysmal atrial fibrillation and severe OSA (AHI 32/hr) showed a reduction in arrhythmias from 73→24 events on CPAP and further to 12 on BiPAP (IPAP 17/EPAP 12 cm H₂O), with complete apnea resolution

Results: PAP therapy demonstrated profound, system-wide benefits:

1. **ComOSAR:** Resolution of PLMS and RLS symptoms, improved sleep efficiency and PAP adherence—critical as coexistence of OSA and RLS correlates with higher insomnia, cognitive, metabolic, and psychiatric comorbidity .
2. **MS + OSA:** Reduction in daytime fatigue and cognitive load, with enhanced quality of life.
3. **UARS:** Significant decreases in flow-limited breathing episodes and daytime dysfunction following targeted CPAP therapy.

4. **Chronic pain & parasomnias:** Rapid cessation of sleep disturbances and reduction in fibromyalgia-induced fatigue, paralleling research showing PAP benefits in chronic pain conditions.
5. **Cardiovascular:** Substantial reduction in atrial arrhythmias; literature supports a ~30–40% reduction in AF recurrence with PAP therapy, due to improved oxygenation, reduced sympathetic activity, and attenuation of atrial remodeling.

Conclusions: PAP therapy not only treats sleep-disordered breathing—it also mitigates neurophysiological disturbances, chronic pain, and cardiovascular comorbidities. Proactive screening and management of OSA is essential in populations with MS, ComOSAR, and AFib to enhance overall health and quality of life.

Acknowledgments: References:

3. Surani S, Taweessedt P. *Obstructive Sleep Apnea: New Perspective*. Medicina (2023).
4. AASM campaign: “OSA is more than a snore.”
5. Gothi D, et al. Prevalence of RLS in OSA and consequences of co-occurrence (*Lung India*, 2023 Jul); ComOSAR concept endorsed

Obstructive sleep apnea prevalence and underlying mechanisms in young individuals with post-traumatic stress disorder symptoms

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Introduction: Obstructive sleep apnea (OSA) has been reported to occur in ~75% of people with PTSD. Most prior studies have assessed military populations who commonly have other OSA risk factors. The aims of this study were to determine whether 1) OSA is more common in individuals with PTSD symptoms exposed to non-military traumas as compared to individuals without PTSD symptoms; and 2) the ventilatory response to arousal from sleep - an OSA endotypic trait - differs according to PTSD symptoms.

Materials and methods: 61 individuals with a range of PTSD symptoms (PTSD symptom checklist for DSM-5, PCL-5) completed an overnight sleep study. OSA prevalence and the ventilatory response to arousal were compared between those with likely PTSD (PCL-5 >33 plus intrusions and Criterion A trauma exposure), sub-syndromal PTSD (PCL-5 = 15-33 plus intrusions and Criterion A trauma exposure) and No-PTSD (PCL-5 <15 and no intrusive symptoms).

Results: Data from 52 participants (36 female) have been analysed: 17 with likely PTSD, 12 sub-syndromal PTSD and 23 No-PTSD. The 3 groups were comparable in age (25±7 years), sex (69% women) and BMI (24.1±4.3 kg/m²). In total, 7 participants had OSA; 4 in the Likely PTSD group, 2 in the sub-syndromal group and 1 in the No-OSA group. The ventilatory response to arousal was assessed in the participants without OSA and found to be significantly larger in individuals with likely and sub-syndromal PTSD as compared to the No-PTSD group (Peak response = 178±17%, 193±23% and 124±8% respectively, ANOVA interaction $p < .001$).

Conclusions: The prevalence of OSA in a young mixed-trauma PTSD population is not as high as that observed in military populations. However, the ventilatory response to arousal is elevated in PTSD and sub-syndromal PTSD, which may predispose to OSA when other risk factors are present such as older age or elevated body mass.

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Obstructive Sleep Apnea Syndrome and Recurrent Vasovagal Syncope: Insights from a Multicentric Observational Study

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Introduction: This study evaluates the impact of diagnosing and treating obstructive sleep apnea syndrome (OSA) on the frequency of recurrent vasovagal syncope (RVS) episodes in OSA patients with comorbid RVS.

Materials and methods: A multicentric interventional observational study was conducted in patients with both OSA and recurrent RVS. Patients underwent CPAP therapy for a minimum of 12 months. The frequency of RVS episodes (with (LC+) and without (LC-) loss of consciousness), quality of life, and polysomnographic parameters, during the 6 months prior to CPAP initiation and during the last 6 months before the follow up visit after CPAP, were assessed.

Results: A total of 27 patients (66.7% female; mean age 42.1 ± 12.8 years; mean BMI 25.6 ± 3.5 kg/m²; mean AHI 22.2 ± 12.1 events/hour) completed 12 months CPAP therapy. The frequency of RVS episodes significantly decreased following treatment. The LC+ declined from 25.7 ± 38.6 to 17.7 ± 40.3 ($p < 0.05$), and LC- dropped from 39.7 ± 78.6 to 9.3 ± 8.5 ($p < 0.05$). CPAP therapy was also associated with significant improvements in daytime sleepiness (Epworth Sleepiness Scale: 9.3 ± 6.5 to 3.9 ± 5.7 , $p < 0.01$), fatigue (Pichot Scale: 16.0 ± 9.8 to 3.9 ± 5.1 , $p < 0.001$), and percentage of patients with positive depression scores (35.3% to 9.1%, $p < 0.001$). No statistically significant changes were observed in heart rate variability or 24-hour blood pressure parameters.

Conclusions: CPAP therapy significantly reduces RVS recurrence in patients with OSA, suggesting that OSA is a modifiable risk factor for RVS. These findings highlight the importance of OSA screening in patients with unexplained syncope. Randomized controlled trials are required to mitigate potential bias of the results due to the observational study design.

Obstructive Sleep Apnea Treatment Regulates Monocyte Inflammatory Phenotype and Function

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Introduction: Obstructive sleep apnea (OSA) is associated with chronic intermittent hypoxia and systemic inflammation, contributing to vascular and metabolic complications. Monocytes, as key mediators of innate immunity, have been implicated in this inflammatory state. However, the effect of OSA treatment on monocyte function and inflammatory phenotype remains poorly understood.

Materials and methods: In this prospective cohort study, OSA patients were evaluated before and after 4 months of continuous positive airway pressure (CPAP) therapy. Circulating monocytes were isolated, and inflammatory cytokine production (TNF- α , IL-1 β , IL-6) was assessed at baseline and post-treatment, both at rest and after LPS stimulation. Monocyte subset distribution (M1/M2) was evaluated by flow cytometry. Clinical severity parameters such as the apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) were correlated with immune changes.

Results: CPAP therapy significantly reduced serum levels of TNF- α and IL-1 β and attenuated LPS-induced cytokine responses. A shift in monocyte phenotype toward an anti-inflammatory M2 profile was observed. These changes were significantly associated with baseline ODI, but not with AHI. Patients with higher ODI showed greater reductions in cytokine levels and more pronounced monocyte reprogramming after CPAP treatment.

Conclusions: CPAP alleviates systemic inflammation in OSA by reducing hypoxic burden and reprogramming monocytes toward an anti-inflammatory phenotype. The magnitude of immune modulation was more closely linked to ODI than AHI, supporting the use of hypoxemia-based metrics for identifying inflammation-prone OSA endotypes and guiding personalized therapy.

Obstructive Sleep Apnoea (OSA) and Continuous Positive Airway Pressure (CPAP): Experience of Chinese Patients in Australia

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Introduction: People of Chinese ethnicity have physiological vulnerabilities for Obstructive Sleep Apnoea (OSA) resulting in high disease prevalence and increased burden of cardiometabolic consequences. While Continuous Positive Airway Pressure (CPAP) therapy is the treatment of choice, treatment engagement among Chinese patients is often suboptimal. Cultural and systemic influences may shape treatment experiences in this group, however, remain under-researched. As such, this study aims to explore the beliefs, experiences, and attitudes towards OSA management from the perspectives of patients of Chinese ethnicity.

Materials and methods: Semi-structured interviews were conducted in a convenience sample of Chinese Australian participants using CPAP treatment for OSA. Participants first completed an online questionnaire and were given an option to be interviewed about their illness and treatment experiences. The interviews were conducted in English or Mandarin depending on participant's preference, recorded, transcribed verbatim and analysed using the Framework Approach to identify emergent themes.

Results: Of 32 returned surveys, 26 participants (mean age 55.1, SD 13.4 years; range 36-81 years, 54% male) were eligible and completed interviews. Eighty-one percent were first-generation immigrants, and 23% of interviews were conducted in Mandarin. The mean duration of CPAP use was 7.7 years (SD 6.6 years), whilst mean duration from diagnosis was 8.9 years (SD 6.9 years). Preliminary analyses unveiled four key themes: disease recognition; help seeking; treatment initiation/acceptance, and ongoing management. Limited awareness of OSA as a medical condition, failure to associate common symptoms with the disease, and notable stigma surrounding OSA and CPAP therapy, were identified as prominent themes that may delay help seeking. Cultural norms such as the perception of snoring as normal, along with influences from family members and social networks, impacted treatment-related decision-making and behaviours. Sustained CPAP use was driven by perceived treatment benefits and fear-based motivation. Lack of systematic follow-up after CPAP initiation, lack of perceived need for follow-up, and uncertainty about appropriate contacts for follow-up were identified as challenges with ongoing disease management.

Conclusions: Findings highlight the need for culturally sensitive education to improve OSA awareness and reduce stigma within Chinese communities. Involving family members or social networks in treatment discussions and emphasising OSA comorbidities and treatment benefits may improve engagement. Scheduled follow-up and ongoing management may support long-term CPAP adherence and reduce attrition.

Opioid-related Central Sleep Apnea Not Detrimental to Key Respiratory and Sleep Parameters: Results from the OpSafe Multicentre Trial

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Introduction: Opioid-related central sleep apnoea (CSA) is increasingly common, but its clinical implications are poorly understood. Without clear evidence of adverse outcomes, sleep physicians find it difficult to make treatment decisions regarding opioid-related CSA. We analyzed the "OpSafe" (Opioid Safety Program in Pain Clinics) cohort, a large prospective multicenter study of chronic opioid users, to investigate whether opioid-related CSA worsens key respiratory and sleep outcomes.

Materials and methods: Participants on a stable opioid dose for chronic pain were recruited from five university-affiliated tertiary care pain clinics. Measurements included resting daytime oxygen saturation (SpO₂), Epworth Sleepiness Scale (ESS), and overnight in-lab polysomnography (PSG). PSGs were analyzed for sleep-disordered breathing, oxygenation parameters, sleep architecture and quantitative electroencephalography (qEEG).

Results: A total of 160 participants were divided into three groups: 21 CSA, 66 obstructive sleep apnea (OSA), and 73 no-apnea. CSA participants had ~4 times higher opioid dose and exhibited a ~3% lower daytime SpO₂ than OSA and no-apnea participants (all $p < 0.001$). However, during sleep, oxygenation

measures were similar between CSA and OSA groups (all $p > 0.2$). Comparing daytime SpO_2 to sleep mean SpO_2 , OSA group decreased significantly (95.1 ± 1.9 vs $93.9 \pm 2.1\%$, $p = 0.001$), no-apnea group moderately dropped (95.9 ± 1.9 vs $95.1 \pm 2\%$, $p = 0.05$), whereas CSA group had no change in oxygen saturation (92.9 ± 3.4 vs $93.5 \pm 2\%$, $p = 0.66$). CSA event duration was significantly shorter than that of OSA (15.6 ± 4.1 vs 19.4 ± 6.8 seconds, $p = 0.005$). CSAs primarily occurred during non-rapid eye movement (NREM) sleep, with the REM CSA index being a third less than the NREM index [$7.9(1.7-13.9)$ vs $27.7(10-50.1)/hr$, $p < 0.001$]. Sleep architecture and arousal indices in CSA patients were normal except for a reduced REM sleep linked to higher opioid doses. During REM sleep, while CSA was rare, the CSA group exhibited significantly higher Sigma, Alpha and Theta power than the OSA and no-apnea groups. Conversely, during NREM sleep, where CSA predominantly occurred, none of those qEEG band powers significantly differed among the three groups. We also found positive correlations between higher opioid doses and increased Sigma, Alpha, and Theta power during REM sleep. Furthermore, CSA was not a significant predictor of daytime sleepiness, explaining only 1.5% of the variance of ESS. In contrast, opioid dose was a significant predictor of daytime sleepiness.

Conclusions: Our novel findings showed that opioid-related CSA did not worsen key respiratory and sleep outcomes. Instead, it may act as a compensatory response through an augmented hypoxic ventilatory responses/loop gain to counteract opioids' central depressant effects. Opioid-related CSA would diminish if the respiratory depression were resolved, usually through reducing the opioid dose. While a positive airway pressure therapy could potentially improve daytime sleepiness in some chronic opioid users by alleviating hypercapnia, hypoxia, and co-existing OSA, this mechanism is unlikely through treating CSA. While it is essential to mitigate respiratory depression, targeted therapies to reduce opioid-related CSA may be unnecessary.

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Opioids-Related Modulation of Nocturnal Cardiac Autonomic Responses to Apneas and Hypopneas

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Introduction: Heart rate (HR) responses to sleep-related breathing interruptions, such as apneas and hypopneas, reflect autonomic arousal and are linked to cardiovascular risk. Opioids, commonly prescribed for chronic pain, may alter these responses, potentially increasing cardiovascular vulnerability. This study investigated the impact of chronic opioids therapy on heart rate responses to respiratory events during sleep and examined sex-specific differences.

Materials and methods: In this preliminary retrospective case-control study, we analyzed sleep electrocardiogram (ECG) recordings from 20 individuals (≥ 18 years, 10 female) receiving chronic opioids therapy for > 3 months with stable daily dosing for at least 4 weeks. For each opioids-treated participant, 2 matched controls were selected from the Sleep Heart Health Study database using Mahalanobis distance matching based on age, sex, and body mass index (BMI), excluding individuals with major comorbidities. Respiratory events were annotated by sleep physicians following the American Academy of Sleep Medicine guidelines. ECG segments spanning 10 seconds before the start and 10 seconds after the end of each respiratory event were preprocessed, and R-peaks were extracted. All peak detections were visually validated, and segments with unreliable peak detection were excluded. Two outcome measures were used to evaluate heart rate responses to respiratory events: 1) HR_{post} , defined as the average heart rate during the 10 seconds following the end of respiratory event, and 2) HR_{diff} , defined as the difference between HR_{post} and the average heart rate during the 10 seconds preceding the end of the respiratory event. A linear mixed-effects model was used to assess the effect of opioids use on HR responses (HR_{post} , HR_{diff}), accounting for multiple respiratory events per individual and adjusting for sex, age, and BMI. Additional sex-stratified analyses were performed to evaluate sex-specific effects. P-value of 0.05 was considered statistically significant.

Results: The study population had a mean age of 54.7 ± 8.4 years and BMI of 31.7 ± 6.9 kg/m² with no significant difference between individuals with and without opioids therapy (age: 53.5 ± 9.0 vs. 54.9 ± 7.7 years, $p = 0.582$; BMI: 31.9 ± 7.7 vs. 31.8 ± 6.6 kg/m², $p = 0.972$). The average daily opioids dose among treated participants was 201.4 ± 207.5 morphine milligram equivalents. Our results showed that opioids therapy and female sex were independently associated with significantly higher HR_{post} , with

increases of 6.0 bpm and 5.7 bpm, respectively (both $p = 0.014$). In sex-stratified analyses, HR_{post} increase was more pronounced among men (+9.1 bpm, $p = 0.005$), whereas among women the estimated increase was smaller (+3.1 bpm) and not statistically significant ($p = 0.386$). While HR_{diff} did not differ significantly in the overall sample, men using opioids exhibited a significantly greater HR change following respiratory events (+1.15 bpm, $p = 0.047$), in contrast to women, who showed a non-significant reduction (-0.93 bpm, $p = 0.178$).

Conclusions: Chronic opioids therapy is associated with elevated post-event heart rate during sleep, particularly among men, suggesting sex-specific modulation of autonomic cardiac responses to respiratory events. Characterizing these alterations may provide insight into mechanisms underlying opioids-related cardiovascular risk and inform safer clinical management strategies for individuals using opioids.

Oscillometric Lung Function and Its Association with Obstructive Sleep Apnea Risk

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Introduction: Obstructive sleep apnea (OSA) is a sleep disorder characterized by repeated episodes of upper airway blockage during sleep, leading to apnea or hypopnea. An apnea is defined as a episode as a reduction in airflow of $\geq 90\%$ lasting at least 10 seconds. A hypopnea is defined as a reduction in airflow of $\geq 30\%$ lasting at least 10 seconds and associated with a $\geq 4\%$ decrease in pulse oxygenation. Collapse or narrowing of the upper airway during sleep is OSA patient can increase resistance airflow in the upper airway. Oscillometry provides a non-invasive comprehensive assessment of lung function by analyzing airway resistance, reactance, and compliance. This multi-dimensional approach allows for detecting abnormalities in the peripheral airways. Oscillometry is a method used to assess upper airway resistance by applying small pressure oscillations to the airway during normal breathing. It measures respiratory system impedance, which includes airway resistance (Rrs) and reactance (Xrs). In OSA patients, increased upper airway resistance, usually in the supine position, can be detected using oscillometry.

Materials and methods: A total of 262 subjects aged 40 years and older were included in this study. The risk of OSA was determined using the STOP-Bang questionnaire, which evaluates clinical parameters including snoring, tiredness during daytime, observed apnea, and high blood Pressure-body mass index, age, neck circumference, sex. Pulmonary function was assessed and evaluated using an oscillometry. Subjects were categorized into low-risk and high-risk groups for OSA. Statistical analyses were performed using independent t-tests and chi-square tests, with a p-value < 0.05 considered statistically significant.

Results: There was no significant difference in age between the groups. High-risk subjects for OSA were more likely to be male ($p = 0.02$), have a higher BMI ($p < 0.05$), and a larger neck circumference ($p < 0.05$). Smoking was also more common in the high-risk group ($p = 0.03$). Comorbidities such as diabetes, cardiovascular disease, and kidney disease were significantly more prevalent in the high-risk group. Oscillometry parameters and respiratory patterns showed no significant differences between the groups.

Conclusions: Individuals at high risk for OSA had significantly higher BMI, neck circumference, smoking prevalence, and comorbid conditions. However, oscillometry findings did not differ between the risk groups, suggesting that respiratory impedance may not be a sensitive marker for differentiating OSA risk.

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Oximetry-based devices in diagnosis of obstructive sleep apnea: a systematic review and meta-analysis

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Introduction: Obstructive sleep apnea (OSA) is a common disorder, associated with significant morbidity and mortality. Polysomnography (PSG) or a home sleep apnea test (HSAT) is required for OSA diagnosis. Recently, several oximetry-based devices have been developed to assist with diagnosing OSA. This study aims to evaluate the diagnostic performance of these oximetry-based devices compared to PSG.

Materials and methods: We performed research in MEDLINE, EMBASE, Google Scholar, and Lilacs databases. We included studies that evaluated oximetry-based devices in comparison to PSG for OSA diagnosis in adults. Selected studies were divided into two subgroups: consumer wearable devices and medical devices.

Results: A total of 18 studies were included in the analysis, with 4 studies in consumer wearable devices subgroup and 14 studies in medical devices subgroup). The overall sensitivity was 97% (95% Confidence Interval [CI]: 96 – 97%) and specificity was 63% (95% CI: 61 – 65) of oximetry-based devices for OSA diagnosis. In the consumer wearable devices subgroup, sensitivity was 93% (95% CI: 90 – 96) and specificity was 63% (95% CI: 53 – 71). In the medical devices subgroup, sensitivity was also high as 97% (95% CI: 96 – 97) with a specificity of 63% (95% CI: 61 – 65). The summary area under the curve was 0.90 and the estimated post-test probability was 90%.

Conclusions: Oximetry-based devices have high sensitivity and high post-test probability but low specificity in adults at high risk for OSA diagnosis. Further research is necessary to assess these devices, particularly wearable ones, especially in low-risk individuals and those with comorbidities.

PAP titration in patients with OSAS and depression: more difficult, more variable and more complex

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Introduction: It has been known for 20 years that 21% of adults with depression also suffer from OSAS. Jens Acker and colleagues showed in 2017 that of 322 patients with a polysomnographic AHI of > 9/hour, 21.5% also suffer from clinically significant depression. Conversely, 23.7% of psychiatric patients were found to have OSAS when measured polygraphically in German psychiatric clinics (Behr et al. 2018). The effects on PAP therapy have so far been based primarily on the clinical impression of a more difficult handling of depressed patients.

Materials and methods: We compared OSAS parameters and PAP therapy in 203 patients with OSAS and clinically relevant depression with 125 OSAS patients without psychological comorbidity. All patients underwent an adjustment night with manual PAP titration followed by a first control night with fixed pressure measurement. The entire procedure took place on the same day for the patients in the control group as for the respective patients in the depression group in order to avoid bias due to different practitioners (MTAs and physicians). Depression was considered clinically significant if at least one antidepressant was taken at clinically relevant doses. Antidepressants or antipsychotics in only sleep-improving doses (19.7%) are not considered as an antidepressant medication.

Results: The groups did not differ in terms of age (56.2 ± 11.9 vs 57.3 ± 11.2 years), gender, BMI (33.8 ± 7.8 vs 32.83 ± 5.9), ESS (8.4 ± 4.3 vs 7.6 ± 4.1), AHI (30.2 ± 19.9 vs 32.2 ± 22.1), desaturation index or other OSAS parameters before the start of treatment. Patients with comorbid depression reported significantly more frequent sleep onset difficulties (45.8 vs 23.2%) and took additional sleep medication more often (19.7 vs 3.2%); sleep maintenance difficulties were equally distributed.

PAP therapy was initiated in 90 (44.5%) of patients with depression and in 69 (54.4%) of control patients. Bilevel S titration was more frequent in patients with comorbid depression (41 vs 27 patients). Significantly more depressed patients discontinued treatment after the first night (8.5 vs 4.8%). There were also significantly more patients who underwent polysomnography to check their PAP pressure (e.g. drivers, n=67 vs 42) who were fitted with a bilevel S device (16.4 vs 7.1%). In cases of inadequate PAP therapy on the night of recruitment, 5 patients (4%) in the control group were mostly (80%) switched to bilevel ST/ASV or NIV. In patients with OSAS and depression (n=24, 11.8%), these switches were much more variable. For example, 37.5% switched to bilevel ST, 33.3% to bilevel ST/ASV or NIV and a further 25% switched back from bilevel ST to CPAP/APAP.

Conclusions: Sufficient PAP therapy is much more difficult to achieve in patients with comorbid depression than in patients without concomitant psychiatric illness. Switching to a different PAP modus after one night of measurement was three times as common. Depressed patients therefore require much more time and material resources in the sleep laboratory. A single night of adjustment is not sufficient. A second subsequent night with the possibility of a change in therapy modus including a new practice phase on the day before the second night is necessary.

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Pathway for bariatric/metabolic surgery candidates with obstructive sleep apnea(OSA) at a private Hospital in Brazil

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Introduction: Obstructive sleep apnea (OSA) is highly prevalent among individuals undergoing bariatric or metabolic surgery (MBS). Studies estimate that over 85% of patients with class III obesity suffer from OSA, highlighting the importance of addressing this comorbidity to reduce surgical risks, particularly respiratory complications, and improve long-term health outcomes. Developing specialized management strategies that integrate care for both obesity and OSA is vital for enhancing patient prognosis. One effective strategy involves the use of Continuous Positive Airway Pressure (CPAP) during the immediate postoperative period to prevent respiratory issues. However, surgeons often avoid using positive pressure in patients undergoing anastomoses in the upper digestive tract due to the risk of air swallowing, which could exert pneumatic pressure on the sutures.

Materials and methods: OSA evaluation begins during the initial medical consultation when MBS is proposed. This evaluation can be conducted by the patient's clinician (such as an endocrinologist, cardiologist, or other specialist) or the bariatric surgeon. The process incorporates standard diagnostic tools as well as specific questionnaires, namely the STOP-BANG questionnaire and the Epworth Sleepiness Scale(EES). Patients identified as having moderate or high risk for OSA are referred for Polysomnography (PSG) or Peripheral Arterial Tonometry (PAT). Those diagnosed with moderate to severe OSA immediately begin a CPAP adaptation program, which educates and trains patients to breathe using CPAP.

The typical preoperative preparation period for MBS lasts at least one month. During this time, medical, nutritional, psychological evaluations, as well as laboratory and imaging tests, are conducted. CPAP adaptation is seamlessly integrated into this timeframe, ensuring it does not prolong the preoperative preparation period.

Results: Patients who successfully adapt to CPAP therapy prior to surgery are encouraged to continue its use postoperatively. This approach minimizes complications such as aerophagia while effectively managing OSA. Follow-up appointments to adjust CPAP use are scheduled to coincide with the surgeon's routine check-ups, occurring at one, three, and six months after surgery. A follow-up PSG/PAT is performed six months postoperatively to reassess OSA status.

Conclusions: The collaborative efforts of a multidisciplinary team—including physicians, physiotherapists, dentists, nutritionists, nurses, and psychologists—enabled the creation of a comprehensive care pathway at HIAE. This initiative significantly reduces the risks for patients with OSA who are candidates for bariatric/metabolic surgery, thereby improving surgical outcomes and enhancing overall patient care.

Acknowledgments: Medical Sleep Assistance Group Hospital Israelita Albert Einstein(HIAE)/ GMA Department of Critical Care Medicine (CPAP Clinic) Hospital Israelita Albert Einstein

PFKFB3 Drives Endothelial Glycolysis, Promoting Vascular Injury under Obstructive Sleep Apnea

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Introduction: Metabolic-inflammatory crosstalk is a hallmark of cardiovascular pathogenesis. Obstructive sleep apnea (OSA), characterized by chronic intermittent hypoxia (CIH), is an independent risk factor for cardiovascular disease (CVD). While endothelial inflammation driven by CIH is pivotal in CVD progression, the metabolic drivers of this process remain elusive.

Materials and methods: The project included inflammatory and metabolic analyses of ECs under CIH exposure or plasma stimulation model, CIH mouse models, and bioinformatics.

Results: We identified phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (PFKFB3), a key glycolytic activator, was markedly upregulated in ECs exposed to CIH exposure or OSA plasma stimulation, correlating with a metabolic shift characterized by enhanced glycolysis, suppressed mitochondrial respiration, and amplified inflammatory responses. Endothelial-specific PFKFB3 deficiency or pharmacological suppression of PFKFB3 restored the glycolytic balance and attenuated inflammatory responses. Mechanistically, CIH enhanced the expression of hypoxia-inducible factor 1 α (HIF1 α), which directly stimulated PFKFB3 by binding to its promoter, while PFKFB3 overexpression further amplified HIF1 α levels. Targeting the HIF1 α -PFKFB3 axis alleviated the inflammatory and glycolytic signatures of ECs.

Conclusions: Collectively, our findings identified PFKFB3 as a critical driver of endothelial inflammation fueled by abnormal glycolysis under CIH, offering novel insights into the vascular pathophysiology of OSA-related cardiovascular diseases and potential intervention targets.

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Phenotypic and Anatomical Predictors of OSA Severity: Insights from DISE procedure

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Introduction: Obstructive sleep apnea (OSA) severity and treatment responsiveness may depend on the anatomical sites of upper airway collapse. Drug-induced sleep endoscopy (DISE), employing the VOTE classification (Velum, Oropharynx, Tongue base, Epiglottis), offers real-time visualization of these patterns. This study examined how VOTE-defined collapse correlates with apnea-hypopnea index (AHI), hypoxic burden, and clinical phenotypes.

Materials and methods: We retrospectively analyzed 186 adults with OSA who underwent DISE and polysomnography. Each VOTE site was scored from 0 (no collapse) to 2 (complete collapse). Multivariable linear and gamma regressions assessed predictors of AHI and hypoxic burden, with anatomical scores and body mass index (BMI) as covariates. Logistic regressions identified demographic predictors of high collapse (score ≥ 1). K-means clustering (k=5) categorized phenotypes based on anatomical and polysomnographic metrics. Jaw-thrust responses during DISE were assessed in 182 patients.

Results: Velum and oropharyngeal collapse were strongly associated with disease severity. Patients with complete velum collapse (V=2) spent approximately 25 minutes with SpO₂ <90%, compared to under 3 minutes for V ≤ 1 . Oropharyngeal collapse (O=2) was linked to a mean AHI of 42/h, compared to 23/h for O=0. In multivariable models, oropharyngeal collapse ($\beta=5.1$, $p=0.001$) and BMI ($\beta=0.83$, $p=0.003$) emerged as the strongest predictors of AHI ($R^2=0.38$). Velum and oropharyngeal scores significantly predicted hypoxic burden, with each point increase associated with a 25–32% longer desaturation duration ($p<0.01$). Age was a significant predictor of high velum and oropharyngeal collapse (OR 1.06–1.07/year), BMI predicted high velum collapse (OR 1.11), and male sex predicted tongue-base collapse (OR 1.9). Five phenotypic clusters were identified: mild velar, classic oropharyngeal, pan-collapse severe, epiglottic curious, and mixed. Jaw-thrust improved airway patency in 90% of patients. Tongue-base collapse was the only independent predictor of a successful jaw-thrust response (OR 1.69, $p=0.03$), although response rates were consistently high across all phenotypes.

Conclusions: This study demonstrates that anatomical sites of collapse distinctly influence OSA physiology: the oropharynx drives AHI severity, while velar collapse predominantly impacts oxygen desaturation. Demographics such as age, BMI, and sex shape anatomical vulnerability. DISE-based phenotyping highlights the heterogeneity of OSA and supports stratified treatment planning. Jaw-

thrust success, particularly in tongue-base collapse, reinforces the relevance of mandibular advancement simulations.

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Polycystic Ovary Syndrome is associated with Masked Hypertension in Reproductive-Aged Women: Role of Obstructive Sleep Apnea

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Introduction: Women with polycystic ovary syndrome (PCOS) face increased cardiovascular disease risk earlier than others. This study aimed to identify abnormal blood pressure(BP) profile in patients with reproductive-aged PCOS compared to matched controls, and determine whether OSA contributes to elevated blood pressure and masked hypertension in patients with PCOS.

Materials and methods: The study finally included 176 reproductive-aged women who scheduled to receive firstly assisted reproductive technology (ART), including 111 patients with PCOS according to the Rotterdam criteria and 65 controls matched age and BMI, from reproductive center of Peking University People's Hospital between July 2023 and October 2024. All participants underwent standard office BP measurements, and overnight home sleep apnea test (HSAT) by NOX-T3 device before ART cycle, followed by 24-hour ambulatory blood pressure monitoring (ABPM) the next morning. ANCOVA and generalized linear models compared groups in 24-hour BP readings, multivariate linear regression examined links between OSA severity and BP measurements, and logistic regression assessed the relationship between OSA and masked hypertension and its component, all adjusting for confounders such as age, BMI, central obesity, HOMA-IR, and DM.

Results: Women with PCOS demonstrated higher rates of masked hypertension (daytime and 24-hour hypertension) compared to matched controls (3.1% vs. 18.0%, $P=0.018$; 4.6% vs. 17.1%, $P=0.044$), even after adjusting for HOMA-IR factor. This cardiovascular risk profile was accompanied by a markedly higher prevalence of OSA in the PCOS cohort (44.1% vs. 20.0%, $P<0.001$), with a mean AHI of 7 events/hour. Within the PCOS group, we observed a dose-response relationship between OSA severity and the prevalence of masked hypertension and its components (all $P<0.01$). Multivariate regression analysis confirmed that AHI was positively correlated with ambulatory BP measurements, including 24-hour, daytime, and nocturnal systolic/diastolic BP ($\beta = 0.56, 0.34, 0.49, 0.31, 0.77, 0.45$, respectively; all $P<0.001$), and it also as a significant risk indicator for masked hypertension in PCOS patients (adjusted $P<0.05$). Using the clinically relevant threshold of $AHI \geq 10$ events/hour, OSA was associated with substantially increased risks of masked hypertension, including daytime hypertension (aOR=8.20, 95% CI: 1.74-38.62, $P=0.008$), and 24-hour hypertension (aOR=6.33, 95% CI: 1.39-28.90, $P=0.017$). A similar trend was observed for nocturnal hypertension, though this did not reach statistical significance (aOR=3.31, 95% CI: 0.91-12.03, $P=0.069$). Importantly, differences in 24-hour BP profiles between PCOS and non-PCOS groups disappeared entirely when patients with OSA were excluded from the analysis.

Conclusions: Women with PCOS exhibit higher 24-hour BP levels and increased rates of masked hypertension compared to matched controls, primarily mediated by OSA. This finding strongly suggests that OSA may be a key contributor linking PCOS to abnormal blood pressure regulation and increased cardiovascular risk in reproductive-aged women.

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Polysomnographic Diagnosis of Obstructive Sleep Apnea in Patients Presenting with Insomnia Symptoms: A Retrospective Observational Study

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Introduction:

Insomnia and obstructive sleep apnea (OSA) frequently co-occur, and in some cases, OSA may be the underlying aetiology of insomnia. However, this overlap is often under-recognised, particularly when patients present primarily with difficulty initiating or maintaining sleep. Misdiagnosis or missed diagnosis may result in delayed or suboptimal treatment. This study aims to assess the prevalence of OSA in patients referred for insomnia symptoms and to evaluate the utility of overnight polysomnography (PSG) in this population.

Materials and methods:

We conducted a retrospective observational study at Sleep Therapeutics, an advanced sleep medicine center located in Hyderabad, Telangana, India. A total of 166 adult patients who underwent overnight PSG between July 2023 and June 2025 were included. All patients presented with primary complaints of sleeplessness either sleep onset issues or sleep maintenance issues or both. OSA was diagnosed using standard criteria with an apnea-hypopnea index (AHI) ≥ 5 . Gender-specific prevalence and other PSG parameters were analysed.

Results:

Of the 166 patients assessed, OSA was diagnosed in 66.2% of males and 33.8% of females. These findings demonstrate that a significant proportion of individuals presenting with insomnia symptoms had undiagnosed OSA, and they were treated as having insomnia for a long period. Additional parameters-including sleep latency, sleep efficiency, arousal index, respiratory disturbance index (RDI), oxygen desaturation index (ODI), and reasons for arousals-revealed notable disruptions in sleep architecture. These findings will be detailed in the accompanying poster.

Conclusions:

A substantial number of patients with insomnia symptoms were found to have underlying OSA on PSG. These results underscore the importance of considering OSA in the differential diagnosis of insomnia in cases who present with complaints of sleeplessness. PSG should be recommended not only in chronic or refractory insomnia cases but also during initial evaluations when patients report minimal improvement with conventional insomnia therapies.

Acknowledgments: I acknowledge the support of Sleep Therapeutics, Hyderabad, India, my team who support me everyday, and the patients whose participation made this study possible.

Positional Obstructive Sleep Apnoea: When and Why the Neck-based Vibrotactile Device Fails

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Introduction:

The efficacy of positional therapy with a neck vibrotactile device for positional obstructive sleep apnoea (POSA) has been demonstrated, but its inefficacy in changing body position has not been equally explored. The primary aim of this study was to evaluate the failure rate of the neck vibrotactile positional therapy in POSA. Secondary aims were: to investigate the reliability of a single night sleep study for labelling a supine sleeper, any differences on supine time between the laboratory and the home environment, the impact of the device on snoring and the compliance.

Materials and methods: A retrospective observational study reviewed patients with a diagnosis of POSA according to Cartwright and who had received monitoring and/or treatment with a Night Shift™ (NS) Sleep Positioner neck device for 4 nights in Monitor or Therapy mode or both. The diagnosis of POSA was made on respiratory polygraphy or polysomnography and a minimum supine sleep time of 15% was required. A supine sleeper was defined if supine sleep time at home was $> 5\%$ at least in 2 nights of neck vibrotactile device in Monitor mode. Failure was defined as continuous vibration time ≥ 5 minutes and a supine time $> 5\%$ in at least 2 nights.

Results: Ninety two adult patients were enrolled. The failure rate, restricted to 74 patients who had received the neck vibrotactile device in Therapy mode for ≥ 2 nights, was 14.8%, with a compliance rate of 96%. Non-supine sleepers at home were 13/74 (17.5%). A significant reduction of supine sleep time at home was observed in comparison with the diagnostic sleep study (23.9% vs 51%, $p < 0.001$).

Snoring rate was significantly reduced while using the vibrotactile device in Therapy mode versus Monitor mode.

Conclusions: Considering the failure rate of the device in changing body position, and the rate of patients that at home spontaneously do not sleep in supine position, around 32% of positional therapy prescribed might be inappropriate. An adequate trial with the neck vibrotactile device, in diagnostic and therapeutic modality, might disclose these cases. Main reasons for inefficacy are: sedatives, chronic sleep deprivation, motor limitations and cognitive impairment.

Acknowledgments: The statistical analysis was performed by Prof Rossella Baldini.

The idea of the project comes from the collaboration with Prof. Mauro Manconi, Dr Alessia Riglietti and the Sleep Team in Lugano.

Potential Markers of Brain Impairment Secondary to Obstructive Sleep Apnea: The Brain Asymmetry

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Introduction: Obstructive sleep apnea (OSA) is one of the leading causes of sleep disorders and often exhibits psychological impairments. Brain asymmetry (BA) is an important marker of psychological traits. OSA is strongly associated with brain activity and psychological disorders. And BA alterations could be observed in people with psychological disorders and motivational abnormalities. Our previous studies have found that OSA exhibits elevated BA during both sleep and daytime, and is associated with psychological abnormalities. Unfortunately, there is no evidence to support whether BA is secondary change in respiratory events or individual heterogeneity. Therefore, this study aimed to explore BA patterns during peri-obstructive sleep apnea-hypopnea.

Materials and methods: A total of 71 subjects with symptoms of OSA, such as nocturnal snoring, frequent arousal, and daytime sleepiness, were recruited for polysomnography (PSG) at the Sleep Medicine Center of Beijing Tongren Hospital. Inclusion criteria included adults aged ≥ 18 years, while exclusion criteria included severe pulmonary, cardiovascular, or cerebrovascular diseases, history of metal implants in the head, pregnancy, or non-cooperation with the examination. PSG was conducted using the Grael device, and EEG signals were recorded from the frontal, central, and occipital regions. Respiratory events (apnea or hypopnea) lasting >15 seconds with intervals >20 seconds were extracted and analyzed for BA changes. Power spectral density (PSD) was calculated for delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-14 Hz), beta (14-30 Hz), and gamma (30-100 Hz) bands. Statistical analyses were performed using R software, and BA was assessed using the formula $\ln[\text{right}] - \ln[\text{left}]$.

Results: A total of 6445 respiratory events were extracted from 71 subjects, with 1265 events in N1, 3655 in N2, 62 in N3, and 1463 in REM sleep stages. BA was significantly elevated during respiratory events in the frontal and central regions, with a uniform pattern across frequency bands ($P < 0.0001$). In the occipital region, BA decreased during respiratory events and rose abruptly at the end of the event ($P < 0.001$). Subgroup analyses indicated that alpha, beta, and gamma bands were the main contributors to BA fluctuations. Non-severe and severe OSA exhibited similar trends in BA changes.

Conclusions: The findings suggest that respiratory events in OSA patients trigger bilateral cerebral asymmetry, with alpha, beta, and gamma bands playing a significant role in BA fluctuations. This study provides evidence that BA may serve as a marker and characteristic phenotype of brain impairment secondary to OSA, highlighting the causal relationship between sleep disorders and psychological disorders. Further research is needed to explore the implications of BA in the context of OSA-related cognitive and emotional impairments.

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Precision Oral Appliance Therapy :The Leading Non-surgical Alternative to CPAP in the treatment of OSA

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Introduction: In 1981, Dr Colin Sullivan in a landmark paper in the Lancet introduced CPAP for the treatment of Obstructive Sleep Apnea (OSA). Despite being labeled as the "gold standard", compliance has not improved significantly over the last 44 years. Precision Oral Appliance therapy has now emerged as the leading non-surgical alternative to CPAP. The latest studies and research will be reviewed in detail in support the improved effectiveness in Precision Oral Appliance Therapy compared to Oral Appliance Therapy in the past.

Materials and methods: This oral scientific session will review 15 clinical studies that involved 1431 patients over multiple clinical sites. This review is from studies utilizing Precision Oral Appliance Therapy for the treatment of all levels of severity in the treatment of OSA. The studies were conducted in the US Army, Portugal, Belgium, England and multiple clinical sites in the US. Success criteria utilized was the standard criteria utilized in determining surgical success (Sher's Criteria: >50% reduction in the AHI and/or AHI <20).

Results: 15 clinical studies involving 1431 patients across multiple sites showed a Mean Efficacy and Median Efficacy of 85% when utilizing the Sher's Criteria for surgical success. Patient compliance averaged 90% and side effects including jaw pain, tooth movement and TMJ dysfunction were minimal.

Conclusions: Despite the high "efficacy" of CPAP in the treatment of OSA, its real world "effectiveness" is compromised by poor compliance or adherence. While Precision Oral Appliance Therapy has lower efficacy than CPAP in the treatment of OSA, its "effectiveness" may be equal to or greater than CPAP when compliance is taken into account. Since mean disease alleviation and health outcomes show little difference between CPAP and Precision Oral Appliance Therapy these studies support an alternative treatment paradigm. Precision Oral Appliance Therapy may be now considered non-inferior to CPAP in all levels of severity of OSA with the results presented in this scientific oral presentation.

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Preclinical Evaluation of a Dual Target Neurostimulator Implant System for Obstructive Sleep Apnea at 34 Weeks

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Introduction: Neuromodulation for the treatment of obstructive sleep apnea (OSA) is an emerging alternative therapy to positive airway pressure. While hypoglossal nerve (HGN) stimulation solutions are commercially available, research into other nerve targets has identified the ansa cervicalis (AC) as a promising candidate for stimulation in combination with HGN stimulation. Recent acute human studies have demonstrated the ability to improve airway collapsibility when stimulating both targets independently and simultaneously. Here, we present chronic results up to 34 weeks (8.5 months) post-implant of an ongoing study to evaluate the stability of the Restera Dual Target Neurostimulator Implant System in a large animal model.

Materials and methods: One Yucatan minipig (male, 44 kg) was implanted with a prototype of the Restera Dual Target Neurostimulator Implant System (Restera, Inc., Santa Clara, CA, USA), comprising two leads tunneled to an implantable pulse generator (IPG). Both leads were percutaneously inserted under ultrasound guidance. Each lead had two stimulating electrodes and two sets of anchoring fins to provide mechanical stability at the distal end. The leads were deployed adjacent to the corresponding nerve target (either HGN or AC). Follow-up visits were performed under general anesthesia at 2, 4, 8, 11, 22, 26 and 34 weeks to assess stimulation thresholds based on airflow measurements using the SFM3300-D flow sensor (Sensirion AG, Stäfa, Switzerland). For each lead independently, the threshold was defined as the minimum current amplitude (in mA) required to induce contraction of the corresponding muscle (genioglossus or infrahyoid strap muscles) that restored airflow to eupneic levels. Starting from the 11-week visit, dual target stimulation at threshold values (or above) with duty cycle was continuously delivered in the absence of external flow support for about one hour to assess stability over extended periods of stimulation.

Results: Electrical stimulation delivered to electrodes of both leads successfully activated the target nerves. During implant surgery, 3-Hz stimulation led to observable twitching responses of the corresponding muscles, confirming appropriate electrode placement near the nerves. During implant

surgery and follow-up visits, 40-Hz tonic stimulation led to sustained muscle contraction and airflow improvement. Stimulation thresholds remained stable over a period of 34 weeks with values ranging between 1.5-3.5 mA at the HGN target and between 0.32-1.5 mA at the AC target. Extended dual target stimulation consistently resulted in sustained airflow improvement over the entire stimulation period at each follow-up visit.

Conclusions: The prototype system used in this ongoing study to stimulate HGN and AC nerve targets demonstrated appropriate stability for chronic therapy, evidenced by the sustained ability to improve anesthetized airflow through contractions of the genioglossus and infrahyoid strap muscles. Future clinical studies will investigate the applicability of the proposed therapy for human patients with OSA.

Acknowledgments: The study was approved by the Institutional Animal Care and Use Committee (IACUC) and supported by the veterinary staff of LabCorp.

Predictors of successful reduction in AHI after Yoga-based intervention for treatment of obstructive sleep apnea

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Introduction: Non-pharmacological interventions have been shown to improve obstructive sleep apnea (OSA) and result in a 30-40% reduction in the apnea-hypopnea index (AHI). Recently, yoga has emerged as a potential intervention for treating OSA; however, treatment responses vary among patients. The study aims to identify the predictors of effectiveness of yoga in reducing apnea-hypopnea index (AHI).

Materials and methods: We have merged the patient data from two randomized controlled trials who underwent yoga-based intervention for treating OSA. Patients who reduced their AHI by 40% or more (Group 1) on 6-month follow-up after a yoga-based intervention were considered treatment-responsive, while those with less than a 40% reduction in AHI (Group 2) were considered non-responsive to treatment. All baseline clinical and polysomnography parameters were compared between the responsive and non-responsive patients.

Results: Baseline data of 19 patients aged 47.21 ± 10.1 years, and 13 (68.42 %) were male, nine were responsive, and 10 were non-responsive and were included in the analysis. Mean 49.1 and $9 \pm 0.12\%$ AHI reduction occurred in the responsive and non-responsive groups. REM AHI was significantly higher among responsive patients ($64.62, \pm 38.55$ vs $25.36, \pm 15.84657$, $p=.03$). The mean baseline BMI was higher among non-responsive patients. However, there was a lack of statistical significance. (30.74 ± 3.99 vs 35.07954 ± 5.490883 , $p=0.07$). The number of patients with NREM-dominant OSA were significantly more common in Group 2 (11% vs 70%, $p=0.02$).

Conclusions: Morbid obesity and NREM-dominant obstructive sleep apnea (OSA) are predictors of a poor treatment response, and the severity of REM sleep apnea is a predictor of the effectiveness of yoga intervention in reducing apnea-hypopnea index (AHI).

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Predictors of surgical outcomes for limited palatal muscle resection in patients with obstructive sleep apnea

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Introduction: Limited palatal muscle resection (LPMR) is a modified palatal surgical technique to correct retropalatal obstruction without complications. This study aims to determine the associated factors affecting the success and cure rate of LPMR in patients with obstructive sleep apnea (OSA), thus guiding patient selection and improving surgical outcome.

Materials and methods: Thirty-five OSA patients underwent LPMR were enrolled. All patients received routine physical examination, preoperative drug-induced sleep endoscopy (DISE), and polysomnography (PSG). Clinical, polysomnographic, cephalometric variables, and DISE findings were evaluated. These measurements were compared between the surgical success and failure group based on the results of preoperative and postoperative PSG. Furthermore, we compared the cured and non-cured groups in the surgical success group.

Results: Among 35 patients, the overall success rate was 57 % with a cure rate of 31.4 %. Patients with Friedman stage II had a significantly higher success rate ($p = 0.032$). According to DISE results, tongue base obstruction affected the surgical outcome ($p < 0.001$). The success rate was 100 % in the no tongue base obstruction during DISE, 72.2 % in the partial obstruction, and 9.1 % in the total obstruction. Tonsil size is also helpful in predicting surgical success rate ($p = 0.041$). Furthermore, patients with mild AHI were more likely to be surgical cures. when compared with patients with severe AHI ($p = 0.044$).

Conclusions: Patients with larger tonsil size and no tongue base obstruction during DISE may have a higher chance of surgical success with LPMR. The lower AHI may be predictors of surgical cure after LPMR.

Acknowledgments: No

Preliminary study of the effects of Nortriptyline on OSA indices and snoring intensity in patients with OSA: a pilot study

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Introduction: Obstructive Sleep Apnea (OSA) is a common breathing disorder with long-term neurocognitive and cardiovascular consequences. Despite CPAP being the gold standard, many patients are intolerant. This has led to the exploration of alternative pharmacological therapies that can reduce obstruction by modulating the activity of respiratory muscles and neurotransmitters. Tricyclic antidepressants (TCAs), by blocking the reuptake of serotonin and norepinephrine, are among the drugs used. Nortriptyline, from this drug class, has the least affinity for muscarinic and histaminic receptors and has fewer side effects and is better tolerated compared to other drugs in this class. This pilot study investigates the effect of Nortriptyline on key OSA indices.

Materials and methods: This single-arm, open-label pilot study will recruit adult patients diagnosed with obstructive sleep apnea (OSA) [AHI > 15 on polysomnography (PSG)] who report intolerance or refusal to use continuous positive airway pressure (CPAP). Participants will receive oral nortriptyline 25 mg once daily, 30 minutes before bedtime, for a duration of four weeks. Feasibility will be assessed by recruitment and retention rates. Safety and tolerability will be monitored through adverse event reporting using the PRISE questionnaire and clinical assessments.

Preliminary efficacy will be evaluated by comparing changes from baseline to the end of the four-week treatment period in key OSA parameters measured by PSG, including the Apnea-Hypopnea Index (AHI), Arousal Index (Arl), and minimum oxygen saturation. Snoring intensity will be assessed using a Visual Analog Scale (VAS). Descriptive statistics will summarize patient characteristics, feasibility, and safety outcomes. Paired statistical tests will be used to explore potential changes in respiratory parameters and snoring intensity following nortriptyline administration. A sample size of 12 participants will be targeted to provide initial data for future controlled trials.

Results: In this study on 12 patients, after one month of treatment period, the mean Apnea-Hypopnea Index (AHI) decreased from 37.25 to 30.83 ($p=0.0026$). The mean score on the Epworth Sleepiness

Scale (ESS) decreased from 12.5 to 8.33 ($p=0.0001$). Also, the mean Sleep Efficiency (SE) improved from 73.83% to 87.75% ($p=0.0047$), which is considered a statistically significant change. In addition, the mean snoring intensity improved from 8.9 to 3.5, and the mean minimum blood oxygen saturation (Min SpO₂) improved from 82.41% to 83.33%.

Conclusions: The intervention improved sleep efficiency, reduced daytime sleepiness, and decreased the severity of sleep apnea and snoring. However, due to the small sample size, findings should be interpreted cautiously. Further investigation in larger trials is necessary to explore the effects of this intervention and its applicability to a wider population.

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Pressure Pays Off: Reducing Healthcare Burden in Moderate OSA with PAP Therapy

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Introduction: Obstructive sleep apnea (OSA) is a sleep-breathing disorder that can negatively impact daytime functioning, cardiovascular and pulmonary health, and quality of life when left untreated. Generally, the severity of OSA is determined by the apnea hypopnea index (AHI) where an AHI of 5-14.9 events per hour (e/hr) is mild, 15-29.9 e/hr is moderate, and greater than 30 e/hr is severe. Positive airway pressure (PAP) therapy is often recognized as first line treatment for OSA, yet globally there are differing requirements for determining a patient's eligibility to receive PAP. The aim of this study was to test the hypothesis that increased PAP therapy usage would be associated with reduced healthcare resource use and costs in a population of patients with moderate OSA.

Materials and methods: This was a retrospective cohort study conducted among patients with a sleep test (ApneaLink, Resmed) that diagnosed moderate OSA and initiated PAP therapy between March 2015 and October 2021. The sleep test and PAP therapy data were linked to administrative claims data through tokenization. Patients were required to have 1 year of data available prior to PAP initiation (index) and 2 years post. PAP adherence over 2 years was defined as adherent, intermediate, or non-adherent based on US Medicare criteria. Healthcare resource use was defined as occurrence of emergency room (ER) visits and hospitalizations. Healthcare costs were defined as total or associated with ER visits or hospitalizations. Inverse probability of treatment weighting was used to balance PAP adherence groups on baseline covariates.

Results: 9,157 patients met inclusion criteria, 38% were female, had an average age 52.5y and average AHI of 21.2 e/hr. 54.1% of patients had comorbid hypertension, 50.6% hyperlipidemia, 25.1% gastroesophageal reflux disease, 21.3% anxiety, 19.5% depression, and 18.5% type 2 diabetes. 77% were at least intermediately adherent to PAP therapy over 2 years (35% adherent, 42% intermediate, 23% non-adherent). Over 1 year, relative to non-adherence, adherent patients had a 19% lower risk for an ER visit (risk ratio (RR): 0.81, 95% confidence interval (CI): 0.73-0.90), 35% lower risk for hospitalization (RR: 0.65, 95% CI: 0.52-0.82), and lower total (US\$8,203 vs. US\$8,563, $p=0.004$), ER visit (US\$304 vs. US\$342, $p<0.001$), and hospitalization (US\$899 vs. US\$1,405, $p<0.001$) costs. Similarly, over 2 years, relative to non-adherence, adherent patients had a 13% lower ER visit risk (RR: 0.87, 95% CI: 0.80-0.94), 26% lower hospitalization risk (RR: 0.74, 95% CI: 0.62-0.87), and lower total (US\$16,116 vs. US\$16,364, $p=0.013$), ER visit (US\$624 vs. US\$705, $p=0.001$), and hospitalization (US\$1,968 vs. US \$2,474, $p=0.003$) costs. Resource use and costs for intermediately adherent patients generally fell between that of adherent and non-adherent patients.

Conclusions: This analysis supports the usage of PAP therapy in patients with moderate OSA to reduce the risk of hospitalization and ER visits and lower healthcare costs in the first 2 years of therapy. These insights should be used to raise awareness of the importance of assessing for and treating OSA in patients with moderate severity.

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Prevalence and characteristics of obstructive sleep apnea (OSA) comorbid with catathrenia (nocturnal groaning)

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Introduction: Catathrenia (nocturnal groaning) is a rare sleep-related breathing disorder, but the comorbidity of catathrenia with obstructive sleep apnea (OSA) is not uncommon. This study highlights the prevalence, clinical, polysomnographic, and craniofacial characteristics of this comorbidity to raise awareness in clinical practice.

Materials and methods: This study was conducted across two independent sleep centers, including 1,123 participants (741 males/382 females), with an average age of 46.3 ± 14.0 y. Patients were diagnosed using full-night video polysomnography (PSG) and acoustic analysis was conducted to classify snoring and groaning sounds using a deep convolutional neural network. The cluster analysis was conducted to analyze subgroups of catathrenia, and inter-group polysomnographic characteristics were investigated. Additionally, craniofacial cone-beam CT was performed to assess the upper airway and surrounding structures. Mandibular advancement devices (MAD) and positive airway pressure (PAP) were used as treatment, and their efficacy was evaluated using PSG.

Results: Among the 1,123 participants, 865 (77.03%) were diagnosed with OSA, with 78 (6.95%, 76 males/2 females) also having comorbid catathrenia. Conversely, only 10 (0.89%, 5 males/5 females) of participants were diagnosed with primary catathrenia. Acoustically, snoring and groaning sounds exhibited distinct characteristics: snoring displayed an irregular waveform, while groaning had a sinusoidal or sawtooth waveform with a discernible fundamental frequency. Cluster analysis revealed two distinct subgroups of catathrenia. Compared to normal references, patients with OSA presented with a retrusive mandible and narrow palatopharynx, whereas patients with catathrenia had a well-developed mandible, and broad palatopharynx, yet narrow hypopharynx. The groaning index decreased significantly from 5.8(2.7,14.3) to 2.8(1.3, 12.2) ($p=0.014$) with MAD treatment.

Conclusions: This study suggests that catathrenia may be more prevalent among patients with OSA and that those with comorbid catathrenia exhibit distinct characteristics, including differences in sex distribution, AHI, acoustic features, and upper airway anatomy. Groaning sounds might be active, vocal sounds to overcome obstructions in the hypopharynx.

Prevalence and Characteristics of Positional Obstructive Sleep Apnea in a Racially Diverse Pediatric Population: Preliminary Results from a Community-Based Study

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Introduction: Positional obstructive sleep apnea (POSA) is characterized by upper airway obstruction that worsens when individuals sleep in supine position. This OSA subtype is commonly seen in both adults and children. Currently, there is a lack of knowledge regarding the prevalence of POSA in otherwise healthy children who may benefit from personalized treatment, specifically positional therapy, as an alternative to surgical intervention and CPAP. The objective of this study is to determine the prevalence and characteristics of POSA and to evaluate its association with symptoms in racially diverse pediatric population.

Materials and methods: Otherwise healthy children aged 4–17 years undergoing clinically indicated overnight polysomnography at a community-based sleep laboratory were prospectively recruited. Data collected included body size measurements, tonsil size, and OSA symptoms assessed using the Pediatric Sleep Questionnaire (PSQ). A PSQ total score of greater than 0.33 indicates a high risk for OSA based on parent-reported symptoms. POSA was defined as: (1) obstructive apnea-hypopnea index (OAHI) ≥ 1.5 events/hour, (2) supine to nonsupine OAHI ratio ≥ 2 , and (3) at least 30 minutes of sleep in both supine and non-supine positions.

Results: Preliminary analysis included 100 children (mean age 8.5 ± 3.1 years; 67% male; 40% White). Based on overall OAHI, 17 had no OSA (OAHI < 1.5), 38 had mild OSA (1.5–5), 25 had moderate OSA (5–10), and 20 had severe OSA (≥ 10). Among 83 participants with OSA, 18 (22%) were classified as POSA, 60 (72%) as non-POSA, and 5 (6%) were unclassified due to insufficient time in supine or non-supine sleep.

Compared to the non-POSA group, children with POSA spent a significantly lower percentage of sleep

time in the supine position [27.7% (17.2–52.6) vs. 49.8% (31.0–62.1); $p = 0.029$]. They also exhibited a higher OAHl during supine sleep [17.5 (6.3–28.9) vs. 6.2 (3.9–12.0) events/hour; $p = 0.002$] and a lower OAHl during non-supine sleep [4.2 (2.2–6.4) vs. 7.5 (4.4–12.2) events/hour; $p = 0.003$]. Additionally, the POSA group had a higher prevalence of enlarged tonsils [53% vs. 22%, $p=0.030$]. Interestingly, a smaller proportion of the POSA group had a PSQ score greater than 0.33 (47% vs. 75%, $p=0.032$) compared to the non-POSA group. No significant differences were found in age, sex, body mass index, neck circumference, overall OAHl, oxygen desaturation index, and arousal index between the two groups.

Conclusions: In this diverse pediatric cohort, approximately one-fifth of children with OSA were identified as having POSA. POSA was associated with enlarged tonsils, but these children displayed a lower symptom burden according to PSQ scores. These findings suggest that POSA may represent a distinct OSA phenotype in children, potentially amenable to positional therapy. Further studies are warranted to investigate potential racial differences and to evaluate both the short- and long-term effects of positional therapy compared to adenotonsillectomy in children with POSA, especially in those with enlarged tonsils.

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Prevalence and identification of rapid eye movement-related obstructive sleep apnea in the Han Chinese adults

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Introduction: This study investigated the demographic, clinical, genetic characteristics of REM-related OSA (REMrOSA) in the Han Chinese population.

Materials and methods: This is a large-scale cross-sectional study conducted from 2007 to 2022 in our sleep center. The REMrOSA and its subgroups were classified based on the ratio of apnea-hypopnea index during REM (AHI_{REM}) versus non-REM (AHI_{NREM}) with sufficient sleep time during REM and NREM. Anthropometric, physiological, and biochemical indexes were collected. Based on the established raw genetic database, a genome-wide association study for AHI_{REM} and REMrOSA phenotypes was analyzed among matched subjects.

Results: A total of 3,631 OSA subjects were included for REMrOSA analysis, and 3,793 subjects (3,317 OSA and 476 NOSA) were included for GWAS analysis. The prevalence of REMrOSA was 18.09% (95% confidence interval, 16.86% to 19.39%) in OSA, which occurred more in females with younger age, better glucolipid profiles, and milder sleeping parameters (Mann-Whitney U test, $P<0.05$). The GWAS analysis identified 36 and 4 single nucleotide polymorphisms significantly associated with AHI_{REM} and REMrOSA phenotypes, respectively. Common gene loci associated with both phenotypes including *TBXAS1*, *SLCO5A1*, *ABCA1* and *ZNF603P*.

Conclusions: More than 1/6 of Han Chinese subjects with OSA had REMrOSA with unique clinical characteristics. Four common genome-wide significant trait-associated loci were identified and might provide novel insight into the genetic architecture of REM sleep disorders.

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Prevalence and Modulating Factors of Upper Airway Collapse Sites in OSA Patients Assessed by Drug-Induced Sleep Endoscopy: A Meta-Analysis

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Introduction: Drug-induced sleep endoscopy (DISE) is an established diagnostic tool for dynamically evaluating upper airway obstruction sites in patients with obstructive sleep apnea (OSA). However, significant variability in reported prevalence rates of obstruction sites across studies has highlighted the critical need for a systematic and comprehensive analysis.

Materials and methods: This meta-analysis aimed to synthesize the prevalence rates of upper airway obstruction sites (velum, oropharynx, tongue base, and epiglottis) as assessed by DISE. We also sought to quantitatively evaluate the impact of sedative type, method of sedation assessment, and patient demographic characteristics (age, body mass index, apnea-hypopnea index, and male ratio) on both the prevalence of obstruction and inter-study heterogeneity. Methods A random-effects model-based meta-analysis was performed using the metaprop function in R. Prevalence rates were calculated for the four obstruction sites based on the VOTE classification system. Subgroup analyses were conducted according to the type of sedative used and the method of sedation assessment. Publication bias was evaluated using Egger's test and the Trim-and-Fill method. The effects of covariates were analyzed via meta-regression using the rma.glmm function from the metafor package.

Results: In an analysis comprising a total of 3,842 patients, velum obstruction was the most prevalent at 75% (95% CI: 0.67-0.82), followed by tongue base at 40% (95% CI: 0.33-0.48), oropharynx at 31% (95% CI: 0.25-0.37), and epiglottis at 24% (95% CI: 0.17-0.32). High heterogeneity ($I^2 > 80\%$) was observed across all sites. Significant publication bias ($p < 0.0001$, right asymmetry) was identified specifically for epiglottic obstruction. After applying the Trim-and-Fill method, the adjusted prevalence of epiglottic obstruction increased substantially to 0.4611 (95% CI: 0.3373-0.5898), suggesting an underreporting bias in studies that reported high prevalence rates. Multivariate meta-regression analysis revealed that the heterogeneity in velum obstruction ($I^2=37.40\%$) was largely explained by sedation-related variables and demographic factors. However, high residual heterogeneity persisted for other sites (oropharynx, tongue base, and epiglottis). Notably, Midazolam use and sedation assessment based on clinical signs were associated with higher obstruction prevalence in some areas. Age, BMI, AHI, and male ratio also acted as significant moderating variables for site-specific obstructions.

Conclusions: This DISE-based meta-analysis elucidated the multilevel nature and site-specific patterns of upper airway obstruction, reaffirming the velum as the most common obstruction site. Our findings highlight that the high variability in DISE outcomes is influenced by sedation protocols and patient characteristics. This underscores the necessity for standardizing sedation protocols and considering patient characteristics in future research, thereby advocating for personalized treatment approaches.

Prevalence and Risk Factors of Residual Excessive Sleepiness in Chinese Obstructive Sleep Apnea Patients

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Introduction: Some obstructive sleep apnea (OSA) patients continue to experience sleepiness despite receiving continuous positive airway pressure (CPAP) treatment, a condition referred to as residual excessive sleepiness (RES). At present, the prevalence and risk factors for RES among OSA patients in China remain unclear. This study seeks to examine the prevalence and predictors of RES in Chinese OSA patients.

Materials and methods: The study prospectively enrolled patients diagnosed with OSA at the Sleep Medicine Center, West China Hospital, Sichuan University, between January 2022 and September 2024. Patients were included if they had a baseline Epworth Sleepiness Scale (ESS) score greater than 10 and had received effective CPAP treatment (residual apnea hypopnea index [AHI] < 5) for at least 4 hours per day. Data collected included: ESS before and after treatment, demographic details, comorbidities, polysomnography and CPAP parameters. After at least 3 months of CPAP treatment, patients were categorized into two groups based on their post-treatment ESS: the non-RES group (ESS ≤ 10) and the RES group (ESS > 10).

Results: A total of 1058 OSA patients treated with effective and adequate CPAP were included. The average age was 42.98 ± 11.27 years, with a BMI of 26.72 ± 3.72 kg/m², 81.6% were males, and the average AHI was 48.80 ± 27.25 events/hour at baseline. After an average of 4.3 months of CPAP treatment (5.79 ± 0.80 h/day), 339 patients (32.04%) complained of RES. Multivariate logistic regression analysis identified several risk factors for RES: higher ESS (OR=1.307, 95%CI: 1.224-1.396, $p < 0.001$) and arousal index (OR=1.109, 95%CI: 1.083-1.137, $p < 0.001$), greater proportion of sleep in N1 stage

(OR=1.040, 95%CI: 1.023-1.056, $p<0.001$), and lower average blood oxygen saturation (OR=1.080, 95%CI: 1.026-1.136, $p=0.003$) before CPAP treatment. In contrast, lower AHI (OR=0.900, 95%CI: 0.883-0.917, $p<0.001$) and a higher proportion of sleep in N3 stage (OR=0.841, 95%CI: 0.744-0.952, $p=0.006$) were protective factors. Additionally, CPAP adherence (OR=0.702, 95%CI: 0.574-0.859, $p=0.001$) was linked to the development of RES. Receiver operating characteristic (ROC) analysis showed that the multivariate model for predicting RES had an area under the curve (AUC) of 0.841.

Conclusions: In China, over 32% of OSA patients receiving CPAP treatment report experiencing RES. The factors associated with RES include baseline severer sleepiness, reduced sleep stability, lower AHI, and worse CPAP adherence.

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Prevalence of high risk for obstructive sleep apnea in Thai patients undergoing elective general surgery

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Introduction: Limited studies have shown that a high proportion of patients undergoing elective surgery under general anesthesia (GA) are at high risk for obstructive sleep apnea (OSA), with 80% remaining undiagnosed. This study aims to determine the prevalence of high-risk OSA in Thai patients undergoing elective general surgery under GA and to explore its association with surgical categories and perioperative complications based on STOP-Bang scores.

Materials and methods: This cross-sectional study was conducted between August 2020 and February 2021. The inclusion criteria were Thai patients ≥ 18 years admitted to Siriraj Hospital for elective general surgery under GA. Exclusion criteria included patients scheduled for bariatric, airway, or neck mass surgery, those whose surgeries were canceled or had anesthetic substituted, and patients unable to complete the questionnaires. Before surgery, all subjects completed the STOP-Bang and associated questionnaires, and relevant medical records, including anesthetic notes, were reviewed.

Results: Of the 300 participants, 162 patients (54%) were classified as being at high risk for OSA (STOP-Bang values of ≥ 3). Among surgical categories, urologic surgery had the highest prevalence (69%) while breast surgery had the lowest (25.7%). High-risk patients shared several characteristics compared to the low-risk group, including being predominantly male, having a larger neck circumference, older age, higher body mass index (BMI), underlying hypertension, cardiovascular diseases, and higher anesthetic risk. However, no significant association was found between the STOP-Bang scores and postoperative complications.

Conclusions: Up to 54% of Thai patients undergoing elective general surgery under GA were at high risk for OSA, with the highest prevalence seen in those undergoing urologic surgery. Increasing awareness of preoperative OSA screening could help prevent future adverse outcomes.

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Prevalence of High Risk of Obstructive Sleep Apnea in Patients with Vertigo

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Introduction: There is a noticeable absence of research focusing on the prevalence of OSA among Asian individuals experiencing vertigo. Our study aims to address this gap by assessing the prevalence

of high-risk OSA in patients with vertigo and examining the association between OSA risk, the severity of dizziness symptoms, and levels of daytime sleepiness.

Materials and methods: This cross-sectional study was conducted at the Faculty of Medicine Siriraj Hospital, Thailand. Inclusion criteria were patients over the age of 18 with vertigo disorders, such as Meniere's disease, benign paroxysmal positional vertigo (BPPV), vestibular neuritis, and vestibular migraine. Patients with history of psychiatric disorders, brain diseases, and those who regularly used central vestibular suppressants, were excluded. Data was collected using the STOP-Bang questionnaire (SBQ), Epworth sleepiness scale (ESS), and Dizziness Handicap Inventory (DHI) scores.

Results: A total of 190 vertigo patients (48 men, 142 women) with a mean age of 58.9 ± 12.6 years (range 19-88 years) and body mass index (BMI) of 24.7 ± 3.9 kg/m² were recruited. The most common subcategory of vertigo was BPPV (56.8%). Ninety-eight patients (51.6%) were categorized as high-risk for OSA; significant independent risk factors for this group included male gender and hypertension ($p = 0.001$). A higher DHI rating was associated with increased ESS scores, but not with SBQ scores.

Conclusions: The prevalence of high-risk OSA among vertigo patients was 51.6%, which is higher than that observed in the general population. There was a notable correlation between the severity of dizziness and sleepiness. . Thus, screening for high-risk OSA in vertigo patients should be encouraged to promote early detection and treatment.

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Prevalence of High Risk of Obstructive Sleep Apnea in Patients with Vertigo

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Introduction:

Obstructive sleep apnea (OSA) is a common sleep disorder associated with significant comorbidities such as hypertension, cardiovascular disease, and daytime sleepiness. Although polysomnography is the diagnostic gold standard, the STOP-Bang questionnaire offers a cost-effective screening tool. Vertigo is also prevalent and affects quality of life, particularly in older adults. While both conditions may share overlapping symptoms, such as fatigue and poor sleep, the relationship between OSA and vertigo remains underexplored, especially in Asian populations. Previous studies have reported a higher prevalence of OSA symptoms among patients with dizziness, but data remain limited. This study aims to determine the prevalence of high-risk OSA among patients with vertigo and to examine the association between OSA risk, dizziness severity, and daytime sleepiness

Materials and methods: This cross-sectional study was conducted at the Faculty of Medicine Siriraj Hospital, Thailand. Inclusion criteria were patients over the age of 18 with vertigo disorders, such as Meniere's disease, benign paroxysmal positional vertigo (BPPV), vestibular neuritis, and vestibular migraine. Patients with history of psychiatric disorders, brain diseases, and those who regularly used central vestibular suppressants, were excluded. Data was collected using the STOP-Bang questionnaire (SBQ), Epworth sleepiness scale (ESS), and Dizziness Handicap Inventory (DHI) scores.

Results: A total of 190 vertigo patients (48 men, 142 women) with a mean age of 58.9 ± 12.6 years (range 19-88 years) and body mass index (BMI) of 24.7 ± 3.9 kg/m² were recruited. The most common subcategory of vertigo was BPPV (56.8%). Ninety-eight patients (51.6%) were categorized as high-risk for OSA; significant independent risk factors for this group included male gender and hypertension ($p = 0.001$). A higher DHI rating was associated with increased ESS scores, but not with SBQ scores.

Conclusions: The prevalence of high-risk OSA among vertigo patients was 51.6%, which is higher than that observed in the general population. There was a notable correlation between the severity of dizziness and sleepiness. . Thus, screening for high-risk OSA in vertigo patients should be encouraged to promote early detection and treatment.

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Quantitative Analysis of Sleep Electroencephalogram in Patients with Interstitial Lung Disease and Obstructive Sleep Apnea

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Introduction: Patients with interstitial lung diseases (ILD) often experience disrupted sleep architecture due to nocturnal desaturation and co-morbid obstructive sleep apnea (OSA) which negatively impact sleep quality and may worsen both conditions. Existing literature focuses on sleep macroarchitecture which has shown reduced REM and slow wave sleep, increased arousals, and fragmented sleep in these patients. Quantitative EEG (qEEG) analysis offers a deeper evaluation of sleep microarchitecture undetectable by traditional scoring methods. This could serve as a potential biomarker for phenotyping and prognosticating ILD-OSA patients, guiding future therapeutic approaches. We aimed to analyse sleep microarchitecture in patients with ILD-OSA and compare it with that of OSA patients matched for disease severity.

Materials and methods: This retrospective study analyzed EEG-derived sleep microarchitecture in ILD patients who underwent level I polysomnography (PSG). Three groups were analyzed: ILD-OSA, ILD without OSA, and non-ILD OSA patients matched for AHI. PSGs with <4 hours of sleep or excessive artifacts were excluded. EEG signals (sampled at 512 Hz) from central channels were pre-processed using Python toolboxes (MNE, YASA, pyprep, autoreject), and 3s cleaned epochs were used for spectral analysis and the indices obtained were compared across the three groups. For comparing indices between the groups (ILD-OSA and ILD without OSA; ILD-OSA and non-ILD OSA) independent t-test or Mann-Whitney U test was used based on the normality of data.

Results: Eighteen patients each with ILD-OSA, ILD without OSA, and non-ILD OSA (matched for AHI; $p=0.2$) were included. Patients with ILD-OSA had a lower mean BMI (26 ± 4.4) compared to those with non-ILD OSA (30.8 ± 6.4) ($p=0.001$) and were less sleepy with a lower mean ESS (8.2 ± 3.6 vs 11 ± 4.1 ; $p=0.03$). Sleep architecture showed decreased N3% ($p=0.009$) and increased wake after sleep onset ($p=0.006$) in ILD-OSA group. Microarchitecture analysis showed higher slow wave peak to peak (PTP) (111.3 ± 13.9 vs 103.5 ± 7.07 ; $p=0.03$), spindle root mean square (RMS) (43.2 ± 66.2 vs 8.8 ± 2.7 ; $p=0.003$), and absolute spindle power (2.13 ± 0.6 vs 1.66 ± 0.2 ; $p=0.003$) for both high and low frequency spindles in ILD-OSA group. Neuroloop gain for spindles was lower among ILD-OSA compared to non-ILD OSA (39.4 ± 14.7 vs 55.6 ± 15.8 ; $p=0.003$). Comparison between ILD-OSA and ILD without OSA did not show any significant difference in the sleep microarchitecture.

Conclusions: ILD patients with comorbid OSA (ILD-OSA) were less sleepy and had a lower BMI compared to disease severity matched OSA patients. They exhibit distinct alterations in sleep macro- and microarchitecture, including reduced deep sleep (N3%) and increased sleep fragmentation. Spindle metrics were however higher in ILD-OSA (higher spindle power, PTP, and RMS) compared to non-ILD OSA patients, suggesting better cortical synchronisation during spindle generation. Neuroloop gain for spindles was reduced in ILD-OSA, suggesting poorer spindle generation due to altered thalamocortical dynamics. However, no significant differences in sleep microarchitecture were found between ILD-OSA and ILD without OSA.

Reading Your Sleep: Learning SpO₂ Words and Sentences for OSA Detection and Subtyping

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent and serious sleep-disordered breathing condition. However, the current gold standard for OSA diagnosis, polysomnography (PSG), is a complex and costly procedure that relies heavily on expert interpretation of multi-channel signals. These limitations severely hinder its application in early screening and large scale population monitoring. Therefore, developing an accessible, low-cost, and reliable automated diagnostic method is of paramount importance. To this end, our study pioneers a approach that translates continuous SpO₂ signals into discrete "physiological words" and "sentences." By learning to read this oximetry language, we aim to provide an efficient and scalable solution for widespread OSA screening, perfectly suited for home based monitoring via wearable devices.

Materials and methods: We propose a novel pipeline to lingualize SpO₂ time series data. Three large-scale clinical datasets—MrOS, SHHS, and MESA—comprising a total of 14,430 polysomnography recordings are utilized as the foundation for both tokenizer construction and model pre-training. To begin, we augmented overnight SpO₂ signal segments from these datasets to create a diverse and representative training pool. Using unsupervised clustering on this enhanced dataset, we constructed a vocabulary of SpO₂ words. Each patient's full-night SpO₂ time series was then tokenized into sequences of these discrete words, which were subsequently organized into physiological sentences. A Transformer-based architecture was pre-trained on these token sequences, with the objective of learning the underlying grammar and semantics of the oximetry language through masked token prediction. The model was then fine-tuned for patient-level OSA detection and evaluated on independent validation cohorts. In addition, we explored the model's potential for identifying OSA subtypes by analyzing its behavior on misclassified cases to uncover atypical physiological patterns.

Results: Our model demonstrated excellent performance on an internal test set from a Chinese cohort (n=848, from a 4,240-subject fine-tune dataset from Shanghai Sixth People's Hospital), achieving an AUC of 0.958. To assess generalizability, we conducted external validation on three independent, multi-ethnic cohorts: the CFS (n=730), WSC (n=2,568), and STAGES (n=1,820) datasets. The model exhibited robust performance across these external datasets, attaining AUCs of 0.900, 0.926, and 0.823, respectively. Further analysis of misclassified cases revealed a subset of atypical OSA patients who were prone to false negatives. These individuals exhibited only mild, transient, or morphologically irregular oxygen desaturation events, with overall higher SpO₂ levels. While their oximetry patterns reflected underlying respiratory instability, the absence of overt hypoxic features posed a challenge for accurate detection by conventional models.

Conclusions: This study successfully demonstrates that lingualizing single-channel SpO₂ signals and leveraging NLP pre-trained models offers a feasible and highly effective pathway for accurate, automated OSA detection, with its robust generalizability validated across multiple independent cohorts. Furthermore, our framework reveals a powerful analytical capability: by conducting in-depth analyses of cases misclassified by the model, we have identified a set of clinically atypical patterns of subtle or irregular oxygen desaturation. This demonstrates that our method is a potent tool capable of reading deeper into the nuances of sleep-disordered breathing, paving the way for the discovery and understanding of different OSA subtypes.

Real-World Evidence for Surgical and Nonsurgical Sleep Apnea Therapies: safety, Clinical Outcomes and Healthcare Utilization Patterns

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent condition with wide-ranging clinical and economic consequences. While continuous positive airway pressure (CPAP) is the gold standard therapy, its limited adherence has led to increased interest in alternative treatments, including soft tissue and skeletal surgeries and implantable devices like hypoglossal nerve stimulation (HGNS). Randomized controlled trials (RCTs) are limited in their scope to capture long-term systemic outcomes

and healthcare costs. Real-world evidence (RWE) using national claims data offers valuable insights into these broader dimensions of sleep care.

Materials and methods:

We conducted a series of retrospective cohort studies using large-scale insurance claims databases (Truven MarketScan and Arcadia) from 2007–2023. Patients aged 18–90 with a diagnosis of OSA who received either CPAP, soft tissue or skeletal surgery, or HGNS were identified. Primary outcomes included:

- Cardiovascular, endocrine, and neurological event rates
- Healthcare utilization (inpatient, outpatient, pharmaceutical expenditures)
- Chronic opioid use and its risk factors following sleep surgery

Analyses employed high-dimensional propensity score matching, logistic regression, and Kaplan-Meier survival estimates, with follow-up ranging from 2 to 8 years depending on the dataset.

Results: Results:

- **Clinical Outcomes:** Patients undergoing soft tissue surgery for OSA demonstrated significantly reduced risk of cardiovascular (HR 0.91), neurological (HR 0.67), and endocrine complications (HR 0.82) compared to matched CPAP users.
- **Hypoglossal Nerve Stimulation (HGNS):** HGNS was associated with lower long-term rates of arrhythmias, heart failure, and stroke compared to CPAP.
- **Healthcare Utilization:** Over a 2-year period, surgery was associated with significantly lower average monthly healthcare expenditures compared to CPAP or no treatment when the cost of the intervention was excluded (e.g., \$694 vs. \$837/month).
- **Opioid Risk:** Among 10,766 OSA surgery patients, 2.8% developed persistent opioid use. Multivariate analysis revealed perioperative opioid prescription (OR 37.8) and smoking (OR 1.95) as independent predictors of chronic use. Skeletal surgery had the lowest opioid exposure compared to soft tissue procedures.

Conclusions: These RWE studies demonstrate that surgical interventions for OSA—particularly soft tissue surgery and HGNS—are associated with lower systemic complication rates, reduced long-term healthcare expenditures, and nuanced opioid risk profiles compared to CPAP therapy. This body of work supports the integration of RWE in clinical decision-making, policy formulation, and patient-centered sleep care strategies.

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Real-world Incremental Economic Burden of Fatigue among Patients with Obstructive Sleep Apnea in the Medicare Fee-for-Service Population

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Introduction: Fatigue, distinct from sleepiness, is one of the most common obstructive sleep apnea (OSA) symptoms, and is associated with diminished quality of life, poor psychological and physical functioning and increased risk of occupational and motor vehicle accidents. The aim of this study was to estimate the incremental healthcare cost burden of fatigue among patients with OSA in the Medicare fee-for-service (FFS) population.

Materials and methods: Retrospective observational claims analysis was conducted comparing newly diagnosed OSA patients with fatigue to matched OSA patients without fatigue. Medical and pharmacy claims from the 2017–2022 Medicare FFS database were used to identify incident cases of fatigue

among newly diagnosed OSA patients who met the following criteria: ≥ 1 inpatient or ≥ 2 outpatient claims (with ≥ 7 days apart) with an ICD-10-CM diagnosis code of OSA (G47.33, G47.30, G47.39); ≥ 1 procedure code for polysomnography or home sleep apnea test in 12 months prior to OSA diagnosis index date; continuous insurance coverage ≥ 12 months before OSA diagnosis index (baseline period) and ≥ 12 months after fatigue index date (follow-up period). Fatigue cases had ≥ 1 claim for fatigue (R53.1, R53.81, R53.82, R53.83) after the OSA diagnosis index date. Controls had no diagnosis of fatigue and were propensity score matched to fatigue cases.

Results: A total of 71,710 newly diagnosed OSA patients met eligibility criteria, of whom $\sim 36\%$ had ≥ 1 diagnosis claim for fatigue. Mean (SD) age was 72.8 years (5.3), 51% male, and 88% White. After OSA diagnosis, mean all-cause healthcare costs were significantly higher (all $p < 0.001$) for patients with fatigue vs. matched controls: Per-patient-per-year (PPPY) all-cause hospitalization (\$7,457 vs \$1,598); outpatient visits (\$5,122 vs \$2,177); emergency department visits (\$846 vs \$237); other medical visits (\$10,628 vs \$4,201); and pharmacy costs (\$5,075 vs \$2,926). Overall, the mean PPPY all-cause total costs (\$29,128 vs \$11,140, $p < 0.001$) in OSA patients with fatigue were significantly higher than those without fatigue, indicating over a two-fold increase.

Conclusions: Fatigue is significantly associated with an increase in all-cause total healthcare costs in newly diagnosed OSA patients as compared with matched patients without fatigue. Addressing fatigue may be useful as part of OSA screening, diagnosis and treatment due to the incremental humanistic and economic burden.

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Reduced N3 Sleep Is Associated with Cognitive Impairment in Elderly Patients with Obstructive Sleep Apnea

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Introduction: This study aimed to identify the prevalence and severity of cognitive impairment in elderly patients with obstructive sleep apnea (OSA), and to explore the association between sleep structure and mild cognitive impairment in elderly patients with OSA.

Materials and methods: 207 elderly patients were diagnosed with OSA (AHI ≥ 5) were continuously enrolled this study from the Division of Sleep Medicine of Peking University People's Hospital between February 2023 to November 2024. Montreal Cognitive Assessment Scale (MoCA)-Beijing was used to assess the prevalence and severity of cognitive impairment. Overnight polysomnography (PSG) was used to evaluate the sleep structure respiratory event. The sleep structure respiratory event are manually scored by trained sleep technicians, and all the scores are carried out in accordance with the criteria of the AASM (American Academy of Sleep Medicine) Manual for the Scoring of Sleep and Associated Events, Version 3.0. The Spearman analysis was used to assess the correlation between sleep structure and MCI score. Multivariate logistic regression was applied to analyze the relationship between MCI and sleep structure after controlling for confounding variables.

Results: 45.8% elderly patients with OSA were diagnosed with MCI (MoCA ≥ 26). Compared to patients without MCI, elderly patients with OSA complicated by mild cognitive impairment had significantly reduced total sleep time, sleep efficiency, and the percentage of N3 sleep stage, while the increased percentage of N1 sleep stage. Multivariate analysis found that a reduction in N3 - stage sleep was correlated with total MCI ($P < 0.05$), a reduced in N3 - stage sleep is a risk factor for MCI in patients with OSA ($P < 0.05$), (OR = 0.95, 95% CI : 0.91, 1.00).

Conclusions: In elderly patients with OSA, The prevalence and severing of MCI is increasing. a reduction in N3 - stage sleep is associated with mild cognitive impairment.

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Refining the Detection of Sleep-disordered Breathing Events: Improving Annotations in National Sleep Research Resource (NSRR) Polysomnography Data

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Introduction: The Sleep Heart Health Study (SHHS), the Osteoporotic Fractures in Men Study (MrOS), and the Multi-Ethnic Study of Atherosclerosis (MESA) are frequently used public sleep study datasets provided by the National Sleep Research Resource (NSRR). These datasets contain full overnight polysomnography recordings with annotated sleep events. However, apnea and hypopnea were labeled solely based on flow reduction, ignoring sleep stages, desaturation, or arousal as required by American Academy of Sleep Medicine (AASM) guidelines. This discrepancy could introduce considerable inconsistency and ambiguity in future studies. Here, we aim to develop a standardized process for analyzing respiratory event annotations from major NSRR datasets and provide updated labels.

Materials and methods: This retrospective study examined polysomnography annotations from SHHS1 (n=5,793), SHHS2 (n=2,651), MrOS1 (n=2,904), MrOS2 (n=1,026), and MESA (n=2,054). Dataset characteristics, including scoring methods and known issues, were analyzed. Then, we evaluated the discrepancy between the reported apnea-hypopnea index (AHI) and the AHI derived from raw annotations and the recalculated AHI adjusted for sleep stage, desaturation, and arousal based on AASM guidelines. Subsequently, we performed identical analysis on the Korea Image-based Sleep Study (KISS) dataset (n=7,745) for comparison.

Finally, we highlighted the importance of precise annotations by developing an electrocardiogram-based sleep-disordered breathing event detection model using original and adjusted annotations from SHHS1, SHHS2, and MESA and comparing sleep apnea (SA) severity classification (Normal, Mild to Moderate, Severe) performance.

Results: The raw labels consistently overestimated AHI across all cohorts, with the largest mean absolute error (MAE) in SHHS1 (23.55 events/hour). Other datasets showed moderate overestimations: SHHS2 (10.45), MrOS1 (11.16), MrOS2 (10.31), and MESA (13.09). After adjusting the annotations per AASM scoring criteria, MAEs were dramatically reduced across all datasets: SHHS1 improved to 1.29 events/hour, SHHS2 to 1.20 events/hour, MrOS1 to 1.03 events/hour, MrOS2 to 0.56 events/hour, and MESA to 0.78 events/hour. Notably, the KISS, which strictly followed the contemporary scoring guidelines in its raw annotations, demonstrated inherently high accuracy with a MAE of 0.6 events/hour, requiring no further processing. Lastly, SA severity classification significantly improved with our annotations compared to the original ones, with the F1 score rising from 0.35 to 0.66.

Conclusions: Annotations of SHHS, MrOS, and MESA require additional processing to accurately identify respiratory events consistent with AASM guidelines. Our updated labels will facilitate unambiguous annotation usage, promoting reproducibility and enabling comparisons in future studies, as shown by our deep learning experiment result. KISS offers the most reliable annotations among the datasets studied.

REI4% Compared to REI3% Leads to Missed OSA Diagnoses and/or Restricts Access to Care in >50% of Pregnancies In a Real-World Symptomatic Clinical Cohort Characterized by Advanced Maternal Age, Morbid Obesity and Chronic Hypertension

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Introduction: Evidence is rapidly accumulating that obstructive sleep apnea (OSA) can complicate healthy as well as high risk pregnancies. NuMom2b, the largest prospective study of gestational sleep apnea (gOSA), has demonstrated an increased risk of gestational diabetes, gestational hypertension and preeclampsia in otherwise healthy pregnant subjects with even "mild" OSA, defined as a respiratory event index (REI) 3% 5-15/hr. Although the REI, just like the apnea hypopnea index (AHI), has limited

predictive value for OSA morbidity and/or treatment outcomes, it is a cornerstone for "severity" designation and eligibility for treatment in US clinical practice. In other words, the REI, rather than clinical diagnostic and risk/benefit assessments, determine recommendations for and access to positive airway pressure (PAP) as the gold standard treatment for OSA. Specifically, PAP insurance coverage for REI 5-15/hr is contingent upon insurance pre-determined, inconsistent and largely non-validated metrics such as the Epworth score. Here we add pregnancy as a clinical population where REI4% compared to REI3% criteria lead to both missed diagnoses and "severity" estimation disparities, and also limit access to insurance-covered gold standard PAP therapy in a vulnerable population, despite evidence that PAP treated OSA is associated with reduced pregnancy morbidity.

Materials and methods: This is a retrospective analysis of 188 home sleep apnea tests (HSATs) completed in gravidae who screened as high risk for OSA using the 4-variable "Facco" questionnaire and were tested for OSA with the Respironics Alice PDx® HSAT. In this analysis, we only included data from HSATs which were reported using both AASM-recommended 3% (REI3%) and Medicare 4% desaturation criteria (REI4%).

Results: Cohort characteristics included average age at referral of 33 yo and average pre-pregnancy BMI of 42 kg/m²; 32% had chronic hypertension, 21% - asthma, 14% - type 2 diabetes and 15% - hypothyroidism; 10% were Black/African American, 7% Hispanic/Latinx, 3% Asian or Indian and 75% White/Caucasian; 61% had one or more living children. Finally, 71% and 65% reported frequent and/or loud snoring respectively, 18% endorsed witnessed apneas, and 65% endorsed being tired during the daytime.

56% of gravidae who received diagnosis of no OSA by 4% criteria (REI4% < 5/hr) were diagnosed with OSA by 3% criteria (REI3% ≥ 5/hr) (n=60/108). 58% of gravidae who were diagnosed with mild OSA by 4% criteria (REI4% 5-15/hr), were reclassified as moderate to severe OSA by 3% criteria (REI3% ≥ 15/hr) (n=34/59).

Conclusions: Our findings from a real world cohort demonstrate that using REI4% rather than REI3% criteria misses the diagnosis of OSA in 56% of pregnant women in our clinical pipeline and results in a change in "severity" from "moderate to severe" to "mild," thus restricting automatic eligibility and insurance coverage for gold standard PAP treatment in 58% of gravidae. Pregnancy complications are significant determinants of long-term adult health, so interventions that improve pregnancy health drive population-based outcomes. In this context, it is imperative to reassess the application of non-validated, restrictive, and non-physiological REI criteria to OSA "severity" classification and determination of access to PAP treatment during pregnancy.

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Relationship between Framingham cardiovascular disease risk profile and pulse-oximetry derived measures of hypoxic burden and vascular reactivity in a sleep clinic cohort

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Introduction: Pulse-oximetry derived measures of respiratory event related hypoxemia and autonomic vascular reactivity during an overnight sleep study – quantified by hypoxic burden (HB) and the pulse wave amplitude drop (PWAD) index – have recently been proposed as biomarkers of cardiovascular disease (CVD) outcomes in patients with obstructive sleep apnoea (OSA). This study examined the relationship between Framingham 10-year CVD risk profile and a range of HB and PWAD characteristics in patients attending a sleep clinic for suspected OSA.

Materials and methods: This study examined HB and PWAD characteristics (from photoplethysmography) in 725 individuals (38% Female; age [mean ± standard deviation]: 50±15y; body mass index: 29.9±7.4kg/m²) who underwent diagnostic polysomnography and had sufficient clinical data to determine history of CVD and calculate a Framingham 10-year CVD risk score. Individuals were categorised as either having an established CVD (CVD_{ESTABLISHED}, n=110) or a Framingham 10-year CVD risk score that was elevated (CVD_{ELEVATED}, n=407) or low (CVD_{LOW}, n=208). Standard polysomnography variables as well as respiratory event related HB (cumulative area of respiratory event related hypoxemia, %min/h) and PWAD characteristics including PWAD_{INDEX} (number

of drops in pulse wave amplitude of >30% from baseline per hour of sleep, events/h) and PWAD_{DURATION} (mean duration of PWAD events, seconds) were derived and compared between CVD groups.

Results: A significantly higher HB ($p < 0.01$) was observed in patients with CVD_{ESTABLISHED} (72.1 ± 93.7 %min/h) and CVD_{ELEVATED} (76.1 ± 121 %min/h) than in patients with CVD_{LOW} (26.7 ± 86.6 %min/h), while HB was similar between CVD_{ESTABLISHED} and CVD_{ELEVATED} ($p = 0.380$). A significantly lower PWAD_{INDEX} ($p < 0.01$) was observed in patients with CVD_{ESTABLISHED} (37.8 ± 19.1 events/h) and CVD_{ELEVATED} (42.2 ± 22.3 events/h) than in patients with CVD_{LOW} (50.6 ± 19.3 events/h), and PWAD_{INDEX} was significantly lower in CVD_{ESTABLISHED} than CVD_{ELEVATED} ($p < 0.01$). A significantly longer PWAD_{DURATION} ($p < 0.01$) was observed in patients with CVD_{ESTABLISHED} (11.6 ± 4.5 seconds) and CVD_{ELEVATED} (9.0 ± 2.1 seconds) than in patients with CVD_{LOW} (8.0 ± 1.4 seconds), and PWAD_{DURATION} was significantly longer in CVD_{ESTABLISHED} than CVD_{ELEVATED} ($p < 0.01$). Similar group differences were observed during REM and non-REM sleep, and group differences in HB, PWAD_{INDEX} and PWAD_{DURATION} remained statistically significant after adjusting for age, sex, body mass index and apnoea-hypopnea index.

Conclusions: These data indicate that a high HB, low PWAD_{INDEX} and longer PWAD_{DURATION} may provide a marker of worsening Framingham 10-year CVD risk score in sleep clinic patients, independent of the presence and severity of OSA (as measured by the apnoea-hypopnea index). The mechanistic link between altered nocturnal PWAD characteristics and CVD risk requires further study.

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Residents, Fellows, and Advanced Practice Providers' Awareness of Clinical Practice Guidelines in Managing Perioperative Obstructive Sleep Apnea: A Multi-Institutional Survey

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Introduction: Patients with obstructive sleep apnea (OSA) undergoing surgery are at significant risk for perioperative morbidity and mortality. Physicians-in-training (Residents, Fellows) and Advanced Practice Providers (APPs; Nurse Practitioners, Nurse Anesthetists, Nurse Midwives, Clinical Nurse

Specialists, and Physician Assistants) are increasingly frontline patient care providers in managing patients worldwide. They often may not receive sufficient education in their clinical training or practice regarding OSA and the associated perioperative risks.

Materials and methods: Electronic surveys were sent to providers in three clinical roles (Residents, Fellows, APPs), four major categories of practice, at nine major United States academic institutions between May 9-June 30, 2021. Chi-square and Fisher's exact tests assessed association between survey question responses and participant characteristics. False discovery rate (FDR) adjustment was used to account for multiple comparisons, with FDR threshold $q < 0.05$ for statistical significance. Cochran-Mantel-Haenszel (CMH) tests evaluated associations stratified by institution, with the homogeneity of odds ratios from CMH tests evaluated using Breslow-Day tests.

Results: 2236 of 6724 (33.3%) participants responded, including 40.6% Residents, 11% Fellows, and 48.4% APPs. The primary category of practice included 20.3% in Anesthesiology, 8.9% Family Medicine (FM), 34.1% Internal Medicine (IM)/subspecialties, 6.7% Obstetrics/Gynecology/Gynecologic Oncology (OB), 25.9% Surgery/subspecialties, and 4.1% Other.

Almost all (93.2%) felt OSA was a risk factor for perioperative complications, with no differences based on clinical roles or categories of practice. However, one-third of providers did not routinely ask elective surgery patients about OSA risk. Many institutions have a written policy outlining the approach to evaluating and managing perioperative patients with concerns for OSA. Most respondents (74.6%) stated they "do not know" if their institution had a written policy, 18.2% reported that their institutions did, and 7.1% reported they did not have written policies. By reference, 6 of 9 (66%) participating institutions did have a written policy regarding the perioperative management of OSA. This lack of knowledge of institutional policy included all clinical roles, with 71% of APPs, 79% of fellows, and 73% of residents reporting that they did not know. Importantly, 50% of participants in Anesthesiology, 70% of Surgery, 76% of OB/GYN, 85% of Internal Medicine and 78% of Family Medicine did not know if there was an institutional policy.

Interestingly, most (79.3%) respondents indicated that clinical practice guidelines would assist in the care of perioperative patients with concerns about OSA, while 18.7% responded, "I'm not sure."

Conclusions: We found that many providers are not aware of institutional policies regarding the approaches to perioperative OSA-risk assessment and management based on clinical roles and categories of practice. This represents a critical void where standardized education regarding OSA and perioperative management may present significant opportunity to improve provider understanding and patient care.

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Respiratory Arousal Threshold and Clinical Features in patients with Isolated Obstructive Sleep Apnea and Comorbid Insomnia (COMISA)

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Introduction: Comorbid insomnia and obstructive sleep apnea (COMISA) affects up to 40% of patients with either disorder, suggesting shared pathophysiological mechanisms. The respiratory arousal threshold (ArTH) – the respiratory effort required to trigger sleep arousal – in COMISA remains uncharacterized. We hypothesized that low ArTH and complications occur more frequently in COMISA than in OSA alone.

Materials and methods: Participants referred for OSA diagnosis underwent a polysomnography (PSG) and answered the Athens insomnia scale (AIS) and the Epworth sleepiness scale (ESS). Participants with an AIS score ≥ 7 were defined as having insomnia. OSA was defined as an apnea hypopnea index (AHI) ≥ 5 events/h. A low ArTH was determined by an ArTH score of 2 or above (one point for each:

apnoea–hypopnea index (AHI) < 30/h, nadir oxygen saturation (SaO₂) >82.5%, fractions of hypopnoeas > 58.3%).

Results: A total of 387 subjects (158 OSA only and 229 COMISA) were analysed. There was a significantly higher proportion of low ArTH patients with COMISA compared with OSA only (35.37% vs 25.32%, $P = 0.036$). After adjusting for confounding factors, including age, sex, BMI, low ArTH was still independently associated with COMISA (OR: 1.696, 95% CI 1.054–2.738, $P=0.030$). Comparing the individual components of the ArTH scoring criteria, there was significantly higher proportions of COMISA subjects who had a fraction of hypopnoeas > 58.3% (68.22% vs 54.65%, $P = 0.010$). There was a significantly higher proportion of EDS, anxiety and depression in patients with COMISA. To illustrate the correlation between phenotypes and cardiovascular responses in patients with OSA alone and COMISA, Spearman correlation analyses were conducted; 18 pair-wise correlations were assessed and statistically significant correlations are shown in Figure 2.

Conclusions: A low respiratory arousal threshold is a predominant phenotypic feature in individuals with COMISA and may exhibit a greater relative contribution to OSA pathogenesis in these patients. Complications, include anxiety, depression and EDS, occur more frequently in COMISA than in OSA alone.

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Respiratory-related motor unit activity in human strap muscles

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Introduction: To maintain upper airway patency, neural drive must be coordinated across 24 pairs of skeletal muscles, including the largest airway dilator muscle, genioglossus, located at the base of the tongue and the strap muscles of the neck. Imprecise multiunit surface recordings of muscle activity suggest that the strap muscles have inspiratory modulation. However, the relative activity of the sternohyoid and sternothyroid muscles is not known. Similarly, the extent to which strap muscle activity changes with increases in respiratory drive is unknown. This study aimed to characterise the pattern and discharge rate of single motor units (SMU) of human strap muscles during quiet and stimulated breathing.

Materials and methods: To date, SMU activity was recorded during quiet breathing, increased CO₂ breathing and deep breaths in the supine position in 2 healthy males and 1 female participant. EMG activity was recorded from the right sternohyoid and sternothyroid (5-10 sites each) using a monopolar needle electrode probe inserted via ultrasound guidance. Genioglossus EMG was recorded using intramuscular wire electrodes. Airflow, mouth pressure and end-tidal CO₂ were recorded via nasal mask and pneumotachograph. SMUs were discriminated to determine their discharge pattern, the timing of activity relative to the respiratory cycle, and firing frequency.

Results: Data collection and analysis are on-going, but during quiet breathing, most sternothyroid SMUs have phasic activity during inspiration with a peak discharge rate of 10-20Hz. Some SMUs have tonic activity with inspiratory modulation. There was a variable response to increased CO₂ and deep voluntary breaths. The inspiratory discharge of some sternothyroid motor units responded to changes in end-expiratory lung volume and inspiratory flow. Thus far, very limited respiratory-related motor unit activity has been seen in sternohyoid.

Conclusions: This is the first comprehensive description of respiratory-related motor unit activity in human strap muscles. Respiratory-related motor unit behaviour is sensitive to changes in chemical and voluntary neural drive as well as lung volume changes which highlights the dynamic control of their output by the central nervous system. The findings of this study will underpin future studies on strap muscle activity in conditions in which upper airway patency is compromised, such as obstructive sleep apnoea. Importantly, this study informs emerging electrical stimulation approaches that target the strap muscles as a potential treatment for obstructive sleep apnoea.

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Respiratory self-similarity is a sleep apnea endotype that predicts cardiovascular disease related mortality in community-dwelling subjects

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Introduction: The effect of sleep apnea phenotypes on cardiovascular disease and mortality remains unclear. It is plausible that pathological respiratory chemoreflex activation (high loop gain) in sleep apnea may independently add to the risk of adverse outcomes. This study is going to determine if high loop gain of the respiratory control system during sleep, estimated by respiratory self-similarity (SS), and the related algorithm detected central respiratory event index (CREI), are related to new onset of cardiovascular disease (CVD) and CVD related mortality.

Materials and methods: A secondary analysis of The Sleep Heart Health Study (SHHS) and Multi-Ethnic Study of Atherosclerosis (MESA) was done, generating SS% and CREI, measured using chest and abdominal RIP signal. Cox regression and restricted cubic spline were done to explore the relationship between SS%, CREI and CVD, CVD-mortality and all caused mortality. The cumulative incidence function and a Fine-Gray subdistribution hazard model were used to evaluate this outcome accounting for competing risks.

Results: A subset of 4,871 SHHS participants and 2,049 MESA participants were included in the analysis of incident CVD. In SHHS, 1,147 new-onset CVD cases were identified, compared to 217 in MESA. After adjusting for confounders, both SS% and CREI demonstrated significant associations with incident CVD in both SHHS (SS%: OR 1.263, 95% CI 1.069-1.492, p:0.006; CREI: OR 1.286, 95% CI 1.099-1.506, p:0.002) and MESA (SS%: OR 1.666, 95% CI 1.193-2.327, p:0.003; CREI: OR 1.620, 95% CI 1.148-2.286, p:0.006). Among SHHS participants, 1,219 deaths were attributed to all causes, including 342 deaths due to CVD, whereas MESA recorded 89 all-cause deaths and 31 CVD-related deaths. A SS% > 9.3% was related with CVD-mortality (HR 1.439, 95% CI 1.127-1.838, p: 0.003) in SHHS and >7.0% with CVD mortality (HR 2.189 95% CI 0.991-4.834, p:0.053) in the MESA study. Male sex had a stronger relationship in all the analysis. In males, a significant initial increase in CVD mortality was observed up to an SS% of approximately 2.9%, followed by a decrease and subsequent linear increase beyond SS% 6.7% (HR 1.04, 95% CI 1.00-1.08) in the non-linear association analysis. Similar results were found for CREI. No significant linear relationship was found between SS% and CVD mortality in females.

Conclusions: An endotype of sleep apnea reflecting high loop gain is associated with CVD and CVD mortality, especially in males.

Rethinking Sleep Apnea Severity: Beyond AHI versus multidimensional Polysomnographic Indices

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Introduction: Obstructive sleep apnea (OSA) is a clinically and pathophysiologically heterogeneous disorder. Standard metric AHI alone fails assess spectrum of disease severity or predict consequences such as metabolic dysfunction or neuropsychiatric impairment. Each OSA phenotypes, has physiological signatures on polysomnography. Metabolic phenotype: ODI, duration saturation below 90%, Dmax duration), sympathetic activity. Neurocognitive/psychiatric: arousal index, REM duration. Hypoxic burden-phenotype. Due to limitations of AHI other polysomnographic parameters to be incorporated . This study evaluates whether AHI-based severity grading aligns with key physiologic markers in patients undergoing diagnostic polysomnography.

Materials and methods: This observational study included adult patients who underwent diagnostic polysomnography at a tertiary care center. Of 150 enrolled, data from the first 30 patients were analyzed. Subjects were divided into two groups: Group 1 (mild to moderate OSA, AHI < 30; n = 17) and Group 2 (severe OSA, AHI ≥ 30; n = 13). Parameters compared included , REM sleep duration, arousal index, lowest oxygen saturation, time spent with SpO₂ < 90%, oxygen desaturation index (ODI), desaturation maximum (Dmax) duration, and heart rate metrics. Statistical comparisons were made using independent t-tests or Mann-Whitney U-tests, and correlations with AHI were explored using

Pearson/Spearman coefficients. Complete data from 130 analyzable patients will be presented at the conference.

Results: In Group I, 14 subjects had REM less than 5% of Total Sleep time(TST). No correlation between AHI and NREM Arousal Index. Heart rate greater than 100 observed in 11 subjects (64%) not correlation AHI values. Duration with below 90 percent saturation, 13 subjects(76%) spent less than 2 minutes, 2 with moderate and one mild AHI spent 30 to 40 minutes and one mild grade with Arousal index 2 spent 119 minutes. Lowest Oxygen saturation less than 70% overserved in 3 subjects of moderate AHI.

In Group II, 11 subjects had REM less than 5% of Total Sleep time(TST) and 4 had no REM sleep. 10 Subjects with NREM AI less than 5 had AHI of more than 40. All 13 subjects had arousal index values less than 50% their corresponding AHI values. All subjects with less AI value had & more sever grade AHI, statistically not correlated. 7 subjects(50%) had longest duration of obstructive apnea more than 60 seconds. Among 12 subjects (92%)Highest Heart rate greater than 100 observed not corelating with AHI values. Duration with below 90 percent saturation, 6 subjects(46%) spent more than 100 minutes one subject 410 minutes. Lowest Oxygen saturation less that 70% overserved in 8(60%) subjects. 5 subjects(38%) had less ODI value compared to corresponding AHI values while 8 (62%) had ODI values at least 20% more than their AHI values. No correlation between AHI, ODI and D max duration.

Conclusions: Early findings suggest that AHI-based severity grading does not consistently align with other key physiological indicators of OSA burden. Metrics such as REM percent, AI, HR variability, ODI, Dmax duration, and hypoxic load may better reflect disease severity and clinical risk. Full analysis of 130 patients will further clarify these relationships and support a multidimensional severity framework in OSA assessment.

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Revealing the knowledge gap: Maxillomandibular Advancement for Obstructive Sleep Apnea in Skeletal Class III Patients

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Introduction: Maxillomandibular advancement (MMA) is a well-established and effective surgical intervention for the treatment of obstructive sleep apnea (OSA). It involves surgical repositioning of the maxilla and mandible to a more forward position, usually with a greater focus on the latter. In addition to functional improvements, it has been commonly cited to improve facial aesthetics in Skeletal Class I and II patients, especially for patients with a smaller lower jaw profile. However, the same cannot be applied to Skeletal Class III patients. The prevalence of OSA in Skeletal Class III patients is 11.22%. These patients have a longer lower jaw profile relative to their upper jaw. Thus, the principles applied to the classic MMA may no longer apply. Unfortunately, the application of MMA in skeletal Class III patients with OSA is not well documented.

Materials and methods: The aim of this scoping review was to explore the variations and outcomes of MMA techniques in this unique subgroup. A comprehensive search of PubMed, Embase, and Cochrane databases was conducted for articles published up to May 2025. The Inclusion criteria were: (1) Primary research articles; (2) Patients with skeletal Class III deformities; (3) Use of MMA or skeletal advancement surgery, (4) Diagnosis of OSA . The exclusion criteria were (1) Review articles; (2) Absence of skeletal Class III patients with OSA; (3) Inability to isolate data specific to Class III patients, (4) No skeletal advancement or MMA performed; (5) Lack of full-text availability or; (6) Presence of craniofacial syndromes

Results: Seven studies and 25 patients met the inclusion criteria. Three main variations of MMA were identified: (1) Bimaxillary advancement. Apnea-hypopnea Index (AHI) reduced by an average of $85.24 \pm 10.84\%$ after this variation of MMA was performed. This variation provided the most significant airway enlargement across all pharyngeal regions but carries the highest risk of facial aesthetic distortion in skeletal class III patients; (2) Maxillary advancement with mandibular auto-

rotation. The AHI was reduced by 81.7%. This is a less invasive option but is only suited for patients with isolated maxillary retrusion and symmetrical mandibular anatomy; (3) Maxillary advancement with mandibular setback. Mean AHI reduction was 68.23%. While this variation, addresses aesthetic concerns in patients with mandibular excess, it may compromise oropharyngeal airway space. The extent to which maxillary advancement can compensate for this potential airway reduction remains unclear. Essentially, all variations were reported to be effective in treating OSA.

Conclusions: Three surgical variations—bimaxillary advancement, isolated maxillary advancement, and maxillary advancement with mandibular setback—were identified, offer differing benefits depending on facial structure, obstruction site, and aesthetic goals. Surgical planning for skeletal Class III patients with OSA cannot rely on standardized protocols but must instead be tailored to patient-specific anatomy and functional needs. Further research with larger samples and detailed reporting is needed to guide evidence-based practice in this underrepresented subgroup.

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Risk of mild cognitive impairment in relation to sleep apnea parameters: an 8-year longitudinal study in a community-based cohort

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Introduction: obstructive sleep apnea (OSA), has been linked to cognitive impairment. However, few studies have examined how AHI severity over time relates to the development of mild cognitive impairment (MCI) in community populations.

Materials and methods: A total of 1,508 cognitively intact participants (K-MMSE ≥ 24) at baseline (2011–2014) who underwent in-home polysomnography (PSG) across three exam periods (baseline ~4-year intervals) were drawn from the Korean Genome and Epidemiology Study (KoGES) for this retrospective study. Sleep apnea parameters included overall and positional AHI, and REM and Non-REM AHI from PSG over 8 years. Participants were classified as cognitively unimpaired (CU) or Mild Cognitive Impairment (MCI) at the 2nd follow-up using the Seoul Neuropsychological Screening Battery-II (SNSB-II). Linear mixed regression estimated how 8-year trajectories of sleep parameters differed retrospectively by MCI status at the 2nd follow-up.

Results: Among the sleep apnea parameters assessed via PSG, although CU group has statistically insignificant change ($p=0.09$), the MCI group showed a slightly steeper increase in N1% of sleep duration from 2011–2014 to 2019–2022 (β [95% CI] = 0.57 [0.18, 0.95], $p = 0.004$). Also, the MCI group has marginally greater increase rate of supine AHI over 8-year periods from baseline (0.87 [0.002, 1.73], $p = 0.049$). Other sleep parameters, including overall AHI, non-supine AHI, REM AHI, and NREM AHI, did not show differential slopes between MCI groups; however, each group presented independent increases over time ($p < 0.05$).

In men, CU group showed a greater increasing rate in hypoxic burden index (HB) compared to MCI group (-2.64 [-5.19, -0.09], $p = 0.043$). Within-group analyses indicated significant increases in both groups over 8 years (5.45[4.12, 6.78], $p<0.001$ and 2.81[0.63, 4.99], $p=0.012$, respectively). In women, N1% of sleep duration differed significantly between groups, with the MCI group showing a greater 8-year increase (0.50 [0.04, 0.96], $p = 0.035$). Women with MCI also had a significantly steeper increase in REM AHI (1.36 [0.08, 2.64], $p = 0.037$). For sleep parameters without group–time interactions, overall AHI, supine AHI, and non-supine AHI increased independently in both CU and MCI groups ($p < 0.05$). Unlike men, women showed an additional independent increase in NREM AHI over time in both groups ($p < 0.001$), without group differences.

Conclusions: In this cohort, the MCI group showed modest increases in N1% of sleep duration and supine AHI, while men demonstrated no clear group differences aside from a rise in HB among CU participants. In women, however, MCI was associated with steeper increases in N1% of sleep duration and REM AHI. Given the established link between OSA and cognition, our findings suggest that rising REM AHI may contribute to elevated MCI risk, particularly in women. The significance of positional

parameters further highlights posture-related vulnerability. Overall, sleep parameters in future MCI cases may diverge years before diagnosis.

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Screening prediction models using artificial intelligence for moderate-to-severe obstructive sleep apnea in patients with acute ischemic stroke

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Introduction: Obstructive sleep apnea (OSA) is common after stroke. Still, routine screening of OSA with polysomnography (PSG) is often unfeasible in clinical practice, primarily because of how limited resources are and the physical condition of patients. In this study, we used several artificial intelligence techniques to predict moderate-to-severe OSA and identify its features in patients with acute ischemic stroke.

Materials and methods: A total of 146 patients with acute ischemic stroke underwent PSG screening for OSA. Their baseline demographic characteristics, including age, sex, body mass index (BMI), Epworth Sleepiness Scale (ESS) score, and stroke risk factors, were recorded. Logistic regression analysis was conducted to identify significant features associated with moderate-to-severe OSA in patients with stroke. These significant features were used with six machine learning and ensemble learning algorithms, namely decision tree, support vector machine, random forest, extreme gradient boosting (XGBoost), adaptive boosting (AdaBoost), and gradient boosting, to compare the performance of several predictive models.

Results: Multivariate logistic regression analysis revealed that age, sex, BMI, neck circumference, and ESS score were significantly associated with the presence of moderate-to-severe OSA. According to the machine learning and ensemble learning results, the XGBoost model achieved the highest performance, with an area under the receiver operating characteristic curve of 0.89 and an accuracy and F1 score of 0.80.

Conclusions: This study identified key factors contributing to moderate-to-severe OSA in patients with ischemic stroke. The XGBoost model exhibited high predictive performance, indicating it has potential as a supporting tool for decision-making in health-care settings.

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Self-Administered Home Sleep Testing Model in Screening of OSA in Healthcare Workers – SOHEW Study: A National Multi-Centre Study in Vietnam

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Introduction: Sleep disorders, including snoring and obstructive sleep apnea (OSA), are significant health concerns. OSA affects an estimated 4 million individuals in Vietnam, with 2.3 million suffering from moderate-to-severe conditions. Despite the high prevalence, underdiagnosis and limited accessibility to sleep diagnostics remain challenges. This study aims to assess the feasibility and effectiveness of a guided, self-administered home sleep study using a Level-3 diagnostic model.

Materials and methods: A cross-sectional multicenter survey conducted from October 2023 to March 2024 included healthcare professionals (HCPs) across Vietnam. Participants completed questionnaires (Epworth Sleepiness Scale, STOP-BANG), and high-risk individuals underwent respiratory polygraphy

using ApneaLink Air devices. Standardized instructions and technical support were provided remotely by trained technicians.

Results: This study involved 1,721 participants recruited from 16 hospitals across 4 regions of Vietnam. Screening and respiratory polygraphy (RPG) identified obstructive sleep apnea (OSA) in 21.9% of the participants. Among 358 high-risk individuals who underwent RPG using ApneaLink Air devices, 61.2% were diagnosed with OSA. The severity distribution in this subgroup was 32.5% mild, 19.5% moderate, and 9.2% severe OSA, while 38.8% had no OSA. Common symptoms reported across the total sample included memory impairment (49.4%), excessive daytime sleepiness (40.7%), and insomnia (22.8%). Regarding technical feasibility, 27 out of 358 RPG recordings (7.5%) were unsuccessful due to device-related or operational issues.

Conclusions: A Level-3 home sleep study model is effective for large-scale OSA screening. Integrating such approaches into public health initiatives can enhance early diagnosis and treatment access, reducing OSA-related health and economic burdens.

Self-reported continuous positive airway pressure (CPAP) therapy use for patients located in metropolitan and regional areas across Australia

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Introduction: Obstructive sleep apnoea (OSA) is a prevalent and underdiagnosed sleep disorder for which continuous positive airway pressure (CPAP) is typically considered the first-line treatment. Due to the geographical expanse of Australia, many Australians live in regional locations and may experience difficulty accessing CPAP. Metropolitan and regional differences in OSA care pathways have been explored previously, however differences in CPAP adherence within that sample had not been evaluated. Emerging evidence suggests that greater remoteness may be associated with poorer CPAP adherence in an Australian setting.

Materials and methods: Data are from a nationwide online survey to investigate pathways to diagnosis and management, use of treatments and health status of Australian adults with a diagnosis of OSA. Data collection took place in 2021. Participants were recruited via email, phone alerts and advertisements. Metropolitan and regional residence was coded according to Australian Bureau of Statistics criteria. Univariate analyses (Chi-Squared and Fisher's Exact tests) were conducted examining associations between demographic variables and CPAP usage variables. Demographic variables included age (<50, 50-67, 68+ years of age), sex, location (regional, metropolitan). CPAP usage variables included ever using CPAP, currently using CPAP, CPAP adherence (defined as self-reported use ≥ 4 hours/night and ≥ 5 nights/week). A multivariable binomial logistic regression was run with CPAP adherence as the dependent variable, and age and location as independent variables.

Results: Of the 412 respondents, 354 (86%) were recommended CPAP therapy (44% female), 138 (39%) resided in regional areas and 216 (61%) in metropolitan areas. 190 (54%) reported receiving a diagnosis of OSA 5+ years prior to participating in the survey. 'Moderate' and 'severe' self-reported OSA occurred in 37%, and 42% of respondents, respectively. 213 (69%) respondents who have used CPAP purchased their machine privately. Geographical location showed no significant associations with ever using CPAP ($p=.909$), currently using CPAP therapy ($p=.218$) or self-reporting as CPAP adherent ($p=.104$). Age group was not significantly associated with ever using CPAP ($p=.635$) or current use ($p=.838$). Age was significantly associated with CPAP adherence (<50 years: 54%; 50-67 years: 94%; 68+ years: 98%; $\chi^2(2, 245)=64.84, p<.001$). Sex was not significantly associated with ever using CPAP ($p=.717$), current use ($p=.929$) or CPAP adherence ($p=.687$). Compared to those aged <50, participants aged 50-67 were 13.8 times more likely to be CPAP adherent (95% CI: 5.48-40, $p<.001$), with those aged 68 and over 36.1 times more likely to be CPAP adherent (95% CI: 9.97-233, $p<.001$).

Conclusions: CPAP adherence was high (86%) which may have been related to sample characteristics, including socioeconomic advantage, and highly motivated individuals undertaking a survey. CPAP adherence did not vary significantly as a function of geographical location of participants, which may be related to the high proportion of private purchases of CPAP machines. Older age groups were

associated with a higher odds of CPAP adherence, though the lowest adherence observed was 54% (<50 years old). Limitations include the lack of objective CPAP data and regional location including both regional and remote.

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Sex differences in endocrine, metabolic and psychological disturbance in obese patients with OSA

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Introduction: Obstructive sleep apnea (OSA) is associated with increased risks of glucolipid metabolic disruption, endocrine disturbances and psychological distress. There is scarce research regarding the influence of sex on these associations. The current study aimed to evaluate the effects of sex on metabolic, endocrine and psychological changes in patients with OSA.

Materials and methods: One hundred sixty-four young adult women and one hundred sixty-two age-matched men with OSA completed polysomnography assessments, questionnaires (including the Epworth Sleepiness Scale [ESS], Self-Reported Anxiety Scale [SAS], Self-Rating Depression Scale [SDS], and 12-Item Short-Form Health Survey [SF-12]) and biochemical analyses for glucolipid metabolism and endocrine function, including the pituitary-adrenal (PA), pituitary thyroid (PT), and pituitary-gonadal (PG) axes.

Results: Homeostasis model assessment of insulin resistance (HOMA-IR), thyroid hormone and midnight PA axis activity levels were greater in female patients with severe OSA compared to those with mild-to-moderate OSA, and these metabolic and endocrine changes were associated with nocturnal hypoxia only in female patients. Additionally, midnight cortisol was associated with HOMA-IR (independent of anthropometry and sleep disturbance parameters) in females ($\beta = 0.545$, $P = 0.012$, adjusted $R^2 = 0.217$). ESS was higher for male patients with severe OSA compared to females with the same level of OSA ($P = 0.003$), and ESS was associated with nocturnal hypoxia in males ($\beta = -0.494$, $P = 0.001$, adjusted $R^2 = 0.224$). SAS was higher for female patients with severe OSA compared to males with the same level of disease ($P = 0.001$).

Conclusions: The metabolic, endocrine and psychological consequences of OSA may differ across sexes. The associations of nocturnal hypoxia with glucose metabolic disturbance and the activation of the PA and PT axes were observed in females, whereas the association of nocturnal hypoxia with ESS was limited to males. This could indicate a distinct metabolic, endocrine and psychological phenotype for female patients with OSA, who may require different disease management strategies compared to males.

Simultaneous Polysomnography and Cardiotocography Reveal Temporal Correlation Between Maternal Obstructive Sleep Apnea and Fetal Hypoxia

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Introduction: Obstructive sleep apnea syndrome (OSAS) during pregnancy is a prevalent complication that can negatively affect fetal outcomes. However, quantitative studies on the immediate effects of maternal hypoxia on fetal heart rate (FHR) changes are lacking, which could provide valuable clinical insights into the potential link between maternal OSAS and fetal hypoxia.

Materials and methods: Time-synchronized polysomnography (PSG) and cardiotocography (CTG) data from two prospective cohorts were used to analyze the temporal correlation between maternal hypoxic events and FHR changes (accelerations or decelerations). Maternal hypoxic event characteristics were analyzed using generalized linear modeling (GLM) to assess their associations with different FHR alteration. To accurately capture the dynamic fetal response, we employed a phase-specific analysis framework that explicitly divided each maternal hypoxic event into pre-, during-, and post-event

phases, enabling precise temporal mapping of FHR fluctuations in relation to maternal oxygenation changes.

Results: A total of 118 pregnant women were included, with 35 from Peking University People's Hospital and 83 from the Maternal Sleep in Pregnancy and the Fetus (MSP) dataset. Immediate FHR changes were significantly associated with maternal hypoxic events, primarily characterized by accelerations as a compensatory response. Notably, a longer hypoxic duration was strongly correlated with increased FHR accelerations ($P < 0.05$), while both prolonged hypoxia (Coef. = 0.012, $P < 0.001$) and greater SpO₂ drop value (Coef. = -0.151, $P = 0.046$) were significantly linked to FHR decelerations in the MSP dataset. Across both cohorts, maternal hypoxia induced a transient increase in FHR, which subsequently returned to baseline following the resolution of hypoxic episodes, reflecting dynamic and reversible fetal responses.

Conclusions: The immediate impact of maternal hypoxia on FHR changes highlights the link between maternal and fetal hypoxia, suggesting that maternal OSAS may contribute to fetal hypoxia. These findings underscore the risks of pregnancy-related OSAS and the importance of maternal-fetal interactions, providing a foundation for future research on interventions to improve fetal health.

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Sleep and cardiovascular outcomes are worse in people with co-morbid obstructive sleep apnoea and chronic respiratory disease: insights from consumer data

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Introduction: Respiratory disease and obstructive sleep apnoea (OSA) are individually associated with increased risk of cardiovascular disease (CVD) and all-cause mortality. People with co-morbid respiratory disease and OSA (co-ROSA) may be at increased cardiovascular risk due to worse night-time hypoxemia which may be exacerbated by disrupted sleep. However, there is a lack of data assessing sleep and cardiovascular risk in co-ROSA.

Materials and methods: We used an international consumer sample of 321,307 nights of sleep data (Withings Sleep Analysers and Scan Watches) from 2573 people with a self-reported doctor diagnosis of respiratory disease (asthma, chronic obstructive pulmonary disease, emphysema) and/or OSA. The odds of self-reported CVD (heart attack, stroke, coronary heart disease, congestive heart failure) and sleep metrics were compared in co-ROSA, respiratory disease and OSA using logistic regression and ANCOVA, respectively, while controlling for age, sex, and BMI. It was hypothesised that people with co-ROSA would have poorer sleep (less total sleep time, higher sleep irregularity, and decreased sleep efficiency), and greater incidence of cardiovascular disease, than people with respiratory disease or OSA alone.

Results: Participants were middle-aged (53.2 ± 13.7 yrs, mean $\pm$ SD), predominantly male (73.2%), with high BMI (31.1 ± 6.5 kg/m²), and normal sleep duration (7.2 ± 1.2 hrs). People with co-ROSA had shorter sleep duration (7.07 hrs $\pm$ 82 minutes) than people with respiratory disease (7.41 hrs $\pm$ 65 minutes), as well as higher night to night variability (rmssd of sleep duration = 137.78 ± 93.41) compared to respiratory disease alone (122.89 ± 58.90), and poorer sleep efficiency ($85\% \pm 9.17$) than respiratory disease alone ($89\% \pm 7.33$). However, there were no differences between co-ROSA and OSA. Co-ROSA was associated with 53% increased odds of CVD compared to respiratory disease 95%CI [30, 92], $p=0.02$, but not OSA, OR 66%, 95%CI [42, 105], $p=0.08$.

Conclusions: Overall sleep quality was worse in co-ROSA than respiratory disease alone, with shorter sleep duration, greater night to night variability, and poorer sleep efficiency. In line with this finding, CVD is also more prevalent in co-ROSA than respiratory disease alone. OSA often goes undiagnosed in people with co-morbid respiratory disease as it can be more challenging to diagnose in this population. OSA diagnosis should be prioritised in people with respiratory disease to improve sleep outcomes and better identify CVD risk. The nearable and wearable technology utilised in this study is a promising new tool that could aid in the diagnosis and management of OSA in more challenging and under-diagnosed populations.

Sleep and hematological diseases

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Introduction: Sleep is fundamental in global health and multidisciplinary is the key. We focussed on the link between hematologists and sleep specialists. In clinical practice patients are referred to Sleep Unit by the hemathologists to detect obstructive sleep apnea (OSA) in case of : Sickle cell disease (SCD) and erythrocytosis. The aim of this abstrct is to make a state of the art of data in Literature.

Materials and methods: A research on Pubmed was performed for "sickle cell disease and sleep disorders"; "sickle cell disease and OSA" , "erythrocytosis and OSA". For the 2 pathologies datas about epidemiology, prevalence, physiopathology, recommandations and treatment have been collected.

Results: Sickle cell disease is the most common genetic disease worldwide. Studies describe an higher prevalence of OSA in SCD (17-44%) than in general population (4-8%). That can be partially due to origin of patients (african more than caucasian), social profile (underprivileged population), increased attention to diagnosis as OSA can aggravate SCD. The mechanisms of this aggravation in OSA patients are: intermittent hypoxia that can trigger Hbs polymerisation and red blood cells (RBC) sickling; oxydative stress and inflammation; impaired vascular function and autonomic nervous system dysfunction that can generate venocclusive crisis. In Literature in the last 40 years few papers and only 3 clinical trials with small population have been published on this subject. They confirmed the strong association OSA and SCD.

OSA signs and symptoms in SCD patients are unusuals : patients are younger, with lower IMC, less sleepy, blood pressure is not higher, and at polygraphy there are more désaturations. More than 50% of patients are Insomniacs.

The complications in SCD seem to be associated to hypoxia on the contrary the apnea hypopnea index (AHI) doesn't seem to be a reliable marker of SCD crisis. There is still no evidence that treating OSA in adults reduces SCD complications.

Erythrocytosis is an abnormally elevated number of RBC and screening OSA is recommanded if a secondary erythrocytosis is suspected. Intermittent hypoxia in OSA is considered a potential trigger for erythropoietin production. Among the 171 papers analysed in the metalalysis publishd in 2022 (Martelli et al; HEMATOLOGY) the prevalence of erythrocytosis in OSA is 2% and in severe OSA 6.2%. The effects of CPAP were a reduction of 3.7- g/l of Hb and 1,1% of HCT.

Erythrocytosis in OSA can be also relative : due to nycturia if the blood test is done in the morning the hemoconcentration during sleep can be responsable of a higher HCT that will be normalised if the blood test is controlled in the afternoon (differences up to 7%).

Conclusions: Hematologists are concerned by OSA diagnosis in SCD and erythrocytosis. In both diseases the physiopathology of the association is well known but we still need studies to determine the threshold of AHI or hypoxic burden to propose treatment and the efficacy of CPAP in reducing crisis in SCD patients and reducing HCT in erythrocytosis

Studies about sleep and hematology are a good exemple of the multidisciplinary of sleep medicine

Sleep and Survival: A Low-Cost Home Ventilation Strategy for Children with Neuromuscular disease in Resource-Limited Settings

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Introduction: Children with neuromuscular disorders are especially vulnerable to sleep-related breathing disturbances and chronic respiratory failure, which is a leading cause of death in these children. In many low- and middle-income countries, delivering comprehensive care is challenging due to high out-of-pocket costs and limited access to specialized equipment. This study presents real-world

data from a pediatric neuromuscular clinic in India, highlighting how low-cost, innovative strategies can support effective home ventilation and sleep care in resource-limited settings.

Materials and methods: This is a retrospective observational study. We included children with NMD up to 18 years of age who attended our tertiary pediatric neuromuscular clinic between January 2018 and February 2025. Clinical profiles, Level-1 Polysomnography (PSG) data when available, along with treatment and outcomes, were analysed.

Results: 415 children (63.6% male) diagnosed with NMD were included. The majority of our cohort had spinal muscular atrophy (SMA, n=213), followed by Duchenne muscular dystrophy (DMD, n=96), and the remaining had other NMD (n=106).

302/415 (72.2%) children had a PSG done with a median Apnea-Hypopnea Index (AHI) of 7.6 (0.3 to 78) per hour of total sleep time, with 64.14% of children having moderate to severe OSA.

HMV was initiated in 351/415 (84.5%) of children. 78/213 (36.6%) of children with SMA1 and SMA2 received DMT-like gene therapy (n=35), Risdiplam (n=22), and Spinraza (n=21). 18 children had a tracheostomy, 55 used mechanical insufflation-exsufflation (MI-E), 34 were on NG feeds, and 28 had a PEG tube with fundoplication done. Optimizing care in these children reduced recurrent hospital admissions in 74% of children. 25 children expired due to respiratory failure.

Among 351 children on HMV, 68% were remotely monitored via video and telephone consultations. A 24/7 emergency contact number along with technician support was provided to families, many of whom travel from across India and often lack access to specialized respiratory care locally. Smaller hospitals frequently hesitate to initiate BiPAP in acutely unwell children, making remote guidance and continuity of care essential.

To overcome the financial burden of out-of-pocket healthcare expenses in India, families utilize affordable Indian-manufactured BiPAP devices (costing <\$500 USD) or rent BiPAP and MI-E machines for \$40 and \$120/month, respectively. Additional support through crowdfunding has helped cover the cost of diagnostics and treatment, while the donation of 40 BiPAP units to our neuromuscular disease unit has further expanded access. Equally important has been the role of family WhatsApp groups, which have become a powerful tool for real-time support, shared learning, and fostering a sense of community among caregivers facing similar challenges and simultaneously raising awareness.

Conclusions: A low threshold for initiation of BiPAP when indicated without a PSG initially is a reasonable practical approach in resource-limited settings. Early initiation of cough assist and HMV helped reduce morbidity and mortality.

This model of care—combining remote monitoring, low-cost locally manufactured respiratory devices, rental options, and philanthropic support—demonstrates a sustainable approach to delivering HMV. Such strategies provide a practical framework for scalable and equitable chronic respiratory care in other low- and middle-income countries.

Sleep Apnea-Hypopnea Events Detection Using a Wireless Abdomen-Worn Sensor with SpO₂ Monitoring

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Introduction: Obstructive sleep apnea (OSA) is traditionally diagnosed using polysomnography (PSG), a costly and inconvenient procedure requiring specialized facilities and long wait times. To address these challenges, wireless wearable devices have been explored as alternatives. However, most of these devices do not classify apnea and hypopnea events, which are essential for determining appropriate treatment for OSA. Detecting hypopnea is particularly challenging due to its subtle characteristics compared to apnea. This study presents a deep learning method for classifying apnea and hypopnea events using a wireless abdomen-worn sensor and SpO₂ monitoring.

Materials and methods: Two hundred participants suspected of OSA underwent overnight in-laboratory PSG, along with data collection from a wireless abdomen-worn sensor (sampling rate: 5 Hz). PSG data were manually scored by clinicians, classifying respiratory events as apnea or hypopnea. SpO₂ and pulse rate data were extracted from PSG and downsampled to 5 Hz. Capacitive and 3-axis accelerometer data from the abdomen-worn sensor were synchronized with the PSG data and preprocessed. Features such as normalized capacitance, local capacitive gap, sleep position, and the length of the acceleration vector were extracted from the capacitive and accelerometer data, serving as primary inputs for the classification model. The MLP-Mixer model was employed for automated classification, utilizing inputs that included the extracted features along with or without SpO₂ and pulse rate information. The apnea-hypopnea index (AHI) was computed as the total number of apnea and hypopnea events detected by the model divided by the recording time. Seven recordings were excluded due to poor data quality, leaving 100 subjects for training and 93 for testing. The area under the curve (AUC) metric was used to evaluate the model's performance in detecting apnea and hypopnea across three configurations: Model 1 (abdomen-worn data with SpO₂ and pulse rate), Model 2 (abdomen-worn data with SpO₂), and Model 3 (abdomen-worn data alone). The agreement between AHI measured by PSG (AHI-PSG) and the predicted AHI (AHI-Model) was assessed through Pearson correlation.

Results: On the test set, the hypopnea detection resulted in AUC values of 0.856, 0.8762, and 0.7571 for Model 1, Model 2, and Model 3, respectively. The apnea detection resulted in AUC values of 0.9483, 0.9511, and 0.9035 for Model 1, Model 2, and Model 3, respectively. The combined features of Soomirang and SpO₂ achieved a sensitivity of 0.7786 and specificity of 0.8082 for hypopnea detection, and a sensitivity of 0.9436 and specificity of 0.8015 for apnea detection. The correlation coefficient between AHI-PSG and AHI-Model2 was 0.9694.

Conclusions: This study highlights the effectiveness of using a wireless abdomen-worn sensor combined with SpO₂ data for accurately classifying apnea and hypopnea events. The results underscore the promise of a non-invasive, wireless, wearable solution for reliable OSA screening.

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Sleep apnea phenotypes based on multi-night assessment of sleep perception

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Introduction: Sleep time misperception has been reported in obstructive sleep apnea (OSA) patients during polysomnography (PSG). However, little is known about multi-night sleep perception patterns in OSA patients' daily lives. We leveraged recent developments in wearable technology to identify OSA phenotypes based on patients' sleep perception patterns over multiple nights in their regular sleeping environment.

Materials and methods: The study included newly diagnosed OSA patients who were instructed to track their sleep for 14 days using objective and self-report metrics. Objective sleep parameters were calculated using a four-class sleep staging algorithm (distinguishing Wake, combined N1/N2, N3, and REM) that takes instantaneous heart rate and body movements acquired through a validated wrist-worn photoplethysmography and accelerometry device as input. A digital sleep diary was used to assess self-reported sleep parameters. All measurements were completed after diagnostic PSG and prior to starting OSA treatment. The perception of total sleep time (TST) was evaluated using the misperception index (MI), using the following formula: (objective TST – self-reported TST)/objective TST. K-means clustering was used to identify multi-night sleep perception patterns using two features: the median and the median absolute deviation of patients' MI values. Clusters were compared across several clinical characteristics and sleep parameters. For continuous parameters, the Kruskal-Wallis test (KW) was performed, with Dunn's post-hoc test (D) in case between-group comparisons were significant. For dichotomous variables, the chi-square test was performed, with pairwise Fisher Exact tests for post-hoc analysis.

Results: The study included 120 OSA patients, with 1605 recording nights in total (median=12.00, IQR=7.00). We identified four distinct sleep perception clusters: accurate estimation (n=64), underestimation (n=33), severe underestimation (n=6) and variable overestimation (n=17). Patients in the variable overestimation cluster were older (median age = 57.00) than patients in the accurate estimation cluster (median age = 46.50, $D p=0.005$), and had a higher apnea hypopnea index (AHI) than participants in all other clusters (KW $p=0.003$). Moreover, the sleep architecture of patients in this cluster was more disrupted compared to the other clusters, with a lower sleep efficiency than the accurate estimation cluster ($D p=0.007$), and a higher N1/N2% (KW $p=0.001$), a lower N3% (KW $p=0.044$) and a lower REM% (KW $p=0.024$) than the accurate and underestimation cluster. Both underestimation clusters had a higher prevalence of insomnia symptoms (Chi-square $p=0.001$), a lower self-reported sleep quality (KW $p<0.001$) as well as a higher Insomnia Severity Index (KW $p=0.001$), Pittsburgh Sleep Quality Index (KW $p<0.001$), and Pre-Sleep Arousal Scale (KW $p=0.013$) score than the other clusters. The severe underestimation cluster reported a particularly high pre-sleep cognitive arousal which significantly differed from the accurate estimation and variable overestimation clusters (KW $p=0.004$).

Conclusions: Distinct OSA phenotypes can be identified based on patients' multi-night sleep time perception patterns. Different phenotypes present with distinct clinical characteristics. For instance, they exhibited distinct profiles with regards to their AHI, insomnia symptom prevalence, as well as objective and self-reported sleep characteristics, highlighting the heterogeneity of the OSA population. These insights may facilitate more personalized treatment approaches.

Sleep Apnea-Specific Hypoxic Burden and Postoperative Outcomes Of Major Non-Cardiothoracic Surgery

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent and heterogeneous condition that predisposes to postoperative complications. Adequate metrics of OSA severity to stratify postoperative risk in clinical setting are needed. This study evaluates whether quantifying OSA severity by the sleep apnea-specific hypoxic burden (SASHB) would predict postoperative cardiovascular (CV) complications and mortality among patients undergoing major non-cardiothoracic surgery.

Materials and methods: Multicenter clinic-based cohort linked with health administrative database, involving adult patients diagnosed with OSA between May 2007 and December 2018 who underwent major non-cardiothoracic surgery between OSA diagnosis and December 2021.

Exposure SASHB is defined as the area under the desaturation curve associated with sleep-related obstructive respiratory events.

The primary outcome was a composite of stroke, atrial fibrillation, heart failure, myocardial infarction, venous thrombo-embolism, and all-cause mortality within 30 days of surgery. The association of SASHB and other OSA severity metrics with the primary outcome was investigated using univariable and multivariable analyses.

Results: Among 1,962 patients with OSA (median [IQR] age of 58 [49-66] years; 64% men) who underwent major non-cardiothoracic surgery 3.5 [1.6-5.8] years after OSA diagnosis, the primary outcome occurred in 71 patients (3.6%) within 30 days of surgery. Compared with patients with SASHB<32%min/h, patients with higher SASHB at diagnosis exhibited increased odds for the primary outcome (adjusted OR [95%CI], 3.291 [1.407-7.699] and 4.217 [1.829-9.723] for SASHB 32 to <80%

and $\geq 80\%$ min/h respectively). A risk score based on age, history of CV diseases and SASHB was predictive of the primary outcome (area under receiver operating characteristic curve, 0.72 [95% CI, 0.68-0.79]).

Conclusions: Among OSA patients undergoing major non-cardiothoracic surgery, SASHB was significantly associated with the risk of 30-day postoperative mortality and CV complications. Further research is needed to determine whether interventions guided by SASHB scores can modify postoperative risk in patients with OSA.

Sleep Architecture and Quality of Life in Comorbid OSA and Depression: Cross-sectional analysis of the Sydney Sleep Biobank

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Introduction: Obstructive sleep apnoea (OSA) and depression are individually associated with changes in sleep architecture and reduced quality of life. However, there are few studies which report on the joint impact of comorbid OSA and depression.

Materials and methods: 1217 participants from the Sydney Sleep Biobank database were assessed (38% female; age 49.5 ± 15.6). Participants were patients who were referred for and underwent an overnight sleep study on suspicion of sleep disordered breathing. Participants were divided into 4 groups based on the presence or absence of OSA and depression. Participants who were diagnosed with an alternate sleep disorder (i.e. central sleep apnoea, restless legs syndrome, insomnia, narcolepsy) were excluded. Criteria used to divide the groups were an apnoea-hypopnoea index greater than 5/hour ($AHI \geq 5$) and a depression subscore greater than 4 ($D > 4$) from the Lovibond and Lovibond Depression Anxiety Stress Scale-21; (1) no OSA-no depression ($AHI < 5$, $D \leq 4$), (2) OSA-only ($AHI \geq 5$, $D \leq 4$), (3) depression-only ($AHI < 5$, $D > 4$), (4) comorbid OSA and depression ($AHI \geq 5$, $D > 4$). Sleep architecture, quality of life (Epworth Sleepiness Scale, ESS and Functional Outcomes of Sleep, FOSQ-10), and cardiovascular comorbidities and cardiovascular risk as indicated by Framingham risk scores were compared between groups. Covariates considered included age, gender, body mass index, smoking, alcohol, and psychiatric medications.

Results: Data from 821 participants were included in the final analysis. Comorbid OSA and depression was associated with a longer REM latency (REML) than OSA-alone (141min vs 123min, $p=0.043$). However, further analysis excluding patients on psychiatric medications revealed that the prolonged REML was a medication effect. After psychiatric medications were accounted for, there were no other significant differences in sleep architecture between comorbid OSA and depression and OSA-alone. Depression groups had worse ESS and FOSQ-10 scores. There was no increase in cardiovascular risk or comorbidities with comorbid OSA and depression compared to OSA-alone.

Conclusions: Despite the lack of changes in sleep architecture, it is still important to identify comorbid OSA and depression as it can be associated with worse quality of life and this may affect treatment compliance.

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Sydney Sleep Biobank Investigators:

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Sleep breathing impairment index predicts incident atrial fibrillation in obstructive sleep apnea: a prospective cohort study

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Introduction: Respiratory-event-associated hypoxia is crucial in cardiovascular comorbidities of obstructive sleep apnea (OSA). Intermittent hypoxia is an independent risk factor for atrial fibrillation (AF). The sleep breathing impairment index (SBII) is a novel metric that quantifies respiratory events and hypoxia, showing exceptional efficacy in predicting cardiovascular diseases. This study aims to evaluate the association between SBII and AF in OSA patients and compare the predictive performance of various OSA severity indices in predicting incident AF.

Materials and methods: This study included 1660 OSA patients without pre-existing AF from the Sleep Heart Health Study. Baseline SBII values were stratified into quartiles. Multivariate logistic regression analysis and restricted cubic spline analysis were conducted to explore the association between SBII and incident AF. Harrell's concordance statistic (C-statistic) was performed to compare the predictive value of SBII against other OSA severity indices.

Results: During a mean follow-up of 5.3 years, 190 (11.5%) OSA patients developed AF. SBII and hypoxic burden (HB) were associated with an increased risk of incident AF, with adjusted odds ratios of 1.87 (95%CI: 1.14, 3.11; $P=0.015$) and 2.01 (95%CI: 1.20, 3.41; $P=0.009$) for the third and fourth quartiles of SBII, respectively, and 1.70 (95%CI: 1.04, 2.81; $P=0.038$) for the fourth quartile of HB. Moreover, SBII had the largest C-statistic (0.75, 95% CI: 0.709, 0.782) compared with HB, AHI, and ODI.

Conclusions: This study demonstrated that elevated SBII and HB levels increased the risk of incident AF in OSA patients, with SBII outperforming other OSA severity indices in predicting AF.

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Sleep-disordered breathing in children with Prader-Willi syndrome and the effect of growth hormone therapy

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Introduction: Growth hormone (GH) therapy may influence sleep-disordered breathing in children with Prader-Willi syndrome (PWS). This study analyzes polysomnographic data collected before and after GH initiation and compares longitudinal data on sleep-related respiratory parameters between children who received GH and those who did not.

Materials and methods: This retrospective study analyzed longitudinal polysomnographic data from children with PWS who underwent polysomnography at Cincinnati Children's Hospital between 2000 and 2024. Participants were categorized based on whether they received GH therapy. In the GH-treated group, pre- and post-treatment sleep parameters were compared using the Wilcoxon signed-rank test. Additionally, longitudinal polysomnographic data were compared between GH-treated and untreated children.

Results: A total of 49 children with PWS were included, with a median age of 1.3 years at their initial polysomnography. GH therapy was initiated in 32 of these children at a median age of 1.9 years. At baseline, the median obstructive apnea-hypopnea index (AHI) was 1.8 events/hour, with 25% of children exceeding 5.0 events/hour. Although the median obstructive AHI did not change significantly following GH therapy ($P = 0.639$), 56% of children showed an increase in obstructive events. In contrast, the median central AHI significantly decreases after GH therapy ($P = 0.014$). There were no significant differences in obstructive or central AHI between the GH-treated and untreated groups.

Conclusions: The rise in obstructive AHI among most children with PWS after GH therapy underscores the need for surveillance polysomnography to enable early detection and proper management.

Sleep-disordered breathing increases all-cause and cardiovascular mortality in patients with diabetes mellitus - SHHS study

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Introduction: Sleep-disordered breathing (SDB) and diabetes mellitus (DM) frequently coexist; however, limited data are available on the effect of SDB on mortality in individuals with DM.

Materials and methods: The analysis included data from the Sleep Heart Health Study, a multicenter prospective observational study encompassing 5,780 participants with polysomnography and mortality data, among whom 453 had diabetes mellitus (DM). The study aimed to evaluate the influence of sleep-disordered breathing (SDB) variables and the presence of DM on all-cause, cardiovascular disease (CVD), and non-CVD-related mortality. Survival analysis and proportional hazard regression models were employed to determine adjusted hazard ratios (aHR) for mortality outcomes.

Results: Patients with diabetes mellitus (DM) who had an average SpO₂ greater than 91.4% demonstrated significantly lower risks of all-cause mortality (aHR 0.52, CI 0.34–0.80) and cardiovascular disease (CVD) mortality (aHR 0.44, CI 0.22–0.87) compared to those with SpO₂ below this threshold. In participants with DM receiving treatment, an apnea-hypopnea index above 31 (aHR 1.58, CI 1.10–2.28) and an oxygen desaturation index greater than 13.3 (aHR 1.58, CI 1.10–2.25) were linked to higher all-cause mortality. Sleep efficiency and the proportion of rapid-eye movement (REM) sleep did not affect mortality in patients with DM, differing notably from individuals without DM, where reduced sleep efficiency (<81.4%; aHR 0.77, CI 0.68–0.87) or lower REM sleep (<14.9%; aHR 0.78, CI 0.68–0.89) was associated with increased all-cause mortality.

Conclusions: Patients with diabetes undergoing treatment and moderate to severe sleep-disordered breathing face an elevated risk of all-cause mortality. Lower average oxygen saturation was a predictor of both all-cause and cardiovascular mortality in individuals with diabetes.

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Sleep-disordered breathing is associated with adverse short - and long-term outcomes in acute ischemic stroke and TIA: Findings from the Bern Sleep-Stroke Registry

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Introduction: Sleep-disordered breathing (SDB) is prevalent after stroke and has been associated with poor outcomes; however, data from large cohorts following acute ischemic stroke remain limited. This study aimed to evaluate the impact of SDB on all-cause mortality, major adverse cardiovascular events (MACE), and functional outcomes.

Materials and methods: This retrospective cohort study included consecutive patients with acute ischemic stroke at the Stroke Center at Inselspital Bern who underwent respiratory polygraphy within 72 hours of admission. SDB severity was stratified by the apnea-hypopnea index (AHI) into mild (AHI ≥ 5 events/h), moderate (AHI ≥ 15 events/h), and severe (AHI ≥ 30 events/h). Outcomes included poor functional outcome (modified Rankin Scale [mRS] ≥ 3 at 3 months), all-cause mortality, and MACE. Associations were evaluated using multivariable Cox and logistic regression models, adjusted for age, sex, body mass index, hypertension, diabetes, dyslipidemia, atrial fibrillation, and initial stroke severity (NIHSS). Results were reported as adjusted hazard ratios (HR) or adjusted odds ratios (OR) with 95% confidence intervals (CI).

Results: A total of 1083 patients were included (678 males, 62.6%; mean age 66.0 ± 14.5 years; mean follow-up 84 months). SDB (AHI ≥ 5 /h) was present in 819 patients (75.6%), including 323 (29.8%) with mild, 248 (22.9%) with moderate, and 248 (22.9%) with severe SDB. Central sleep apnea was identified in 69 (6.4%) patients. Severe SDB was significantly associated with all-cause mortality (adjusted HR 2.77, 95% CI: 1.20–6.40). Moderate (adjusted HR 1.81, 95%CI: 1.18–2.79) and severe SDB (adjusted HR 1.55, 95%CI: 1.01–2.40) were linked to increased an increased risk of MACE, and severe SDB was associated with poor functional outcome (mRS ≥ 3) at 3 months (adjusted OR 2.50, 95%CI: 1.46–4.38). **Conclusions:** In this large cohort from the Bern Sleep-Stroke Registry, SDB was highly prevalent and independently associated with mortality, cardiovascular events, and impaired functional recovery, with risks increasing by severity. These findings support routine SDB screening and severity-based risk assessment in stroke care.

Sleep fragmentation during REM and NREM sleep and glucose metabolism in patients with obstructive sleep apnea

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Introduction: Although numerous studies have demonstrated the positive relationships between apnea-hypopnea index (AHI), micro-arousal index (MAI) and glucose metabolism, the associations between sleep fragmentation during REM-phase and NREM-phase and abnormal glucose metabolism is not clear yet.

Materials and methods: Subjects with initially suspected obstructive sleep apnea (OSA) in the Shanghai Sleep Health Study (SSHS) were selected. For each subject, MAI-REM and MAI-NREM data from overnight standard polysomnography; fasting plasma glucose and insulin (FINS) were also collected. The relationships between MAI and glucose metabolism in REM and NREM phases were assessed by logistic regression and multivariable linear regressions.

Results: A total of 4448 participants (mean age: 41.336 ± 12.374 years and mean BMI: $26.261 \pm 3.713 \text{ kg/m}^2$) were finally included in this study. Of all the subjects, the mean MAI-REM was 25.496 ± 19.279 events/h, and the mean MAI-NREM was 25.540 ± 18.204 events/h. Linear regression analyses revealed that MAI-NREM was independently associated with FINS ($\beta = 0.014$, $P = 0.011$). This association remained significant after sensitivity analyses excluding subjects with MAI-REM higher than the median ($\beta = 0.032$, $P = 0.026$). However, logistic regressions showed that no significant correlations were found between MAI-REM, MAI-NREM and hyperglycemia, hyperinsulinemia or insulin resistance (all $P > 0.05$), after adjustment for confounders including age, sex, BMI, smoking and alcohol consumption.

Conclusions: In OSA patients, a significant positive correlation was observed between MAI-NREM and FINS. Further prospective cohort studies are needed to determine such relationships.

Sleep quality and sleep symptom manifestation in patients with atrial fibrillation and sleep apnea

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Introduction: Sleep apnea is highly prevalent in patients with atrial fibrillation (AF). Daytime sleepiness is an important consequence of sleep apnea, which can compromise quality of life. The current guidelines recommend screening for signs and symptoms of sleep apnea in patients with AF and considering treatment of sleep apnea to improve AF treatment outcomes. There have been suggestions that patients with AF tend to have poor quality of sleep but manifest less pronounced sleep symptoms. We investigated objective sleep quality and subjective daytime sleepiness in patients with AF.

Materials and methods: We included patients with and without (1:1 match) a history of AF who underwent clinically indicated in-lab sleep study at a single academic sleep center. Sleep apnea was defined by apnea-hypopnea index ≥ 15 . We compared sleep quality metrics (total sleep time, sleep efficiency, and deep sleep time [N3]) based on polysomnography by sleep apnea status. In patients with sleep apnea, we compared the subjective report of daytime sleepiness as measured by the Epworth sleepiness scale (ESS). We then examined whether excessive daytime sleepiness (EDS) ($ESS \geq 11$) is associated with sleep apnea in patients with AF, adjusting for sex, obesity, and age category by AF status.

Results: The cohort included 465 patients (AF 51%, male 57%, mean age 63). The prevalence of sleep apnea was similar between patients with and without AF (58 vs. 52%, $p=0.16$). While there was no difference in total sleep time (276 vs. 291 min, $p=0.18$), sleep efficiency (68 vs. 73%, $p=0.01$) was lower in patients with AF. The amount of deep sleep (N3) was similar between the two groups (10.6 vs. 11.6 min, $p=0.48$). In patients with sleep apnea, the reported degree of daytime sleepiness (ESS 10.1 vs. 10.7, $p=0.32$) and the prevalence of EDS (36 vs. 40%, $p=0.46$) were similar between the two groups. In multivariable analysis, EDS was associated with the risk of sleep apnea (odds ratio: 1.87 [1.1, 3.3], $p=0.03$). However, such an association was not found in patients with AF (odds ratio: 1.23 [0.71, 2.15], $p=0.46$).

Conclusions: Patients with AF had lower sleep efficiency but comparable total sleep time and deep sleep compared to patients without AF. In patients with sleep apnea, the subjective reporting of EDS was similar to that of patients without AF. In patients with AF, EDS was not predictive of sleep apnea. Thus, more rigorous sleep apnea screening beyond symptoms may be indicated in patients with AF.

Sleep Quality with EPAP Enhanced Novel Mandibular Advancement Device versus Continuous Positive Airway Pressure in Severe Obstructive Sleep Apnea

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Introduction: The study was performed to compare self-reported sleep quality, treatment compliance, and respiratory event index (REI) after 6 months of treatment with EPAP enhanced mandibular advancement device - O2Vent Optima+ExVent (EMAD) versus continuous positive airway pressure (CPAP) in severe obstructive sleep apnea (OSA). O2Vent Optima is a novel oral appliance that incorporates both mandibular advancement to reduce pharyngeal collapsibility and an air channel that allows airflow through the device to circumvent nasopharyngeal obstruction. The ExVent is an accessory to the novel oral appliance and provides oral Expiratory Positive Airway Pressure (EPAP) to support upper airway by passive dilatation of the airway, which reduces flow limitation.

Materials and methods: A total of 26 patients with severe OSA who either declined or failed CPAP were treated with EMAD. The comparison group was 26 severe OSA patients who were treated with CPAP therapy. Both groups were prospectively followed for 6 months. Data were collected through Level 1 polysomnographic sleep recordings, CPAP downloads, Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale (SSS) and Functional Outcomes of Sleep Questionnaire (FOSQ-10). Data was analyzed to assess compliance, ESS, SSS, FOSQ-10 scores and REI, respectively. Reliable change index (RCI) was used to evaluate change in FOSQ global score.

Results: More patients were compliant with EMAD treatment (89.5%) than CPAP treatment (67.9%) at 6-month follow-up ($P<0.01$). Both groups had improved ESS, SSS and FOSQ-10 scores: EMAD (ESS: 12.8 ± 3.6 to 7.9 ± 2.6 ; SSS: 3.4 ± 1.2 to 2.2 ± 0.7 FOSQ-10: 13.2 ± 2.9 to 17.3 ± 3.1 ; mean difference - 2.9, (95% CI -3.5 to -2.4); $P<0.001$) and CPAP (ESS: 13.2 ± 3.5 to 6.7 ± 3.4 , SSS: 3.3 ± 1.1 to 2.2 ± 0.9 ; FOSQ-10: 13.9 ± 2.5 to 17.8 ± 3.6 ; mean difference -3.1 (95% CI -3.2 to -2.4); $P<0.001$). Patients in both groups had improved FOSQ global score according to the RCI, EMAD group (38.6%) and CPAP

group (36.7%) ($P > 0.05$). Both treatments reduced REI to $< 10/\text{hr}$. similarly; EMAD (82%) and CPAP (94%) ($P > 0.05$).

Conclusions: Both EMAD and CPAP treatments improved self-reported sleep quality in patients with severe OSA. EMAD treatment was associated with better compliance; however, the improvement in sleep quality was similar with EMAD and CPAP, REI was reduced similarly with both the treatments. We conclude that EMAD treatment should be considered an effective therapeutic option for severe OSA patients who decline or fail CPAP therapy.

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Sleep-Related Tongue-Biting Events Associated with Obstructive Sleep Apnea: A Case Report

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Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder, but it is very rare to be combined with sleep-related facial mandibular myoclonus (SRFMM). The relationship between OSA and SRFMM is not clear.

Materials and methods: This case reports the medical history, auxiliary examination, diagnosis and treatment, and prognosis of a patient with OSA complicated with SRFMM.

Results: A 69-year-old male presented with a 10-year history of nocturnal tongue biting and fragmented sleep. After video-polysomnography (v-PSG) examination, severe OSA was diagnosed, and epilepsy and sleep bruxism were excluded. v-PSG captured a tongue-biting episode triggered immediately after an obstructive respiratory event in REM sleep, featuring abrupt masseter/temporalis electromyography bursts without epileptiform activity. Continuous positive airway pressure (CPAP) initially failed due to poor adherence and persistent biting. Switching to bi-level positive airway pressure (BiPAP) eliminated tongue biting within 1 month. At 3-month and 6-month follow-ups, SRFMM remained fully controlled only with consistent BiPAP use. Cessation of BiPAP invariably triggered recurrence.

Conclusions: This case demonstrates severe SRFMM directly triggered by OSA-induced respiratory events and cortical arousals. BiPAP therapy, potentially by reducing respiratory effort and sleep instability more effectively than CPAP, achieved complete remission. SRFMM should be considered in OSA patients with unexplained nocturnal tongue injury.

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Sleep spindle characteristics in children with OSA and their associations with declarative memory function

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Introduction: Sleep spindles serve as one of the biological markers for cognitive function development in children, while children with Obstructive Sleep Apnea (OSA) exhibit varying degrees of cognitive impairment. This study systematically examined the spindle characteristics of children with OSA and explored the relationship between spindle parameters and declarative memory.

Materials and methods: Children aged 6 to 12 years old with snoring were included in this study, alongside age-matched healthy controls. Participants with OSA were divided into three distinct groups: primary snoring (PS), mild OSA (M OSA), and moderate-severe OSA (MS OSA) based on OAH1. All enrolled children completed a full-night polysomnography (PSG) and declarative memory task tests before and after sleep monitoring. During the N2 and N3 sleep stages recorded on the C3 channel, an advanced automatic detection of sleep spindles was implemented through a deep learning framework based on the BiLSTM-attention network. The characteristics of spindle activity were assessed using a

comprehensive set of parameters, including number, density, duration, intensity, amplitude, absolute power, relative power, center frequency, and the number of oscillations. Spindles were classified as fast spindles ($13 < f \leq 16$ Hz) and slow spindles ($11 \leq f \leq 13$ Hz) based on their central frequency, enabling the investigation of fast and slow spindle characteristics in OSA children and their correlations with declarative memory task performance.

Results: A total of 51 children were included: 15 PS, 13 M OSA, 13 MS OSA, and 10 healthy control. The results showed that the proportion of REM in children with MS OSA decreased, while N1 increased. Compared with children with M OSA, MS OSA had lower numbers, densities, durations, and intensities of total and slow spindles. In the assessment of declarative memory function, no significant differences were observed across varying degrees of OSA. Notably, the consolidation rate of recall demonstrated significant positive correlations with the absolute power of spindles, a pattern consistently observed across total, slow, and fast spindles.

Conclusions: Children with OSA, particularly those with MS OSA, exhibit sleep architecture disturbances and spindle activity impairments, which may underlie its cognitive dysfunction. The absolute power of sleep spindles could potentially serve as a more sensitive objective biomarker for assessing cognitive function in children.

Sleep-stage dynamics predicts current sleep-disordered-breathing and future cardiovascular risk

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Introduction: Sleep-disordered breathing (SDB) is a well-established contributor to cardiovascular morbidity and mortality, including hypertension, stroke, and heart failure^{1,2}. In addition to its respiratory effects, SDB disrupts sleep-macrostructure³ and, as emerging evidence suggests, alters sleep-stage dynamics⁴⁻⁶. This implies that both macrostructure and dynamics may be statistically linked with cardiovascular risk, as they can reflect downstream effects of SDB—thus enabling predictive modelling. Previous studies have primarily examined static macrostructural features, such as total-sleep-time (TST) or N3/REM durations, concerning cardiovascular outcomes⁷⁻⁹. However, the temporal organisation of sleep—specifically, transitions between stages—remains largely unexplored as a predictor of long-term cardiovascular risk. To address this gap, we present the first study evaluating whether sleep-stage dynamics can predict future cardiovascular outcomes in a large prospective cohort.

Materials and methods: We analyzed data from the Sleep Heart Health Study (SHHS)¹⁰, a prospective cohort of SDB-untreated individuals, examining the links between SDB and cardiovascular health. 5791 participants underwent baseline (SHHS1) in-home polysomnography (PSG); 2651 repeated it on-average 5 years later (SHHS2), and were followed for over 10 years. The PSG was scored into five stages (W, N1–3, REM), and apnea-hypopnea index (AHI) was calculated using the "recommended" definition, consistent with AASM guidelines (v2.2, 2015). We focused on 2581 SHHS1 participants without prior cardiovascular events or sleep-altering medications (e.g., antidepressants, diuretics, alpha/beta-blockers). The primary outcome was the first occurrence of a composite cardiovascular event: heart failure, stroke, myocardial infarction, angina, or cardiovascular surgical procedure since baseline. Predictors included: 25 (5x5) sleep-stage transition proportions, conventional sleep markers (e.g., TST), BMI, smoking status, and demographics. We used Random Forest (RF) for SDB detection and Random Survival Forest¹¹ (RSF) for cardiovascular risk prediction, both non-parametric methods robust to predictors' multicollinearity and non-linear effects.

Results: RF model for detecting moderate-to-severe SDB (AHI>15) achieved cross-validated ROC>75%, with stable performance across REM/NREM subtypes and strong generalization (ROC>70%) even to patients with medications or prior events, suggesting that SDB can be accurately predicted from sleep-stage features and demographics alone. RSF predicting future cardiovascular outcomes achieved concordance indices and time-dependent-ROC >75% across 1–10 year horizons, with significant log-rank separation ($p<0.05$, for high- vs. low-risk groups). Analysis of partial effects confirmed known risk factors like age and smoking, while revealing novel U-shaped risk profiles for many predictors—suggesting optimal ranges with increased risk at both extremes—including BMI (~25),

TST (~350 min), and sleep-stage continuities such as N1-to-N1 (~2%), N2-to-N2 (~40%), N3-to-N3 (~10–30%), and REM-to-REM (~20%). Specific atypical transitions, such as R-to-N3 and N3-to-N1, increased risk by >10% per single nightly occurrence; N3-to-REM and W-to-N3 were associated with ~5% increased risk when occurring ≥2 times per night.

Conclusions: Sleep-stage dynamics are sensitive markers for both SDB and long-term cardiovascular risk. Our findings, including confirmed effects of N3/REM^{7,*}, suggest novel risk markers based on sleep-stage transitions, providing deeper physiological insight than traditional macrostructure measures. While cardiovascular risk can be accurately predicted from sleep, further analysis is needed to design optimal treatment and sleep management interventions.

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1. [10.1164/rccm.200911-1746OC](https://doi.org/10.1164/rccm.200911-1746OC)
2. [10.1378/chest.10-2223](https://doi.org/10.1378/chest.10-2223)
3. [10.1007/BF03339872](https://doi.org/10.1007/BF03339872)
4. [10.1038/sj.npp.1300146](https://doi.org/10.1038/sj.npp.1300146)
5. [10.1371/journal.pone.0011356](https://doi.org/10.1371/journal.pone.0011356)
6. [10.1038/s41598-025-97172-3](https://doi.org/10.1038/s41598-025-97172-3)
7. [10.1161/HYPERTENSIONAHA.111.174409](https://doi.org/10.1161/HYPERTENSIONAHA.111.174409)
8. [10.1001/jamaneurol.2020.2108](https://doi.org/10.1001/jamaneurol.2020.2108)
9. [10.1007/s11886-022-01816-z](https://doi.org/10.1007/s11886-022-01816-z)
10. [10.1093/sleep/20.12.1077](https://doi.org/10.1093/sleep/20.12.1077)
11. [10.1214/08-AOAS169](https://doi.org/10.1214/08-AOAS169)

Sleep Surgery Symposium Proposal - "50 years of Sleep Surgery - Does it Work?"

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Introduction: Since 1970s, Sleep surgery has been part of the treatment of OSA. These past 50 years of sleep surgery has seen many changes and evolution of sleep surgery. Palate surgeries have evolved, Nasal surgeries have improved and become an integral part of OSA surgery. Tongue surgery has evolved from reduction to stimulation.

Materials and methods: Medical literature research on sleep surgery

Results: Sleep Surgery Symposium Proposal - "50 years of Sleep Surgery - Does it Work?"

Consisting of 4 oral presentations - by 4 renowned sleep surgeons, each discussing different aspects of sleep surgery over the past 50 years.

The different aspects of Sleep Diagnosis, Upper airway dynamics and Sleep surgery are discussed.

Conclusions: A strong conclusion of what works and what should be done to improve success rates.

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Small vessel disease in obstructive sleep apnea: a peak width of skeletonized mean diffusivity-based study

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Introduction: Peak width of skeletonized mean diffusivity (PSMD) is a novel marker of small vessel disease in the brain. This study aimed to investigate the association between small vessel disease and obstructive sleep apnea (OSA) using PSMD.

Materials and methods: We enrolled patients with OSA and age- and sex-matched healthy controls, and performed diffusion tensor imaging (DTI) using a 3-tesla MRI scanner in them. We calculated the PSMD based on DTI in several steps, including preprocessing, skeletonization, application of a custom

mask, and histogram analysis using the FSL program. We compared the PSMD between patients with OSA and healthy controls and investigated the correlation between PSMD and clinical factors.

Results: Thirty-nine patients with OSA (apnea-hypopnea index > 5; mean = 20.5) and 48 healthy controls were enrolled. The PSMD was significantly higher in patients with OSA than that in the healthy controls (2.521 vs. 2.320×10^{-4} mm²/s, $p = 0.013$). In addition, PSMD positively correlated with age ($r = 0.512$, $p < 0.001$) and body mass index ($r = 0.472$, $p = 0.002$). However, PSMD was not associated with polysomnographic measurements.

Conclusions: The mean PSMD is higher in patients with OSA than that in healthy controls, indicating a white matter injury due to small-vessel disease in patients with OSA. Our study highlights the importance of actively diagnosing and treating OSA. In addition, PSMD can be used to determine the relationship between sleep disorders and small vessel disease.

Snoring Child with Central Apnea: Uncovering a Hidden Neurological Cause

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Introduction: Pediatric sleep apnea is a sleep-related breathing disorder characterized by partial or total obstruction of the upper airway, usually due to an obstructive cause such as enlarged tonsils in children. However, children can rarely present with central sleep apnea (CSA), which in some cases can be associated with various neurological conditions.

Materials and methods: A 7-year-old boy has presented with frequent snoring and morning headaches. Physical examination and PNS X-ray revealed no significant abnormalities in the paranasal sinuses, such as sinusitis, and no enlargement of tonsil and adenoid. Type 1 Polysomnography showed periodic breathing with central apnea and snoring, with minimal obstructive events. Further neurologic evaluation was performed to differentiate the cause of the central apnea, there is no abnormal finding on neurologic tests revealed any central nervous system problems.

Results: A subsequent brain MRI revealed a cerebellar tonsillar hernia extending below the foramen magnum, consistent with a Chiari 1 malformation.

Conclusions: This case highlights the importance of considering a central cause in pediatric patients presenting with snoring and abnormal central sleep apnea on sleep study findings. Early neuroimaging and appropriate management, when indicated, can result in clinical improvement and help prevent long-term complications.

Snoring index, not apnea-hypopnea index, associated with daytime dysfunction in elementary school children

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Introduction:

This study aimed to investigate the independent effects of the Snoring Index, based on parent or guardian reports of snoring frequency and loudness, and the apnea-hypopnea index (AHI) on daytime dysfunction among elementary school children.

Materials and methods:

Two cross-sectional studies were conducted among elementary school children in Tokyo. Parents or guardians completed a questionnaire, and the children underwent overnight tracheal sound recordings. The Snoring Index was calculated as the mean of z-standardized parent/guardian ratings of snoring frequency and loudness. The AHI was estimated using a validated neural network algorithm based on the tracheal sound data. Daytime dysfunction was assessed using parent/guardian reports of hyperactivity/inattention, emotional symptoms, and daytime sleepiness. Generalized linear models

were employed to examine associations between the Snoring Index, AHI, and daytime dysfunction outcomes, adjusting for sex, age, BMI z-score, sleep duration, and nasal symptoms.

Results:

Analyses included 598 children from the Higasiyamato study (grades 1–2, mean age = 7.1 ± 0.7 years; 52.0% boys) and 240 children from the Musashimurayama study (grades 1–6, mean age = 9.3 ± 1.8 years; 58.2% boys). Higher Snoring Index scores were significantly associated with increased hyperactivity/inattention ($p < 0.05$) and daytime sleepiness ($p < 0.01$) in both cohorts. Emotional symptoms were significantly associated with the Snoring Index only in older children (Musashimurayama study; $p = 0.02$). In contrast, objectively measured AHI was not significantly associated with any daytime dysfunction outcomes (all $p > 0.1$).

Conclusions: Our findings indicate that the Snoring Index, which is based on parent or guardian reports of snoring frequency and loudness, was significantly associated with daytime dysfunction, particularly hyperactivity and daytime sleepiness, independently of AHI. These results underscore the importance of recognizing snoring as an independent contributor to cognitive and behavioral dysfunction in pediatric populations.

Sofia Scale: a female-specific screening tool for obstructive sleep apnea

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Introduction: Sleep-Disordered Breathing (SDB) encompasses a spectrum of conditions, ranging from simple snoring to Obstructive Sleep Apnea (OSA), the most severe form of SDB. OSA is a highly prevalent disorder associated with significant cardiovascular morbidity, increased risk of occupational and traffic accidents, and a notable decline in health-related quality of life.

Classically, the hallmark symptoms of OSA include excessive daytime sleepiness (EDS), loud snoring, and witnessed apneas. However, there is increasing recognition that the clinical presentation of OSA in women frequently diverges from this typical phenotype. Women with OSA often report non-specific symptoms such as insomnia, fatigue, morning headaches, mood disturbances, or fragmented sleep, which may not be effectively captured by existing screening tools.

Current widely used questionnaires, such as STOP-BANG and the Epworth Sleepiness Scale, have demonstrated suboptimal performance in female populations, potentially contributing to underdiagnosis and undertreatment in this group.

Materials and methods: To address this gap, we developed the SOFIA scale (Screening Of Female-specific Indicators of Apnea), a novel screening instrument specifically designed to identify OSA in women.

The objective of this study was to validate the SOFIA scale and to compare its diagnostic performance with existing tools. We conducted a prospective study in which 100 women referred for suspected OSA underwent overnight sleep studies. Each participant completed the SOFIA scale, STOP-BANG questionnaire, and Epworth Sleepiness Scale prior to polysomnography or respiratory polygraphy. The primary outcome was to assess the predictive capacity of the SOFIA scale for the diagnosis of OSA, defined as an apnea-hypopnea index (AHI) >15 events/hour.

diagnosis of OSA, defined as an apnea-hypopnea index (AHI) >15 events/hour.

SCALE SOFIA: I feel tired during the day, I feel nervous during the day, I feel a lack of energy or

interest, I usually sleep poorly or have insomnia, I usually snore, headache, I feel that I do not rest properly when I sleep, Sensation of shortness of breath at night or have been told you breathe irregularly, Hormonal dysregulation, Overweight, age.

Results: The SOFIA scale comprises 26 items reflecting female-specific symptoms and risk factors for OSA. A total score above 16 was considered indicative of high risk for OSA.

The SOFIA scale demonstrated superior diagnostic accuracy compared to the STOP-BANG questionnaire, with an area under the receiver operating characteristic curve (AUC) of 0.745 versus 0.648, respectively.

For moderate-to-severe OSA (AHI >15), the SOFIA scale achieved a sensitivity of 71% and a specificity of 73.3%. The positive predictive value (PPV) was 82%, and the negative predictive value (NPV) was 58%. The kappa coefficient for agreement between SOFIA and sleep study diagnosis was 0.42, indicating moderate concordance.

Conclusions: The SOFIA scale represents a promising, female-specific screening tool for the identification of OSA in women. Its superior diagnostic performance compared to traditional questionnaires underscores its potential utility in clinical practice. Implementation of SOFIA could contribute to reducing the current underdiagnosis of OSA among women and support a more gender-sensitive, personalized approach to sleep medicine. Further studies in larger, diverse populations are warranted to confirm these findings and explore its integration into routine screening pathways.

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'S score' - A novel computational algorithm for OSA severity assessment

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Introduction: Obstructive sleep apnea (OSA) is attaining pandemic proportion among non-communicable diseases with ever increasing lifestyle disorders. Assessing severity of OSA holds key in appropriate management this global health crisis. However currently widely accepted "AHI scale" for severity assessment has its own pitfalls. It assigns equal weightage to apnea and hypopnea. Current AHI system of severity grading do not factor in 'duration' of these events, technically events with prolonged duration will have more pronounced impact on physiological parameters like desaturation events and heartrate variability. To address these pitfalls and to provide comprehensive severity assessment tool, we have developed novel computational algorithm "S Score" for severity assessment in OSA . This study was done to validate effectiveness of "S score" in capturing physiological impact of apnea and hypopnea

Materials and methods: Novel computational algorithm "S Score" for severity assessment of OSA is used to assess severity of OSA in confirmed cases of OS following overnight level 1 polysomnography (PSG) were included [$S \text{ Score} = (0.73 (T^A - 10 N^A) + 0.27 (T^H - 10 N^H))/T$]. PSGs were recorded at a tertiary care hospital. Sleep study data including AHI, apnea frequency and duration, hypopnea frequency and duration, number of relative desaturations, mean SPO2 recorded in sleep, minimum SPO2 recorded in sleep, minimum, average and maximum heart rate in sleep, sleep onset, total sleep time, sleep efficiency were retrieved from the system. Logarithm transformed regression model was used for AHI and S score against mean SPO2, minimum SPO2, average HR and maximum HR.

Results: In our study we found that correlation coefficient between AHI and mean SPO2 in sleep is -0.4542 which is moderate correlation. Correlation between AHI and minimum SPO2 is -0.45577 which is also moderate correlation . However the correlation between S score and minimum SPO2 is -0.5940. The R² value of S score for highest heart rate is 0.0715 where as R² value of AHI for highest heart rate is only 0.0342. The R² value of S score for mean saturation is 0.3437 and for minimum saturation is 0.3724, however R² value of AHI for mean saturation is 0.2536 and for minimum saturation is 0.264. Our study objectively demonstrates that R² values for highest heart rate, mean and minimum saturation has better correlation with 'S score' than existing AHI for OSA severity assessment

Conclusions: 'S score' a novel severity assessment tool for OSA, captures the physiological consequences more precisely than existing AHI. S Score provides different weightages to apnea and hypopnea while also factoring in the 'duration' of events in totality. Whereas existing AHI is a mere summation of apnea and hypopnea without any reference to its physiological impact

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Study of OSA biomarkers based on proteomics

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Introduction: Obstructive sleep apnea (OSA) is a complex and heterogeneous disease with great harm. The current diagnosis and treatment system of OSA still has great limitations. It is a hot topic in the field of sleep medicine to determine the risk of OSA and related multi-system injuries and to distinguish the subtypes of subjects most likely to benefit from OSA treatment. The study of OSA biomarkers can promote the development of precision sleep medicine. The purpose of this study is to explore the stage heterogeneity characteristics of biomarkers in OSA, so as to provide new methods for disease risk assessment, early injury warning and curative effect prediction.

Materials and methods: Through rigorous experimental design and research (including the discovery set of 90 samples, the internal validation set of 225 samples, the validation set with continuous positive airway pressure [CPAP] treatment cohort of 208 samples, and the external validation set of 150 samples as series validations). We combined the cross-sectional study with the cohort study. According to the proteomic test results of serum samples, bioinformatics analysis was used to explore the biomarkers of OSA. The diagnostic ability of biomarkers was confirmed in the training set and test set. The predictive ability of biomarkers on prognosis and efficacy was observed in intervention and non-intervention cohorts.

Results: In the proteomics study, we revealed that the distinctive protein combination and protein expression of OSA subjects were different at each severity stage and at each treatment stage of CPAP, namely stage heterogeneity characteristics. Biomarkers screened by proteomics had high accuracy in the diagnosis of OSA with different severity. At the same time, in non-intervention and intervention cohorts, molecular typing based on proteomic biomarkers was carried out, reflecting different susceptibility to OSA-related multi-system injury, blood pressure reactivity and mini-mental state examination improvement after CPAP treatment. These results have important implications for clinical identification of high-risk populations and prediction of treatment benefits, so as to explain the heterogeneity of disease. Growth and differentiation factor-associated serum protein 1 (GASP-1), as a key biomarker screened and verified, had a significant negative correlation with AHI and a significant positive correlation with genioglossal muscle compensatory response index reflecting genioglossal muscle function.

Conclusions: According to the proteomic results of serum samples, combined with bioinformatics analysis, the new combination of heterogeneous biomarkers in OSA stage was identified, and the heterogeneity characteristics of pathophysiology of the disease were further analyzed comprehensively from the molecular level. The combination of biomarkers can carry out disease diagnosis and risk identification with high accuracy. The molecular typing based on this provides a new method for disease risk assessment, early injury warning and curative effect prediction. At the same time, we preliminarily verified the potential biological function of factor GASP-1 found in proteomics research that is significantly related to the severity of OSA, and provided theoretical basis for further exploring the mechanism of biomarkers.

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Study on gene single nucleotide polymorphisms in Han and Uyghur patients with OSA combined with hypertension

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Introduction: The pathogenesis of obstructive sleep apnea (OSA) is complex, involving genetic and environmental factors. Some studies have found that certain genes are related to OSA. Therefore, studying the gene polymorphism of OSA patients is helpful for revealing its mechanism. Some study performed a comprehensive qualitative and quantitative analysis to estimate the contribution of variants from candidate genes to the risk of OSA, which associated with the risk of OSA, which also show ethnicity differences in East Asian and European subgroups. OSA is often accompanied by hypertension. It is very important to explore the related gene polymorphisms between the two diseases. This study to explore the differences in nucleotide sequences of 20 gene loci closely related to obstructive sleep apnea (OSA) in Han and Uyghur patients with hypertension.

Materials and methods: All patients were selected from a total of 433 OSA patients (both with and without hypertension) hospitalized in the respiratory sleep department of Karamay Central Hospital from January 2023 to September 2024. Additionally, 100 hypertensive individuals without OSA from the same period were included as the control group. The patients included 249 cases of OSA with hypertension, of whom 200 were Han and 29 were Uyghur, with an average age of (54.5 ± 12.1) years for Han and (52.2 ± 8.7) years for Uyghur. There were 134 males and 115 females. There were 172 cases of OSA without hypertension, including 138 Han and 34 Uyghur, with an average age of (49.8 ± 13.0) years for Han and (49.9 ± 10.0) years for Uyghur. There were 100 cases hypertension patients from the physical examination group, including 90 males and 10 females, with an average age of (50.6 ± 7.4) years. The genomic DNA was extracted using a Wizard Genomic DNA Purification Kit (Promega, Madison, Wisconsin, USA) as per the product instruction. A multiplex PCR-ligase detection reaction method was used for genotyping four SNPs. For each SNP, the alleles were distinguished by different fluorescent labels of allele specific oligonucleotide probe pairs. Different SNPs were further distinguished by different extended lengths at 3' end.

Results: By comparing the closely related to OSA among the groups (Han OSA with hypertension group, Uyghur OSA with hypertension group, Han OSA without hypertension group, Uyghur OSA without hypertension group, and physical examination hypertensive group), we found that the A/C/T Single-Nucleotide Polymorphism (SNP) in rs1137101 of the leptin receptor LEPR gene on chromosome 1, the G/A/T/C (SNP) in rs1143633 of the interleukin-1 receptor IL1B gene on chromosome 2, the C/G (SNP) in rs12511115 of the gamma-aminobutyric acid (GABA) A receptor GABRB1 gene on chromosome 4, and the C/G/T (SNP) in rs6313 of the 5-hydroxytryptamine receptor HTR2A gene on chromosome 13 showed significant differences between the Han and Uyghur OSA groups ($P < 0.05$).

Conclusions: The variations of the SNP in rs1137101 of the LEPR gene, the SNP in rs12511115 of the GABRB1 gene, the SNP in rs1143633 of the IL1B gene, and the SNP in rs6313 of the HTR2A gene may be related to OSA in different ethnic groups. The mechanisms need further study.

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Study on the Effect of Chemogenetic Regulation of Neurons in the mPFC brain Region on Learning and Memory Impairment and Sleep Structure in Mice with Chronic Intermittent Hypoxia

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Introduction: Young and middle-aged patients with OSA often suffer from cognitive impairments in multiple cognitive functional domains such as attention, memory, and executive function. Chronic intermittent hypoxia (CIH) is one of the possible mechanisms leading to changes in electroencephalogram activity and cognitive dysfunction, but the current research results are controversial. Our preliminary research found that CIH significantly increased c-fos neuronal activity in the medial prefrontal cortex (mPFC) region of mice, suggesting that the mPFC is likely to be the key brain area involved in OSA-related cognitive impairment. Therefore, we intend to investigate the pathogenesis of learning and memory impairment in CIH mice from the perspective of neuronal regulation, aiming to provide new ideas and methods for clinical diagnosis and treatment.

Materials and methods: (1) Construction of an OSA mouse model

C57BL/6 mice aged 6-8 weeks were placed in a hypoxia chamber. Each cycle lasted 60 seconds, with the ambient oxygen concentration (FiO_2) decreasing from 21.0% to $6 \pm 0.5\%$ within the first 30 seconds, and then increasing back to 21% within the next 30 seconds.

(2) Chemogenetics regulates neuronal activity

Chemogenetic viruses were injected into the mPFC region of mice using stereotaxic techniques. The

viruses were allowed to fully express for 2-3 weeks. Half to one hour prior to the start of the experiment, clozapine-N-oxide (CNO) was injected intraperitoneally to activate the chemogenetic pathway.

(3) EEG/EMG recording

Mice were anesthetized and fixed using a stereotaxic apparatus. Electrodes were surgically implanted, with two electrodes for EEG signal recording and two flexible electrodes for EMG signal recording. EEG and EMG signals were amplified and filtered (EEG: 0.5-25 Hz; EMG: 20-200 Hz) and recorded using software.

(4) Cognitive-related behavioral tests

Behavioral tests such as the open field test, novel object recognition test, novel location recognition test, and water maze test were conducted to evaluate the cognitive abilities of mice.

(5) Immunofluorescence technique for observing changes in myelin and glial cells in CIH mice.

Results: 1. Compared to control mice, CIH-exposed mice exhibited increased c-fos expression in the mPFC-IL region.

2. Compared with the control group mice, CIH-exposed mice showed decreased learning and memory indices. However, chemogenetics can improve the learning and memory impairment of CIH mice.

3. Compared with the control group mice, CIH-exposed mice showed reduced myelin basic protein levels in the corpus callosum and decreased numbers of oligodendrocytes and OPCs across all hippocampal regions. Chemogenetics can improve the myelin injury and the decline in the number of oligodendrocytes and precursor cells in CIH mice.

4. Compared with the control group mice, CIH-exposed mice exhibited reduced REM sleep and an increased number of sleep-wake transitions, and chemogenetic regulation could not improve the disruption of sleep structure in CIH mice.

Conclusions: The mPFC brain region is a critical brain region for learning and memory impairment in CIH-exposed mice. Chemogenetic regulation of neurons in the mPFC brain region can improve learning and memory impairment by reducing myelin damage and increasing the number of oligodendrocytes and precursor cells. However, this intervention does not alleviate the disruption of sleep architecture in CIH mice.

Success rate of Portable Polysomnography in Snoring and Obstructive Sleep Apnea Patients in ENT Clinic Srinagarind Hospital, Khon Kaen University

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Introduction: Study objectives: To study the success rate of portable PSG, used in diagnosis and treatment monitoring in the snoring and sleep disorders clinic, Department of Otorhinolaryngology, Faculty of Medicine, Khon Kaen University, Thailand

Materials and methods: This study is a retrospective descriptive study in adult patients over 18 years old who received services at a snoring and sleep disorders clinic, Department of Otorhinolaryngology, Srinagarind Hospital from 2012 – 2019. Patient information was collected from Srinagarind Hospital's medical records. The collected data consisted of general patient information. Data based on the modified STOP BANG questionnaire, clinical data, physical examination, underlying diseases, portable PSG examination data results. All data were analyzed through percentage statistics and spearman correlation.

Results: There were 1,028 new patients, 110 were pediatric patients and 918 were patients over 18 years old. 58 patients were unable to retrieve data. The remaining 858 cases (93.5%) 550 were male (64.1%) and 308 female (35.9). Most of the cases, 256 patients (29.3%) aged between 50-60 years. 680 cases were diagnosed with OSA (79.2%) Most of the patients had modified STOP BANG at 4 points, 30%. There were 659 patients who tested PSG or 76.8%, divided into port PSG 599 cases, 69.8% of the patients were diagnosed with severe OSA 34.4% and moderate OSA 25.5%. There were 12 cases with re-test for PSG, or 1.8%. When studying the relationship between modified STOP BANG and the results of portable PSG, it was found that modified STOP BANG was greater than 2 and AHI with cut off value greater than 15 was found sensitivity 86.7% and specificity 26.4%. The Spearman correlation coefficient was 0.25 at P < 0.01 when comparing modified STOP BANG with portable PSG results. The majority of patients in the clinic 490 patients (57.1%) used CPAP, 83 cases (9.7%) were treated by

surgery and 13 cases(1.5%) used mandibular advancement devices . After treatment with additional life style modifications most of the patients' symptoms improved.

Conclusions: Portable polysomnography has the advantage of ease of use, better accessibility and lower cost. It can be utilized for diagnosis of OSA in areas in which in lab PSG is not yet fully accessible, with minimal data loss or inconclusive diagnoses.

Acknowledgments: This study was approved by Khon Kaen University Ethics Committee project no. HE641573. We thank you Mrs. Arunya Kotelong the clinic nurse for assistance in data collection.

Supplemental Low-Dose CO₂ Delivered by a Novel Device Abolishes Central Sleep Apnea at High Altitude

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Introduction: Lowlanders ascending to high altitude often develop central sleep apnea secondary to hypocapnia. We designed a device that comfortably delivers a constant, low dose of CO₂. This study evaluated whether CO₂ supplementation could alleviate central sleep apnea and improve sleep quality in healthy adults at high altitude.

Materials and methods: Forty-six healthy lowlanders (mean age 25.2 ± 7.5 years; 26 men) were flown to 4,505 m. On their first night, participants were randomised 1:1 to inhale either 4.5% CO₂ or room air via a novel delivery device with virtually no functional dead space and negligible breathing resistance. Full overnight polysomnography was recorded.

Results: Compared with controls, the CO₂ group demonstrated a dramatically lower apnea-hypopnea index (4.0 ± 4.5 vs. 41.0 ± 49.8 events/h), higher mean SpO₂ (82.1% ± 4.0% vs. 65.1% ± 8.0%), and improved sleep efficiency (81.0% ± 8.5% vs. 65.2% ± 14.2%) (all P < 0.01).

Conclusions: Inhalation of low-dose CO₂ via our novel device effectively abolishes central sleep apnea, attenuates hypoxemia, and enhances sleep quality in healthy adults at high altitude.

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Surface electromyography of masticatory muscles in adults with obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is a sleep-related breathing disorder with potential neuromuscular implications for orofacial structures during sleep and possibly during wakefulness. Therefore, the aim of this study was to compare the bilateral electrical activity of the temporalis and masseter muscles in adults with and without OSA using surface electromyography (sEMG) while awake.

Materials and methods: Study approved by the Human Research Ethics Committee of HCFMRP-USP (protocol no. 12634/2010). Fifty-four adults with OSA and fifteen healthy controls, diagnosed via polysomnographic evaluation, underwent bilateral sEMG of the anterior temporalis and masseter muscles while awake. The following indices were analyzed: percentage overlapping coefficient (POC) of temporalis and masseter muscles, torsion index (TORS), occlusal barycenter (BAR), absolute asymmetry index (Asim), and absolute activity index (Ativ). Between-group comparisons were performed using the Mann-Whitney U test. Correlations between the Apnea-Hypopnea Index (AHI) and sEMG values were analyzed using Spearman's correlation coefficient (p < 0.05).

Results: A moderate and significant negative correlation was observed between AHI and POC values of both temporalis and masseter muscles ($p < 0.001$), as well as with BMI and ATiv ($p = 0.03$). No significant correlations were found with age or other sEMG variables. The OSA group showed significantly lower COT values for both temporalis and masseter muscles ($p < 0.001$), indicating reduced muscle activation during clenching. No significant differences between groups were observed for POC, TORS, BAR, Asim, or Ativ indices.

Conclusions: Adults with OSA demonstrated reduced sEMG activation of masticatory muscles compared to healthy individuals. These findings support the hypothesis of orofacial myofunctional adaptations or impairments in OSA and highlight the potential value of muscle function assessment and rehabilitation in the clinical management of these patients.

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Surgically assisted transverse jaw expansion in adult OSA patients

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Introduction: Obstructive Sleep Apnea (OSA) is a prevalent condition that significantly impacts the quality of life and overall health. This study evaluates the outcomes of surgically assisted transverse jaw expansion in adult OSA patients in Hong Kong.

Materials and methods: A retrospective analysis was conducted on OSA patients who underwent surgically assisted maxillomandibular expansion (MME) or maxillary expansion (MxE) between 2012 and 2025 at Department of Dentistry and Maxillofacial Surgery, United Christian Hospital, Hospital Authority, Hong Kong. Inclusion criteria included pre-operative Apnea-Hypopnea Index (AHI) ≥ 5 and age at surgery ≥ 16 . Objective outcomes measures included AHI and Lowest Oxygen Saturation (LSAT) pre- and post-operatively. Statistical analysis was performed with SPSS.

Results: A total of 10 subjects underwent surgical assisted transverse jaw expansion surgery (MME:6; MxE: 4). The median age of patients at surgery was 23.5 (IQR: 20-32). The median AHI significantly improved from 20.8 (IQR: 13.9-32.7) pre-operatively to 6.5 (IQR: 5.4 -26.8) post-operatively ($p = 0.022$). LSAT also showed improvement, increasing from a median of 85.5% (IQR: 78-89%) to 87.5% (IQR: 83-90%), although this change was not statistically significant ($p=0.153$).

Conclusions: This study demonstrates that surgically assisted transverse jaw expansion leads to a significant reduction in AHI and some improvement in LSAT in adult OSA patients. The findings suggest this surgical intervention may be effective to adult OSA patients; further study is warranted to confirm the result.

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Tailored palatal surgery for obstructive sleep apnea patients with lateral pharyngeal wall collapse based on DISE phenotyping

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Introduction: Obstructive Sleep Apnea (OSA) is a heterogeneous disorder caused by a combination of anatomical and physiological factors that lead to upper airway collapse during sleep. Drug-Induced Sleep Endoscopy (DISE) provides real-time visualization of dynamic upper airway obstruction and has emerged as a valuable tool for individualized surgical planning. Among the various sites of collapse, the lateral pharyngeal wall has been increasingly recognized as a key contributor to airway obstruction in OSA. The aim of this study was to evaluate the utility of DISE in guiding the selection of palatal surgical techniques and to assess their clinical efficacy in OSA patients with lateral pharyngeal wall collapse.

Materials and methods: Patients with moderate to severe OSA underwent DISE to determine their patterns of upper airway obstruction. DISE phenotyping revealed a high prevalence of lateral pharyngeal wall collapse in this population. Surgical interventions were selected based on the severity and pattern of collapse observed.

Results: Patients were stratified to undergo soft palate webbing flap pharyngoplasty, relocation pharyngoplasty, or expansion sphincter pharyngoplasty according to their DISE findings. Uvuloplasty (e.g., soft palate webbing flap) was recommended for patients with mild to moderate OSA and minimal lateral wall collapse (< grade I) in DISE findings. Relocation pharyngoplasty was performed in patients with moderate lateral wall collapse (> grade II) and tonsillar hypertrophy (over grade 2 tonsil hypertrophy). Expansion sphincter pharyngoplasty was indicated for those with severe circumferential narrowing and significant lateral pharyngeal wall involvement (> grade III) in DISE findings and over grade 2 bilateral tonsil hypertrophy. Clinical outcomes showed that soft palate webbing flap pharyngoplasty achieved a 40.1% success rate, with mean apnea-hypopnea index (AHI) decreasing from 25.7 to 15.1 in selected cases of primary snoring and mild to moderate OSA. Relocation pharyngoplasty resulted in a 52.9% success rate and a 65.8% response rate in patients with moderate lateral wall collapse and enlarged tonsils. Expansion sphincter pharyngoplasty yielded favorable outcomes in severe OSA cases, with marked improvements in AHI and retropalatal patency.

Conclusions:

DISE-directed surgical planning allows for phenotype-based stratification and targeted correction of airway collapse in OSA. Tailoring palatal surgery according to specific collapse patterns—particularly those involving the lateral pharyngeal wall—leads to improved clinical outcomes and reduced surgical failure. This individualized approach represents a significant advancement in the personalized management of sleep-disordered breathing.

The application of hypoxic burden in evaluating systemic consequences associated with obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder primarily characterized by recurrent episodes of apnea and hypopnea during the sleep period, leading to intermittent hypoxemia, hypercapnia, and fragmented sleep. The prevalence of OSA has been steadily increasing. In recent years, the hypoxic burden (HB) has attracted considerable attention as an index that quantifies the cumulative effects of OSA-associated desaturation events by measuring the area under the curve of the decline in blood oxygen saturation (SpO₂). Compared to the conventional diagnostic metric, the apnea-hypopnea index (AHI), hypoxic burden shows significant promise in predicting the risk of OSA-related comorbidities and treatment outcomes, particularly in the realms of cardiovascular and metabolic diseases as well as cognitive dysfunction, thereby making it a more forward-looking tool for assessing the risk of complications associated with OSA.

Materials and methods: This study systematically reviews the definition, calculation methods, differences from other hypoxic indices, and the clinical utility of hypoxic burden in evaluating systemic damage caused by OSA.

Results: In this review, we provide a summary of the following aspects: the definition and calculation methods of hypoxic burden, comparisons between hypoxic burden and other hypoxia-related indices, the clinical value of hypoxic burden in the diagnosis and treatment of obstructive sleep apnea (OSA) and its associated diseases, and the application of hypoxic burden in OSA-related comorbidities.

Conclusions: As a highly promising metric, HB plays a significant role in the diagnosis and management of OSA, as well as in predicting OSA-related comorbidities. By accounting for the heterogeneity of OSA, it enables diagnosis, stratification according to severity, reflection of hypoxia-induced pathophysiological changes, and prediction of potential complications. Current evidence further suggests that HB provides superior prognostic value compared with the traditional apnea-hypopnea index (AHI). Nevertheless, HB remains an emerging metric, and its prognostic value for OSA-related comorbidities requires further validation. Methodological challenges, particularly the lack of

standardized computational procedures and clear baseline definitions, continue to limit its widespread adoption in clinical practice. Future research should validate HB in diverse populations, establish unified calculation standards, and explore integration with artificial intelligence-based analytic approaches. Collectively, these efforts may establish HB as a robust biomarker to advance precision medicine in OSA management.

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The Association between Obstructive Sleep Apnea and Frailty Traits: A Bidirectional Mendelian Randomization Study

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Introduction: Despite sharing similar risk factors and characteristics, the relationship between obstructive sleep apnea (OSA) and frailty remains unclear due to the predominance of observational researches. This study aimed to explore the genetic association between OSA and frailty traits using a bidirectional two-sample Mendelian randomization (MR) analysis.

Materials and methods: Utilizing summary data from large-scale genome-wide association studies (GWAS) obtained from FinnGen and MRC-IEU on European individuals, we designed a bidirectional two-sample MR analysis to comprehensively assess the genetic-level link between OSA and frailty traits, including frailty index, appendicular lean mass (ALM), grip strength and walking pace. Effect estimates were primarily evaluated using Inverse-variance weighted (IVW), with MR-Egger, weighted median (WM), simple mode, and weighted mode analyses serving as complementary methods. A series of sensitivity analyses, including outlier detection, heterogeneity analysis, and horizontal pleiotropy assessment, was applied to ensure the robustness of the results.

Results: IVW models showed that genetically predicted OSA had no significant effect on frailty index, ALM, grip strength, or walking pace. However, the reverse MR analysis suggested that a higher genetically predicted frailty index increased OSA risk (IVW: OR=1.777, 95% CI: 1.137--2.777, p=0.012) with 14 single nucleotide polymorphisms (SNPs), while a faster genetically predicted walking pace was identified as a protective factor for OSA (IVW: OR=0.204, 95% CI: 0.104--0.399, p=3.39E-06; WM: OR=0.368, 95% CI: 0.193--0.703, p=0.003) with 56 SNPs. MR-Egger indicated no evidence of genetic pleiotropy. Although heterogeneity among the instrumental variable was observed in the reverse MR analysis, the results could be considered robust based on the IVW analysis and other supplementary sensitivity analyses.

Conclusions: The two-sample MR study found genetic evidence supporting OSA causally associated by frailty traits in reverse MR analysis, with frailty index and walking pace as risk and protective factors, respectively. The forward MR analysis did not find significant association between OSA and frailty traits.

The Association of Obstructive Sleep Apnea with Serum and Cerebrospinal Fluid Biomarkers of Alzheimer's Dementia - A Systematic Review and Meta-Analysis

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Introduction: The association between Obstructive Sleep Apnea (OSA) and dementia has been well-documented. Alzheimer's Disease (AD), the most prevalent form of dementia, is marked by the accumulation of extracellular amyloid-beta and the intracellular hyperphosphorylation of tau proteins. Consequently, it is hypothesized that OSA may be linked to elevated levels of AD-related biomarkers. This study seeks to perform a systematic review and meta-analysis to evaluate the relationship

between OSA and concentrations of Alzheimer's Disease biomarkers in both serum and cerebrospinal fluid.

Materials and methods: PubMed, Embase, and Cochrane Library were systematically searched to identify studies that compared serum and cerebrospinal fluid levels of dementia-related biomarkers between individuals with OSA and healthy control subjects. Two independent authors screened articles for eligibility, extracted relevant data into a structured template, and evaluated the risk of bias of included studies using the Risk of Bias of Non-Randomized Studies of Interventions (ROBINS-I) scale. Various meta-analyses of the standardized mean difference were conducted using random-effects models. Further subgroup, sensitivity, meta-regression and publication bias analyses were conducted. **Results:** From 17 studies with 2804 patients, meta-analysis found that cerebrospinal fluid amyloid beta-40 (SMD:-1.13, 95%CI:-1.65 to -0.60) serum total amyloid beta (SMD:0.68, 95%CI: 0.40 to 0.96), serum amyloid beta-40 (SMD:0.60, 95%CI: 0.35 to 0.85), serum amyloid beta-42 (SMD:0.80, 95%CI: 0.38 to 1.23) and serum t-tau (SMD:1.07, 95%CI: 0.27 to 1.88) were significantly higher in OSA patients compared with healthy controls. These results remained robust to various subgroup, sensitivity and meta-regression analyses, and publication bias was absent.

Conclusions: OSA is linked to elevated levels of certain AD biomarkers, and serum biomarkers may help quantify the severity of OSA. Further studies with larger cohort sizes and follow-up periods may offer deeper insights into the association between OSA and neurodegenerative biomarkers.

The combined effect of acetazolamide and oxygen (ACZO₂) on OSA severity and endotypes

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Introduction: Elevated loop gain contributes of OSA pathogenesis in at least one third of patients. Both acetazolamide (ACZ) and supplemental oxygen (O₂) have been demonstrated to reduce loop gain (via different mechanisms) and the apnoea-hypopnoea-index (AHI). This trial assessed the efficacy of combining both ACZ and O₂ (ACZ+O₂) to maximally lower loop gain.

Materials and methods: In a randomised single-blind cross-over trial, participants were first randomised to take ACZ (500mg orally) or placebo for 7 days. During each treatment period, participants undertook two polysomnograms (PSGs) during which they slept with supplemental oxygen (3L/min) or sham (medical air, 3L/min). PSGs were scored by a technologist blinded to intervention. In addition to standard scoring, respiratory events were scored excluding SpO₂ or arousal information to calculate a 'flow-based AHI' (fAHI). OSA endotypes (including loop gain, collapsibility, muscle compensation and arousal threshold) were quantified from PSG signals.

Results: In twenty participants (7 females, Age= 50.3 ± 10.3, BMI= 32.3 ± 4.6, AHI_{baseline}= 51.5 ± 23.6, loop gain_{baseline} = 0.69 ± 0.19), loop gain was significantly reduced by both ACZ (Δ LG = -0.16 [CI₉₅:-0.06, -0.27], p<0.001) and O₂ (-0.14, [-0.04, -0.25], p=0.003). Very large reductions in loop gain were observed for the combination ACZ+O₂ (-0.25, [-0.14, -0.35], p<0.001) relative to the placebo-sham-air condition. All participants achieved a low loop gain (defined by LG<0.7) on ACZ+O₂. Upper airway collapsibility was significantly improved by ACZ relative to both placebo/sham (+13.4 %Veupnea [2.7, 24.2], p = 0.009) and O₂ (+11.6 %Veupnea [0.8, 22.4], p = 0.030). The improved collapsibility effect appeared diminished in the ACZ+O₂ condition which was not different to placebo/sham (+7.5 %Veupnea, p = 0.269) or O₂ (+5.6 %Veupnea, p= 0.523) conditions. OSA severity, as quantified by fAHI, was significantly reduced by all three treatments compared to placebo; ACZ (-20.3 /hr [-13.5, -27.0]), p<0.001, O₂ (-14.5 /hr [-7.9, -21.1], p<0.001) and ACZ+O₂ (-23.5 /hr [-16.8, -30.2], p<0.001). While fAHI was significantly lower on ACZ+O₂ compared with O₂ (-9.0 /hr, p=0.004), the difference between ACZ+O₂ and ACZ was not significant (-5.8/hr, p=0.12). ACZ+O₂ induced a >50% reduction in fAHI in 11/20 participants and 7/20 participants achieved a fAHI<15.

Conclusions: These data demonstrate that the combination of both acetazolamide and oxygen can strongly reduce loop gain in unselected patients, and this effect appears borne out by reductions in fAHI. Future work is required to determine whether reductions in loop gain and OSA severity are larger in patients with high loop gain at baseline.

The correlation between snoring and sleep related breathing disorders using an under-mattress sleep monitoring device

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Introduction: Snoring, often misunderstood as a sign of good sleep in some cultures, is a common but overlooked symptom of sleep-related breathing disorders (SRBD), which are linked to cardiovascular and metabolic complications. This study was conducted to evaluate the correlation between snoring and SRBD, particularly obstructive sleep apnea (OSA), using an under-mattress sleep study device (Sleeptracker-AI). Additionally, we aimed to investigate the differences in this correlation across age groups and between sexes.

Materials and methods: The validated Sleeptracker-AI Monitor (Fullpower Technologies Inc., CA, USA), which passively detects sleep-disordered breathing via piezoelectric sensors was used in the study. We reviewed de-identified data collected between August 15, 2023, and June 30, 2024.

Results: A total of 155,441 participants (84,183 men, and 71,258 women) with mean age 47.9 ± 12.7 years contributed 27,708,834 recorded nights of data. Predicted apnea prevalence increased from 7% for subjects with little snoring (snoring percentage 3%, 25th percentile) to 15% in those moderate to heavy snorers (snoring 22% of the night, 75th percentile) and 48% in heavy snorers (snoring percentage 55%, 95th percentile). The odds ratios for apnea ($AHI \geq 5$) associated with each 10-percentage-point increase in snoring, expressed as a percentage of total sleep time. Age modified this interaction ($p < 0.0001$), with odds ratios of 1.77 [1.73, 1.81], 1.61 [1.59, 1.63], and 1.45 [1.42, 1.47] at ages 30, 50, 70. Interaction with sex was insignificant ($p=0.54$).

Conclusions: A large-scale analysis revealed a significant age-dependent association between snoring percentage of total sleep time and OSA prevalence across snoring severity. Each 10% increase in snoring elevated apnea odds with a stronger effect in younger individuals. Sex did not significantly modify this relationship.

The different characteristics of polysomnography between stroke and TIA patients

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Introduction: Obstructive sleep apnea is the most common sleep related breathing disorders. The association between cerebrovascular disease and obstructive sleep apnea is bidirectional. However, studies involving polysomnographic data in stroke and TIA patients compared to general population have shown inconsistency results. Data on different effects of OSA on stroke comparing to TIA were scarce

Materials and methods: Patients age over 18 years were recruited from Siriraj Hospital medical records between 2016 and 2023. All patients underwent sleep studies at the Siriraj Sleep Center before the diagnosis of stroke or TIA. Demographic data, stroke and TIA disease characteristics, and polysomnographic data were collected and compared through statistical analysis.

Results: The study aimed to recruit 198 patients in total. We collected 206 patients. Polysomnography were done prior cerebrovascular event 66 months. One hundred fifty patients had hypertension and dyslipidemia, mainly. 102 patients were ischemic stroke and 104 patients were TIA. 161 (78.16%) patients had supratentorial pathologies and 118 (57.28%) patients has cerebrovascular disease from small vessel disease. Mean AHI in stroke and TIA patients were 38.22 ± 24.41 /hr and 36.21 ± 26.22 /hr, respectively (p -value = 0.571). Minimum oxygenation were $82.55 \pm 7.83\%$ and 81.76 ± 11.27 in stroke and TIA patients, serially (p -value = 0.561). There was significant difference in cumulative time with oxygen saturation below 90% in total sleep time (T90) between stroke and TIA patients (10.21 ± 19.41 in stroke patients and 5.22 ± 13.52 in TIA patients with p -value of 0.034). Mixed apnea events were also significantly higher in stroke patients (5.65 ± 14.81) compared to TIA patients (0.26 ± 0.86), with a p -

value of 0.033. Other polysomnographic data were not significantly different between stroke and TIA patients.

Conclusions: Severe OSA is common in patients developing cerebrovascular attacks. Duration of desaturation is significantly affected severity of cerebrovascular diseases. Difference of mixed apneas percentage may underline the different OSA pathogenesis of stroke and TIA.

The Effectiveness of a Smart Sleep Apnoea Self-Management Support Program (4S) in Improving Cardiovascular Risk and Quality of Life in Subjects with Moderate to Severe Obstructive Sleep Apnea: A Randomized Controlled Trial

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Introduction: Obstructive Sleep Apnea (OSA) affects 9% to 38% of the global population, contributing to cardiovascular diseases and a reduced quality of life. Self-management strategies, including increased physical activity, weight control, and regular monitoring, can help reduce symptoms and lower the risk of complications. This study assessed the effectiveness of the 1-year Smart Sleep Apnea Self-Management Support Program (4S) in improving cardiovascular health risks.

Materials and methods: This was a two-arm randomized controlled trial. Eligible patients had moderate to severe OSA, a BMI >23, and engaged in less than 150 minutes of moderate physical activity per week. Participants were recruited from two hospitals and randomly allocated to either the 4S intervention group or the General Hygiene Information (GHI) control group.

The 4S intervention included: (i) Two 30-minute brief motivational interviewing sessions, (ii) Scheduled theory- and theme-based instant messages and phone calls, (iii) Personalized chat-based coaching, and (iv) An e-platform for goal setting and self-monitoring.

The GHI control group received general health information at similar frequencies and in a comparable format. Quantitative assessments were conducted at baseline, 4 months, and 12 months. A linear mixed model was used to compare changes in cardiovascular risk factors between the 4S intervention group and the GHI control group.

Results: A total of 123 participants (73.2% male, mean age 60 years, BMI 30 kg/m²) with moderate to severe OSA were recruited. Baseline characteristics did not differ between the two groups. The intervention group showed increases in Positive Airway Pressure (PAP) use and engagement in moderate physical activity. There was a significantly greater increase in PAP use in the intervention group compared to the control group. However, the difference in changes in engagement in moderate physical activity was not statistically significant between the two groups. The intervention group showed significant reductions in body weight, waist circumference, systolic blood pressure, and triglyceride levels compared to baseline. These reductions were significantly greater in the intervention group compared to the control group.

Conclusions: The 4S program demonstrated significant improvements in cardiovascular health risk factors among physically inactive, overweight individuals with moderate to severe OSA. By promoting self-management and sustainable health behaviors, the program may provide an effective approach to improving outcomes for individuals with OSA.

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The Effect of Bariatric Surgery on Obstructive Sleep Apnea Remission and Outcomes

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Introduction: Obesity is a major global health concern with a steadily rising prevalence. It shares several adverse health consequences with obstructive sleep apnea (OSA). Bariatric surgery is an effective treatment for morbid obesity, offering substantial weight loss. However, its specific impact on OSA such as remission, symptom improvement, and reduced CPAP requirements remains underexplored. This study aimed to assess the effect of bariatric surgery on OSA remission and improvements in clinical and polysomnographic parameters.

Materials and methods: A retrospective cohort study was conducted on patients who underwent bariatric surgery between January 1, 2005, and February 28, 2025, and had both preoperative and postoperative polysomnography (PSG). Relevant clinical and polysomnographic data were collected and analyzed.

Results: A total of 638 patients underwent bariatric surgery, of whom 48 met the inclusion criteria and were included in the study. The mean duration of follow-up PSG after surgery was 3.36 ± 2.5 years. Significant reductions were observed in BMI, AHI, and ESS. BMI decreased from 50.2 ± 13.1 to 33.8 ± 9.9 kg/m² ($p < 0.001$), AHI decreased from 52.8 (IQR 29.4, 121.4) to 27.2 (IQR 13.3, 43.8) ($p < 0.001$), and ESS decreased from 11.4 ± 5.7 to 6.8 ± 4.4 ($p < 0.001$). Other polysomnographic parameters were also significantly improved including sleep efficiency increased from $80.9 \pm 12.3\%$ to $86.6 \pm 9.7\%$ ($p < 0.001$), mean oxygen saturation improved from $87.3 \pm 12.2\%$ to $95.5 \pm 2.2\%$ ($p < 0.001$) and nadir oxygen saturation improved from $71.9 \pm 17.1\%$ to $84.6 \pm 11.2\%$ ($p < 0.001$). Three patients (6.3%) achieved OSA remission. The proportion of mild OSA increased from 4.2% to 22.9%, moderate OSA increased from 20.8% to 25%, and severe OSA decreased from 75% to 45.8% ($p < 0.001$). Postoperative CPAP independence (AHI < 5 /hr or AHI 5-15/hr with ESS < 10) was observed in 25% of patients. Preoperative parameters including ESS < 10 , REM latency < 120 mins, WASO < 30 mins, and arousal index > 15 /hr were significantly associated with postoperative PAP independence. Bariatric surgical procedures, including Roux-en-Y gastric bypass and sleeve gastrectomy resulted in non-significant difference in BMI and AHI reductions.

Conclusions: Bariatric surgery resulted in significant reduction in AHI and BMI along with improvements in sleep parameters from PSG. Although the overall remission rate of OSA remained low, nearly half of the patients with moderate to severe OSA experienced an improvement in disease severity following surgery. Additionally, one-quarter achieved CPAP independence. These findings support bariatric surgery as a potential strategy for OSA management in patients with morbid obesity.

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The effect of positive airway pressure therapy on cardiac remodelling and cardiovascular risk factors in patients with the chronic obstructive pulmonary disease and obstructive sleep apnoea overlap syndrome: The REMAPS study

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Introduction: Patients with chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are classified as overlap syndrome (OVS). OVS is associated with increased cardiovascular comorbidities and mortality compared to patients with COPD alone. The study aims were to assess changes in cardiac structure and function using cardiac magnetic resonance imaging (CMRI) following treatment of sleep disordered breathing with positive airway pressure (PAP) therapy in patients with OVS. The effects of PAP therapy were also assessed on cardiac biomarkers (high-sensitivity troponin, high sensitivity C-reactive protein, brain natriuretic peptide); arterial stiffness; and 6-minute walk distance (6MWD).

Materials and methods: We evaluated 10 patients with COPD (GOLD criteria) and severe OSA (apnoea-hypopnoea index (AHI) >30 events/hour by polysomnography). All participants underwent CMRI, pathology testing for cardiac biomarkers, pulse wave velocity (PWV) assessment and 6-minute walk test. After 3 months of CPAP therapy, these investigations were repeated.

Results: Participants were 90% male, median age 69 (IQR 60.5-71.8) years, AHI 55.2/hr (IQR 43.8-77). Median FEV1% predicted was 58% (IQR 45.3-67.3). Overall, there was no significant change in cardiac dimensions or cardiac function after CPAP therapy. However, there was a significant increase in left ventricular end diastolic volume (LV EDV) in patients without late gadolinium enhancement (LGE) compared to patients with LGE (mean difference 42.4±11 mL, p=0.005, 95% CI 17.1-67.7). There were no significant differences in cardiac biomarkers, PWV or 6MWD after CPAP treatment. The median CPAP compliance was 5.2 hrs/night (IQR 4.6-6) and treatment AHI was 1.4/hr (IQR 0.6-2.4).

Conclusions: The preliminary results from this pilot study demonstrated that CPAP treatment significantly increased LV EDV in patients without LGE compared to patients with LGE, reflecting possibly improved LV diastolic function. These results suggest that PAP therapy may have the greatest cardiac benefits in OVS patients without existing damaged myocardium.

The Effect of Resveratrol on Insulin Resistance in 3T3-L1 Adipocytes Exposed to Intermittent Hypoxia

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Introduction: Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder, characterized by repetitive upper airway narrowing or collapse during sleep that leads to intermittent hypoxia (IH). OSA has been associated with insulin resistance, increased risk of metabolic syndrome, and type 2 diabetes, potentially due to IH. One of the key mechanisms underlying this phenomenon is the generation of reactive oxygen species (ROS), which impairs insulin signaling. Our previous studies have indicated that oxidative stress is one of the key drivers of adipocyte insulin resistance under IH. Since oxidative stress contributes to insulin resistance, antioxidants such as Resveratrol have been explored as potential means to mitigate its effects. Resveratrol, a natural polyphenol found in grapes, berries, red wine, and other fruits and nuts, is known for its antioxidant, anti-obesogenic, and anti-diabetic properties. It modulates insulin signaling in adipose tissue by activating Nrf2-mediated transcription of antioxidant enzymes, such as the Heme-oxygenase 1 (HO-1), which in turn reduce mitochondrial ROS. The present study aimed to examine whether Resveratrol treatment may reduce insulin resistance induced by IH.

Materials and methods: We used 3T3-L1 cells, an established model of adipocytes, with significant similarities to primary human adipose tissues. 3T3-L1 cells were exposed to room air (RA) or IH (2%-17% O₂ 30-min cycles, 8 hrs on / 16 off) for 48 hours with or without Resveratrol (25mM). Western Blot was used to evaluate AKT phosphorylation rates in response to insulin, and mRNA expression of relevant genes [antioxidant capacity (HO-1, GPX2, SOD2) and glucose processing (Glut4)] was measured by RT-PCR.

Results: IH-exposed adipocytes demonstrated reduced pAKT/tAKT ratios in the presence of insulin, indicating impaired insulin signaling. IH exposure led to elevated mRNA expression of the antioxidant enzyme GPX2, suggesting a compensatory response to IH-induced ROS production. Resveratrol treatment, but not IH exposure, increased mRNA levels of HO-1, a direct transcriptional target of the antioxidant regulator NRF2. Glut4 expression remained unchanged. Functionally, Resveratrol treatment led to an improvement in insulin signaling in RA-exposed cells, but did not fully reverse IH-induced insulin resistance.

Conclusions: Collectively, these findings suggest that Resveratrol enhances insulin sensitivity primarily by attenuating oxidative stress, evidenced by an increased pAKT/tAKT ratio, rather than by modulating Glut4 expression. IH-induced insulin resistance may be only partially responsive to antioxidant interventions.

The Effect of Telemedicine-Based CPAP Management on 24-Hour Ambulatory Blood Pressure in Patients with Obstructive Sleep Apnea: A Randomized, Controlled, Non-Inferiority Trial

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Introduction: Previous studies have demonstrated feasibility and availability of telemedicine management of Obstructive Sleep Apnea (OSA) in China, but further evaluation is needed to determine whether these telemedicine approaches can lower 24-Hour Ambulatory Blood Pressure (AMBP), which is one of the intermediary mechanisms leading to increased cardiovascular morbidity. This study aimed at evaluating the effects of telemedicine-based CPAP management on 24h AMBP reductions in OSA patients.

Materials and methods: 344 adult (18-75 years old) OSA patients (AHI $\geq$ 5 events/h) were randomized to either telemedicine management (TM) (web-based questionnaires, self-administered home sleep apnea testing (HSAT), automatic positive airway pressure (APAP) and video-conference for visits) (n=172) or in-person management (IP) (paper questionnaires, in-person HSAT set-up, APAP and face-to-face visits) (n=172) for three months. The primary outcome was the change in 24-Hour mean arterial BP (MAP) from baseline to three months. Secondary outcomes included APAP adherence, depressive symptoms, daytime sleepiness, sleep quality, and serum liver enzyme levels.

Results: A total of 127 and 129 patients in the TM and IP groups, respectively, completed APAP treatment and underwent follow-up 24h ABPM monitoring. Significant reductions in 24-Hour mean arterial pressure (MAP) were observed in both groups: 2.94 mmHg in the TM group (P = 0.016) and 2.98 mmHg in the IP group (P = 0.015). The between-group difference was 0.78 mmHg (95% CI: -2.88 to 1.32; P=0.467), with the upper bound of the confidence interval below the pre-specified non-inferiority margin of 1.5 mmHg. Both groups also showed significant improvements in 24-hour systolic and diastolic BP. Daytime sleepiness, sleep quality, and depressive mood significantly improved in both groups after three months of APAP therapy (all P<0.05), with no significant between-group differences (P=0.48, P=0.50, and P=0.86, respectively). Serum alanine aminotransferase (ALT) levels significantly decreased in both the TM group (38.9 to 30.5 U/L, P=0.001) and the IP group (38.6 to 32.9 U/L, P=0.01), with no significant difference between groups (P=0.40). Aspartate aminotransferase (AST) levels showed a decreasing trend, but the change was not statistically significant.

Conclusions: Comprehensive telemedicine-based CPAP management is non-inferior to conventional in-person management in reducing 24h MAP among patients with OSA. Both groups experienced comparable improvements in sleep-related symptoms and quality of life. Serum liver enzymes, particularly ALT, also decreased following three months of APAP therapy.

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The Effect of Zolpidem on CPAP Acclimatization in Patients with OSA: A Crossover, Randomized, Double-blinded, Placebo-controlled Trial

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Introduction: One factor contributing to the failure of CPAP therapy is difficulty sleeping. Hypnotic medications, particularly eszopiclone, were shown to be beneficial in CPAP adaptation. However, research on zolpidem is limited.

This study aims to evaluate the effect of zolpidem on CPAP compliance in OSA patients compared to a placebo.

Materials and methods: This cross-over, RCT enrolled OSA patients indicated for CPAP therapy but naïve for the device usage. The enrolled participants were randomly allocated into 2 groups with different therapeutic sequences: group (1) 10-milligrams-zolpidem, and group (2) placebo in identical capsules 30 minutes before bedtime for 1-week. In the second week, the participants alternatively received either placebo or zolpidem. The wash-out period was 24 hours.

Results: The endpoint cohort included 28 participants (57.1% male) with an average age of 54.54 ± 13.70 years. The average CPAP usage per night (MD 0.18; 95% CI -0.39 to 0.75) and the percentage of the day utilized CPAP ≥ 4 hours (2.60; -5.65 to 10.87) did not differ significantly between the zolpidem and placebo groups, and treatment sequences had no significant effect ($p=0.87$). Subgroup analysis for gender, disease severity, and arousal index demonstrated no significant effects of zolpidem. No serious adverse events according to zolpidem usage were reported. The most common minor adverse event was dizziness (7.14%).

Conclusions: This article highlights the value of employing various CPAP acclimatization approaches during the CPAP introduction period instead of focusing on the regular use of zolpidem. Further studies with larger sample sizes and long-term follow-up are recommended.

The efficacy and safety of acupuncture for allergic rhinitis: a systematic review of randomised controlled trials

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Introduction: Allergic rhinitis (AR), affecting up to 40% of the global population, causes nasal symptoms and reduces quality of life. Conventional treatments (antihistamines, immunotherapy) often have side effects or require long-term commitment. This systematic review evaluates acupuncture as a safer, cost-effective alternative for AR management, focusing on recent RCTs (2015–2020).

Materials and methods: [https://drive.google.com/file/d/1kgwVqsohlo6ruOWn -MfUHe6T1uG0tp/view?usp=sharing](https://drive.google.com/file/d/1kgwVqsohlo6ruOWn-MfUHe6T1uG0tp/view?usp=sharing)

- **Search Strategy:** Databases (PubMed, Cochrane) were searched for English-language RCTs (2015–2020) using terms like "rhinitis," "acupuncture," and "randomized controlled trial."
- **Inclusion Criteria:** RCTs evaluating manual acupuncture in adults with moderate-to-severe AR (seasonal/perennial). Sham acupuncture, waiting lists, or conventional therapies served as controls.
- **Data Analysis:** Meta-analysis of nasal symptom scores (TNSS) and quality-of-life metrics (RQLQ) using RevMan 5.3. Heterogeneity was assessed via I^2 statistics.
- **Risk of Bias:** Evaluated using Cochrane criteria.

Results: [https://drive.google.com/file/d/1kgwVqsohlo6ruOWn -MfUHe6T1uG0tp/view?usp=sharing](https://drive.google.com/file/d/1kgwVqsohlo6ruOWn-MfUHe6T1uG0tp/view?usp=sharing)
Results

- **Included Studies:** Three RCTs (total 235 participants) from Australia and China met inclusion criteria.
- **Efficacy:**
 - **TNSS:** Acupuncture significantly reduced nasal symptoms post-treatment (SMD: -0.80; 95% CI: -1.54 to -0.05) and at follow-up (SMD: -0.51; 95% CI: -0.79 to -0.22).
 - **RQLQ:** Quality of life improved significantly at follow-up (SMD: -0.54; 95% CI: -0.82 to -0.25).
- **Safety:** Minor adverse effects (e.g., bruising, pain) occurred in 10.8% of patients (McDonald et al., 2016); no serious events were reported.
- **Heterogeneity:** High post-treatment heterogeneity ($I^2=84\%$ for TNSS, 79% for RQLQ) but resolved by follow-up.

Conclusions: This systematic review of recent RCTs assessing the efficacy and safety of acupuncture on the treatment of AR supports the previously performed reviews, suggesting that acupuncture is a safe and beneficial treatment modality for AR and may provide a low-cost non-invasive alternative for conventional treatment options. Further research, including high-quality integrative medicine RCTs will help in providing further objective support and establishing clinical guidelines.

Acknowledgments: CONTRIBUTION OF AUTHORS

LC, MA and SO performed the literature search, applied inclusion criteria and extracted data.

SO reviewed and combined extracted data and risk of bias. LC and MA performed the meta-analysis. First draft of the review was written jointly by the authors. All authors read and approved the final manuscript.

The Efficacy and Safety of Intraoral Negative Air Pressure Device in Obstructive Sleep Apnea Patients: A Systematic Review and Meta-analysis

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Introduction: Oral pressure therapy (OPT) and intraoral negative air pressure (INAP) devices are recent innovations that have emerged as potential treatment options for individuals who cannot tolerate CPAP and are seeking alternatives. These devices alleviate airway blockage during sleep by periodically applying negative pressure to the oral cavity, which moves the tongue and soft palate forward, increasing the cross-sectional areas behind the palate and tongue. Given the recent surge in research, this updated systematic review and meta-analysis aims to investigate the safety and effectiveness of OPT and INAP therapy for OSA patients, based on the latest evidence.

Materials and methods: A systematic search of the Ovid Medline, Embase, and Scopus databases was conducted, without language restrictions, to identify all original studies on the effects of INAP devices in adult OSA patients that reported the apnea-hypopnea index (AHI). Final update was done on December 7, 2024. The risk-of-bias assessment tool for nonrandomized studies (RoBANS) was applied for quality assessments. RevMan was used to conduct the statistical analyses.

Results: From the 72 initially retrieved articles, 9 studies involving a total of 445 individuals were included. Meta-analysis of the pooled data showed that, following INAP treatment, the participants had a significant improvement of mean AHI with mean difference (MD) of 12.4 (95%CI, 7.5 to 17.3), minimum oxygen saturation with MD of -3.6 (95%CI, -5.3 to -1.8), Epworth sleepiness scale with MD of 2.64 (95% CI, 0.23 to 5.05), and oxygen desaturation index (ODI) with MD of 10.8 (95%CI, 7.2 to 14.3). The participants also had a trend of improvement in percentages of time spent with oxygen saturation $\geq 90\%$ after treatment but did not reach statistical significance. The most common device-related adverse events were oral tissue discomfort and irritation, but no serious adverse events were reported.

Conclusions: INAP devices significantly improved AHI and ODI after treatment. No serious device-related adverse events were reported. Based on the current evidence, INAP may be a suitable treatment option for OSA in selected patients.

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The Hyoid Bone's Role in Mandibular Advancement Therapy for OSA: Do Position and Mobility Affect Upper Airway Patency?

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Introduction: Mandibular advancement is a common treatment for obstructive sleep apnea (OSA), but its success rate is variable, and the reasons for treatment failure remain unclear. The mandible and mobile hyoid bone serve as anchor points for key upper airway muscles - some of which directly connect the two - and play essential roles in maintaining airway patency. Accordingly, the hyoid bone may play a significant role in mandibular advancement effectiveness, though this relationship remains underexplored. This study aimed to investigate how hyoid bone position and mobility affect the ability of mandibular advancement to improve upper airway patency. We hypothesized that a lower (more caudal) natural baseline hyoid position and restricted mobility would reduce mandibular advancement

effectiveness, while anterior surgical repositioning of the hyoid would enhance it, regardless of baseline hyoid position.

Materials and methods: A previously validated 2D mid-sagittal finite element model of the rabbit upper airway was used to simulate mandibular advancement under different conditions, alone and combined: (1) baseline hyoid positions at increasingly caudal levels, (2) hyoid either free to move or fixed, and (3) anterior surgical repositioning of the hyoid. For each case, upper airway collapsibility (closing pressure, P_{close}) and cross-sectional area were assessed.

Results: Mandibular advancement decreased P_{close} (indicating reduced airway collapsibility) and enlarged the upper airway at the original baseline hyoid position. In comparison, a more caudal hyoid increased P_{close} and reduced mandibular advancement efficacy, regardless of mobility. Fixing the hyoid also increased P_{close} and produced smaller airway enlargement than when the hyoid was free. Anterior surgical hyoid repositioning consistently reduced P_{close} and enlarged the airway, mitigating the negative effects of a lower hyoid position.

Conclusions: Hyoid bone position and mobility substantially modulate the effectiveness of mandibular advancement in improving upper airway patency. A lower hyoid position - commonly observed in individuals with OSA - diminishes the efficacy of mandibular advancement, while limited hyoid mobility further impairs its benefits. Anterior surgical hyoid repositioning, on the other hand, helps restore and even enhance mandibular advancement outcomes. These findings underscore the potential for individualized OSA therapies by incorporating hyoid mechanics into treatment planning and suggest a complementary role for hyoid repositioning in improving mandibular advancement outcomes.

The impact of body mass index on severity of sleep related breathing disorders in adults with class 3 obesity

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Introduction: Obesity is a well-established risk factor for sleep related breathing disorders (SRBD) and the relationship between the two is multifaceted, although the influence of increasing body mass index (BMI) on the severity of SRBD in adults with class 3 obesity ($BMI \geq 40 \text{ kg/m}^2$) have not been conclusively explored. This study aimed to investigate the effect of BMI on SRBD severity in adults with class 3 obesity enrolled in a multidisciplinary weight management program.

Materials and methods: Adult patients (≥ 18 years) with class 3 obesity enrolled in a multidisciplinary weight management program in Sydney, Australia who underwent polysomnography between January 2020 and December 2024 were included in this retrospective study. Demographic details, anthropometric variables, clinical data, STOP-BANG score, Epworth sleepiness scale (ESS) score, and polysomnography parameters including sleep duration, respiratory indices, and oximetry were collected. Severity of SRBD was classified according to the respiratory disturbance index (RDI). Continuous variables were expressed as mean $\pm$ standard deviation (SD) and categorical variables were expressed as percentages (%). Independent T-tests were used to compare group means. Univariate and multivariate regression analyses were employed to assess associations between BMI and SRBD severity measures using SPSS v29.

Results: A total of 172 patients were included with mean age 42.9 ± 12.5 years and mean BMI $52.9 \pm 9.7 \text{ kg/m}^2$. The cohort was predominantly female (76.2%) and Caucasian (74.5%). The mean STOP-BANG and ESS scores were 4.7 ± 1.3 and 9.1 ± 5.0 , respectively. Majority of the cohort had severe SRBD (70.3%) defined by total sleep time (TST) RDI > 30 events/hour. The mean TST RDI was 54.2 ± 38.5 events/hour with mean hypopnoea index (HI) of 40.0 ± 26.2 events/hour and mean obstructive apnoea index (OAI) of 11.0 ± 22.4 events/hour. Key oximetry findings included mean nadir oxygen saturation (nSO_2) $77.3 \pm 11.6\%$, and mean proportion of total sleep with oxygen saturation $< 90\%$ ($pS < 90\%$) $16.5 \pm 25.7\%$. On univariate and multivariate regression analyses adjusted for age, sex and ethnicity, BMI was significantly associated with TST RDI (β 1.36, $p < 0.001$ univariate, $p < 0.001$ multivariate), nSO_2 (β -0.33, $p < 0.001$ univariate, $p < 0.001$ multivariate), and log transformed $pS < 90\%$ (β 0.055, $p = 0.002$ univariate, $p < 0.001$ multivariate). Patients with BMI $> 60 \text{ kg/m}^2$ ($n = 40$), compared to patients with BMI $40\text{--}49.9 \text{ kg/m}^2$ ($n = 68$), had significantly higher TST RDI (71.3 ± 42.6 events/hour vs 42.8 ± 31.5 events/hour, $p < 0.001$) and significantly lower nSO_2 ($72.4 \pm 13.8\%$ vs $79.6 \pm 9.0\%$, $p = 0.005$) with no

difference in STOP-BANG or ESS scores. Interestingly, 11% of the cohort had TST RDI <15 events/hour and 7.5% of the cohort with BMI >60 kg/m² had TST RDI <15 events/hour.

Conclusions: While there was a high prevalence of severe SRBD in adults with class 3 obesity, increasing BMI was associated with increasing severity of SRBD, as reflected by worsening RDI and greater burden of hypoxia during sleep but not worsening symptoms of SRBD. The relationship of weight loss in this group to improvement in SRBD needs further investigation. Additionally, a small proportion had normal to mild SRBD with RDI <15 events/hour despite having class 3 obesity and further investigation may reveal protective characteristics in this cohort.

The Impact of Early Intensive Nursing Interventions via Telemetric Monitoring on Long-Term Continuous positive airway pressure (CPAP) Adherence in Obstructive Sleep Apnea (OSA)- A single-centre experience in Hong Kong

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Introduction: Long-term adherence to CPAP remains a significant challenge in the treatment of OSA. It has been shown that suboptimal initial CPAP experiences negatively impact patient compliance. Conventional in-laboratory CPAP titration, often limited to a single-night assessment, may fail to address patient adaptation challenges. To enhance early patient support while optimizing resource allocation, our center introduced a home-based CPAP titration protocol incorporating telemonitoring and nursing interventions. We conducted a retrospective comparative analysis to evaluate the efficacy of home-based versus in-laboratory titration.

Materials and methods: Patients with newly diagnosed pure OSA who were naïve to CPAP treatment and underwent either home-based (home group) or in-laboratory titration (in-lab group) between January and September 2024 were included in the analysis.

Both groups participated in an OSA and CPAP education session, followed by a daytime CPAP trial in the sleep center prior to titration. The in-lab group received standard single-night attended CPAP titration, whereas the home group used an auto-adjusting CPAP device with integrated telemonitoring (ResMed AirSense 10 AutoSet for Her) for one week. In home group, telemonitoring was performed via a cloud-based platform, supplemented by phone consultations by trained nurses to assess adherence. Based on patient-reported feedback and objective usage data, personalized guidance was provided to address side effects and troubleshoot issues. Remote CPAP setting adjustments were made when necessary. In both groups, data was reviewed by physician to determine the final PAP prescription. After titration, both groups received an educational pamphlet with written and video instructions on PAP use and troubleshooting.

The following outcomes were compared:

- Titration success rate (the ability to derive prescribed PAP settings from the test)
- CPAP uptake (patient procurement of a CPAP device post-titration)
- CPAP adherence at 3 months (usage ≥4 hours per night for ≥70% of days)

Results: A total of 332 patients were included (110 in-lab, 222 home). The mean age (in-lab: 60.2 years, home: 57.3 years; p=0.08) and pre-treatment apnea-hypopnea index (AHI) (in-lab: 38.8/ hour, home: 36.5/ hour; p=0.18) were similar among both groups. Although titration success rate was higher in the in-lab group (in-lab: 97.3%, home: 89.1%; p=0.01), CPAP uptake rate was similar among both groups (in-lab: 51.8%, home: 59%; p=0.25). Although majority of patients who procured PAP device chose auto-CPAP (in-lab 84.5%; Home 90%; p=0.25), those who had underwent home CPAP titration still demonstrated significantly better adherence at 3 months (in-lab: 19.6%, home: 36.3%, p=0.0002) (Figure 5). Neither pre-treatment AHI ≥30/ hour (p=0.65) nor pre-treatment ESS scores ≥ 11 (p= 0.59) showed significant relationship with good adherence rate.

Conclusions: While auto-CPAP offers a convenient approach to initiating therapy, early identification and management of CPAP-related challenges remain crucial for optimizing long-term adherence. Our findings demonstrate that home-based CPAP titration with telemonitoring and nursing support not only improves adherence but also enables sleep centers to reserve in-laboratory resources for patients with complex sleep conditions.

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The Impact of Exercise Training on the Obstructive Sleep Apnea Endotypes

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Introduction: Weight loss interventions such as exercise are often recommended to manage both obstructive sleep apnea (OSA) and the cardio-metabolic complications associated with obesity. Interestingly, exercise can modestly improve OSA severity even without significant changes in body weight. However, the mechanisms underlying the improvements in OSA severity, separate from those observed with weight loss, are currently unknown. We aimed to assess how exercise affects the OSA pathophysiological endotypes (upper airway collapsibility, loop gain, arousal threshold and upper airway muscle compensation) and to identify individuals most likely to improve their OSA with exercise.

Materials and methods: We retrospectively analyzed data from OSA patients who underwent a 6-month exercise intervention (n=22). OSA endotypes were calculated from routine polysomnographic recordings before and following the intervention. Paired t-tests were used to compare the OSA endotypes before and after the exercise intervention. Correlation analysis was used to assess whether the baseline OSA endotype(s) predict change in OSA severity.

Results: Following 72 sessions of supervised exercise training, there was an improvement in the AHI (37.2[17.1, 57.4] to 27.9[15.9, 48.8] events/hr, p=0.046) but no significant change in body weight. Overall, there was no change in OSA endotypes; however, improvements in AHI were associated with improvements in upper airway muscle compensation ($\rho = -0.54$, p=0.011). Furthermore, poor upper airway muscle compensation at baseline predicted greater reductions in OSA severity ($\rho = 0.51$, p=0.017).

Conclusions: Exercise may improve OSA by strengthening the upper airway muscles. As such, regular exercise may be helpful to improve OSA in those with poor upper airway muscle function.

The Impact of Laparoscopic Sleeve Gastrectomy on Upper Airway Function and Sleep-disordered Breathing

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Introduction: Obstructive Sleep Apnea (OSA) is a global health crisis, strongly associated with obesity, increasing cardiovascular and metabolic risks. Continuous Positive Airway Pressure (CPAP) is the primary treatment but requires lifelong adherence and is not always well-tolerated. Metabolic Bariatric Surgery (MBS) has emerged as a promising intervention by reducing excess weight and improving

upper airway anatomy. Laparoscopic sleeve gastrectomy (LSG) has become the most common form of MBS performed worldwide due to its excellent results and limited complications. This study evaluates the impact of LSG on OSA using Magnetic Resonance Imaging (MRI) and polysomnography to assess structural changes and clinical outcomes.

Materials and methods: This prospective study was conducted on OSA patients referred to bariatric surgical department, in Medical Research Institute Alexandria University during the period between May 2023 and January 2024.

Ethical approval was obtained from the institutional review board (IRB) of the Faculty of Medicine of Alexandria University (No. --0306534-). Informed consent was obtained from the patients. All methods were performed in accordance with the relevant guidelines and regulations. This prospective study included 40 patients aged 18–65 years with BMI >30 kg/m² and confirmed OSA (apnea-hypopnea index (AHI) ≥5). Pre- and post-operative assessments included MRI of the upper airway, polysomnography, and the Arabic version of the Epworth Sleepiness Scale (ArESS) for daytime sleepiness. Statistical analyses, including Generalized Estimating Equations (GEE) and correlation tests, were performed using R software to evaluate changes in weight, BMI, AHI, ODI, and airway dimensions.

Results: The ESS showed an average reduction from 17.0 ± 0.5 to 5.4 ± 0.2 . Regarding polysomnography, there was a dramatic decrease in the AHI from 38.1 ± 2.5 events per hour, the nocturnal oximetry and the ODI was significantly reduced from 30.7 ± 2.2 to 5.2 ± 0.5 events per hour. The need for CPAP decreased dramatically from 80% of patients to 22.5% post-surgery as well as the average CPAP pressure required.

Metabolic parameters showed significant improvements; average reductions in fasting glucose and HbA1c were 15.4 mg/dL and 0.6%, respectively. In addition to the Lipid profiles with average reductions in triglycerides (-44.0 mg/dL), LDL cholesterol (-17.4 mg/dL), and overall cholesterol levels (-26.8 mg/dL).

After surgery diabetes and hypertension were resolved in all cases ($p = 0.023$ and $p = 0.008$, respectively). Hypothyroidism and dyslipidemia improved in 85.7% of cases but did not reach statistical significance ($p = 0.077$ and $p = 0.480$, respectively). Osteoarthritis did not resolve in any patient but showed improvement in all cases (100%), while cardiac conditions improved in 33.3% of cases and resolved in 66.7%, neither reaching statistical significance ($p = 0.480$ for both).

Greater %TWL correlated significantly with improvements in ESS, AHI, and ODI when outliers were excluded.

Conclusions: LSG significantly improves OSA severity, upper airway anatomy, and reducing CPAP dependency. These findings highlight LSG as an effective intervention for OSA patients with obesity, emphasizing the need for long-term research.

The Menopause Effects in Obstructive Sleep Apnoea (OSA) and the use of STOP-BANG score in Hong Kong (MENOSAS-HK)

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Introduction: The median age of menopause in Hong Kong is 51 year-old⁽¹⁾.

In a recent review on OSA and menopause, the reduction in oestrogen and progesterone hormones might cause instability in the ventilatory control system, leading to an overall increased risk for OSA⁽²⁾. This study aimed to assess difference in sleep characteristics and polysomnographic patterns in menopause patients compared to male counterpart in Hong Kong.

Materials and methods: Patients referred for sleep studies were recruited from 15/09/2022 to 28/02/2023. OSA were defined as apnoea-hypopnea index ≥ 5 events/hour⁽³⁾. Menopause was defined as patients > 51 year-old⁽¹⁾. STOP-BANG has been validated in Hong Kong for screening of OSA⁽⁴⁾.

Results: A total of 263 patients were recruited, amongst them 59 patients were menopause (22.4%). Menopausal patients were older than male patients (62.24 ± 7.02 vs 58.40 ± 10.96 years ($p < 0.05$)). BMI, AHI and ESS were similar. Menopausal patients have more snoring (15.67 ± 18.54 vs 8.18 ± 11.58 ($p < 0.05$)) and more hypopnoea (27.98 ± 19.50 vs 21.22 ± 14.58 ($p < 0.05$)). While male subjects present

with more central apnoea (1.46 ± 2.34 vs 5.54 ± 7.49 ($p < 0.05$)).

There was 1 unit difference in STOP-BANG score between menopause and male patients ($p < 0.05$).

Conclusions: Despite the same BMI, AHI and ESS, there was 1 unit difference in STOP-BANG score between menopausal and male patients, reflecting the gender component, while the lack of oestrogen/progesterone in menopausal patients do not confer protection against OSA. Hence, the use of STOP-BANG as screening may underestimate OSA in menopausal patients.

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The nonlinear endotypic characteristics and unique endotypic subtypes in Obstructive sleep apnea

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Introduction: The pathology mechanisms of obstructive sleep apnea (OSA) include high loop gain, low arousal threshold, more collapsible upper airway, and poor pharyngeal muscle responsiveness. Our research aimed to evaluate the dose-effect relationship between OSA endotypes and apnea hypopnea index (AHI), identify OSA endotypic clusters, and compare the cardiovascular disease (CVD) risk in different endotypic clusters.

Materials and methods: Individuals underwent polysomnography (PSG) were recruited. Endotypes were calculated with PSG-derived methods, including LG, ArTH, pharyngeal collapsibility (Vpassive), and muscle compensation (Vcomp). Restricted cubic spline (RCS) analysis was used to assess the non-linear relationship between variables. Latent profile analysis (LPA) was conducted to identify OSA clusters.

Results: This cross-sectional trial included 3616 OSA participants, fully adjusted model indicated loop gain, arousal threshold and upper airway collapsibility were non-linearly related to AHI; muscle compensation was linearly related to AHI. Latent profile analyses identified three OSA endotypic clusters, including high loop gain and upper airway collapsibility cluster, low arousal threshold cluster, low muscle compensation cluster. The high loop gain and upper airway collapsibility cluster had the highest CVD risk, while the low muscle compensation cluster had the lowest CVD risk.

Conclusions: In Chinese OSA participants, endotypes (except for Vcomp) were nonlinearly related to AHI. LPA identified the high LG and low Vpassive cluster, low ArTH cluster, and low Vcomp cluster.

The oral and gut microbiota dysbiosis in OSA

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Introduction: This study based on high-throughput sequencing technology to investigate the characteristics of oral-gut microecological communities in OSA and potential association with oral-gut microbiota and intermittent hypoxia.

Materials and methods: Adult subjects were enrolled from the department of sleep medicine, Peking University People's Hospital. All participants completed overnight PSG, collected fecal and oral pharyngeal swab sampling. 16s rRNA sequencing technology was used to analyze the microbiota structure and functional characteristics of OSA with different severity and healthy volunteers without snoring and apnea.

Results: (1) The alpha diversity of the gut microbiota in the OSA group was changed, the abundance of mild OSA and moderate-to-severe OSA(MSevOSA) group was greater than that of healthy control, but the species uniformity and microbiota diversity (Shannon index and Simpson index) were lower than those of healthy control. Linear discriminant analysis Effect Size analysis(LEfSe) found that *Ruminococcus_torques_group* and *Escherichia-Shigella* were significantly enriched in the gut of the MSevOSA group, and were positively correlated with cumulative time at $SpO_2 < 90\%$ (CT90) and cumulative percentage of sleep time spent with $SpO_2 < 90\%$ (CT90%), and significantly negatively correlated with lowest oxygen saturation(LSpO2). RDA analysis and Envfit test found the

environmental factors with the greatest impact on the gut microbiome were mean oxygen saturation(MSpO₂), CT90, LSpO₂, CT90%, BMI and ODI (r^2 was 0.804, 0.539, 0.525, 0.519, 0.307 and 0.272, respectively, $p < 0.005$), in which AHI had the lowest contribution to the difference in microbiota abundance ($r^2=0.216$, $p=0.006$). BugBase annotation showed that the aerobic phenotype of gut microbiota in MSevOSA group decreased significantly compared with the healthy control group [0.01(0.00-0.02) in the MSevOSA vs 0.02(0.01-0.02) in the healthy control group, $p=0.019$].

(2) The alpha diversity was demonstrated no difference in oropharyngeal microbiome, but there was a significant difference in beta diversity between healthy control and MSevOSA (Adonis test, $R^2=0.042$, adjusted $p=0.017$). In terms of microbial composition, Bacteroides, Lachnospirillum and Porphyromonas endodontalis were enriched in MSevOSA group. Among them, the differential genera Porphyromonas endodontalis, Bacteroides, and Lachnospirillum were positively correlated with AHI ($r=0.470$, 0.366 and 0.362 , respectively, $p<0.01$). RDA analysis and Envfit test showed that CT90% and AHI contributed the highest to the difference in the abundance of oropharyngeal microbiota ($r^2= 0.289$ and 0.254 respectively, $p < 0.01$).

Conclusions: Chronic intermittent hypoxia caused by OSA had a potential effect on the dysbiosis of the human oral-gut microbiota. The abundance of gut microbiome was high in patients with different degrees of OSA, but there was obvious heterogeneity in species evenness and diversity. The Ruminococcus_torques_group and Escherichia-Shigella were characteristic genera in the gut microbiota of MSevOSA, and were significantly correlated with the severity and duration of nocturnal hypoxia, but not AHI. Bacteroides and Lachnospirillum were enriched in oropharyngeal microbiome structure of MSevOSA, which is closely related to AHI and nocturnal hypoxia severity.

The Overlooked component: Proportion of Central Hypopnea in Obstructive Sleep Apnea Patients

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Introduction: Nearly 1 billion people globally are affected by Obstructive sleep apnea (OSA), with 425 million adults aged 30–69 having moderate to severe disease.

OSA involves repeated airflow reduction or cessation due to upper airway narrowing during sleep, causing hypoxia, arousals, and autonomic dysfunction.

These changes contribute to metabolic syndrome, hypertension, cardiovascular diseases, and cognitive decline.

Despite its prevalence, OSA remains underdiagnosed and untreated, and may coexist with central events. Central sleep apnea (CSA) results from impaired respiratory rhythm and is influenced by sleep stage, position, and gas exchange.

Differentiating OSA from CSA is essential, as both require distinct diagnostic and therapeutic approaches.

Materials and methods: This was a prospective cross-sectional single-center study consisting of 172 patients who fulfilled inclusion and exclusion criteria. A structured proforma was used to record demographics, symptoms, comorbidities, family history, and physical exam findings. All patients underwent Level-1 polysomnography.

For those diagnosed with OSA, hypopneas were manually classified as central or obstructive.

Central hypopnea proportion and revised Apnea-Hypopnea Index (excluding central events) were calculated.

The association between central hypopneas and clinical characteristics was then analyzed.

Results:

- 367 patients of OSA, who were diagnosed by level 1 polysomnography laboratory were screened for eligibility, and 172 patients were enrolled in the study. The proportion of central hypopnea in our study population was 7.35% (2.02% -18.95%). When analysed by OSA severity, the median proportion of central hypopnea was highest in mild OSA (22.97%), followed by moderate (11.04%) and severe (3.07%). The differences among groups were statistically significant. Central hypopnea had weak negative correlation with age and Body-mass index (BMI). Central hypopnea was lesser in type-2 diabetes and hypertensive patients.

Excluding central hypopneas from AHI calculation reclassified 23.1% of mild OSA patients as no OSA, 20.9% of moderate as mild with 2.3% as no OSA, and 6.7% of severe as moderate. When central hypopneas were counted as a part of central events, 3 out of 172 patients i.e. 1.7% could be labelled as central sleep apnea.

Conclusions:

- The study was conducted with the thought that although scoring hypopnea into obstructive and central is optional according to AASM scoring manual version-3, it is important to score central and obstructive hypopnea separately. Our study shows that central hypopnea is found in significant proportions in patients of OSA and may have diagnostic and therapeutic implications.

Abbreviations: OSA – obstructive sleep apnea, AHI – Apnea- Hypopnea Index, CPAP- Continuous positive airway pressure

The Prevalence of Obstructive Sleep Apnea among Patients with Secondary Polycythemia in Sultan Qaboos University Hospital

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Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder in the general population. It is usually considered one of the causes of secondary polycythemia. The relationship between OSA and secondary polycythemia is controversial. Multiple studies reported a higher prevalence of secondary polycythemia among patients with OSA, while others did not show any significant relationship. This study aimed to investigate the prevalence of obstructive sleep apnea (OSA) among patients with secondary polycythemia.

Materials and methods: A retrospective cross-sectional study was conducted at Sultan Qaboos University Hospital (SQUH). This study included all patients admitted to the hematology clinic in SQUH with secondary polycythemia and a sleep study was done for them. Study population data was collected from Trackcare and entered into SPSS, and Descriptive Statistics (mean and frequency) were obtained.

Results: The data of 44 patients was collected (male/female). All the study subjects had OSA at different severity; 52% of patients were found to have severe OSA. The mean apnea-hypopnea index (AHI) was 33.27 event/h and the desaturation index of 20.28 event/h. The male population was more likely to develop polycythemia. Polycythemia is more common in the middle-aged population, with a mean value of 40 years old, and it is more common in obese people whose body mass index is more than 30 Kg/m².

Conclusions: Severe OSA is found to be common in patients with secondary polycythemia, and it is more prevalent among patients with obesity and male sex.

The Prognostic Significance of Severe Obstructive Sleep Apnea in Patients Undergoing Surgical Repair for Acute Type A Aortic Dissection

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Introduction: Obstructive sleep apnea (OSA) is prevalent in patients with aortic dissection, yet its long-term effect on prognosis, particularly in those with acute type A aortic dissection (ATAAD), remains inadequately understood.

Materials and methods: This study conducted sleep test for 86 ATAAD patients within 90 days after total aortic arch replacement between January 2018 and December 2018. Severe OSA was defined as an apnea and hypopnea index ≥ 30 events/hour. Multivariable Cox regression analysis was used to evaluate the relationship between severe OSA and major adverse events (MAEs), including all-cause mortality and surgical reintervention.

Results: Over a median follow-up period of seven years, patients with severe OSA ($n = 22$) experienced a significantly higher incidence of MAEs (6 [27.3%] vs. 5 [7.8%], $P = 0.047$) and lower long-term survival rates (81.8% vs. 97.4%, $P = 0.003$) compared to patients without severe OSA ($n = 64$). Cox regression analysis revealed that severe OSA was a significant predictor of MAEs (HR = 3.9; 95% CI: 1.2–12.9; $P = 0.025$), with the association remaining significant after adjusting for age (HR = 3.7; 95% CI: 1.1–12.4; $P = 0.032$). Additionally, partial thrombosis of the false lumen was more frequently observed in patients with severe OSA compared to controls (9 [40.9%] vs. 9 [14.1%], $P = 0.028$).

Conclusions: Severe OSA is associated with poorer outcomes in patients undergoing surgical repair for ATAAD, underscoring the importance of identifying and managing OSA effectively, even following standard surgical intervention.

The relationship between obstructive sleep apnea and visual hallucinations in PD patients--a MRI and PSG study

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Introduction: Parkinson's disease (PD) patients frequently experience visual hallucinations (VHs) and obstructive sleep apnea (OSA). The aim of this study was to describe the prevalence and clinical correlates of VHs and OSAS in the Chinese population with PD. Using magnetic resonance to measure upper airway parameters and explore their relationship with sleep apnea and visual hallucinations in Parkinson's disease.

Materials and methods: A sample of 489 PD patients was recruited for the present study. Patients were categorized as having formed VHs (FVHs) or minor VHs (MVHs) or as non-hallucinators (NVHs) according to the Unified Parkinson's Disease Rating Scale (UPDRS) and an initial questionnaire. Polysomnography (PSG) was used for objective assessment of sleep. Using color Doppler ultrasound to examine the thickness of the genioglossus muscle, the thickness of the tongue, the left-right diameter of the oropharyngeal airway at the end of deep inhalation, and the left-right diameter of the oropharyngeal airway at the end of deep exhalation in patients with OSA. Using MRI to reconstruct the upper airway of OSA patients, measure the volume of oropharynx, glossopharynx, laryngopharynx and nasopharynx.

Results: VHs were observed in 143 (29.2%) patients. Among them, 75 of the hallucinators experienced MVHs, and 68 experienced FVHs. The disease duration, UPDRS Part III score, Hoehn and Yahr (H-Y) stage, Pittsburgh Sleep Quality Index (PSQI) score and rapid eye movement (REM) sleep behavior disorder (RBD) score of hallucinators were significantly greater than those of non-hallucinators ($P < 0.05$). We also observed OSAS in 38.7, 54.7, and 63.3% of the NVHs, MVHs, and FVHs groups, respectively. PSG showed that the VH groups had a lower total sleep time, lower sleep efficiency, higher arousal index, lower sleep latency, lower N1%, higher apnea-hypopnea index (AHI), higher average duration of apnea, higher respiratory-related arousal (RRA), and lower values of the lowest O_2 and mean O_2 . The forward binary logistic regression model showed that AHI, N1%, RRA and lowest O_2 were independently associated with VHs in PD patients. MRI examination indicates that there are abnormalities in the bony structure of the upper airway in patients with OSA. Ultrasonic examination indicates that patients with OSA have a higher degree of airway collapse. CPAP treatment can significantly improve non motor symptoms such as motor symptoms, cognition, and VHs in patients.

Conclusions: Our results confirm the high prevalence of VHs and OSAS as well as their relationship in patients with PD. Emphasizing the treatment of patients with PD combined with OSAS is beneficial for improving the overall symptoms of PD.

The Role of Mouth Tape for CPAP Users in OSA Patients with Mouth Breathing

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Introduction: Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnea (OSA), but its effectiveness depends on patient adherence. Mouth breathing during CPAP therapy is common among patients with OSA and is associated with reduced adherence. Current strategies to address this issue include the use of a chin strap with a nasal mask or switching to an oronasal mask. Mouth taping has recently emerged as a potential intervention; however, its impact on CPAP adherence remains unstudied. This study aims to evaluate whether mouth tape improves CPAP adherence in patients with OSA. Secondary outcomes include daytime sleepiness (Epworth Sleepiness Scale [ESS]), snoring (visual analog scale [VAS]), night awakenings, mouth/throat dryness, air leakage, and adverse effects.

Materials and methods: This randomized crossover study compared CPAP adherence with and without silicone hypoallergenic mouth tape in participants who exhibited mouth breathing during CPAP therapy. Participants received CPAP therapy with or without mouth tape for 30 days, then crossed over to the other intervention for another 30 days, with a 7-day washout period between phases. After each period, CPAP data (adherence, apnea-hypopnea index [AHI], and leakage) and questionnaires were collected. Tape application involved cutting silicone hypoallergenic tape to 2–4 cm based on facial structure and applying it vertically over the philtrum to seal both the upper and lower lips.

Results: Sixty-two patients with OSA (36 males; AHI [mean $\pm$ standard deviation], 45.8 ± 22.2 events/h; age, 57.7 ± 17.6 years; BMI, 27.9 ± 7.1 kg/m²) were randomized. Participants using mouth tape, compared to without mouth tape, showed higher CPAP adherence: average use increased by 51.8 minutes/day (95% CI, 33.1–70.4) and by 41.4 minutes/used day (95% CI, 27.9–55.0). Frequency of use increased by 14.2% (95% CI, 9.3–19.0), with 17.6% more days reaching ≥ 4 hours/night (95% CI, 12.7–22.6). Good adherence increased with an odds ratio of 4.5 ($p < 0.001$). Mouth tape significantly improved ESS, snoring VAS, mouth/throat dryness, and night awakenings ($p < 0.05$). Adverse effects were reported.

Conclusions:

Using mouth tape in patients with mouth breathing during CPAP improved CPAP adherence in both duration and frequency. Unfavorable symptoms related to OSA, or CPAP were alleviated, leading to better sleep quality.

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The Role of TREM-1 in Mediating Atherosclerosis Induced by Obstructive Sleep Apnea Syndrome: Insights into Mechanisms and Therapeutic Implications

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Introduction: To investigate the role of TREM-1 in atherosclerosis (AS) development triggered by obstructive sleep apnea syndrome (OSAS) and understand the underlying mechanisms.

Materials and methods: Mendelian randomization (MR) analysis was conducted using genome-wide association study (GWAS) summary data to assess the causal relationship between OSAS and AS (Finngen R10). Single-cell RNA sequencing (scRNA-seq) analysis was performed to examine the impact of OSAS on cellular transcriptional status in lung tissue (GSE145435) and peripheral blood (GSE214865) at the single-cell resolution. Additionally, single-cell transcriptional landscapes of aortic AS (GSE155512) were constructed to explore the involvement of macrophages in AS pathology. A chronic intermittent hypoxia (CIH) mouse model was established to evaluate atherosclerosis of aorta

formation, polarization of macrophage, and expression level of TREM-1. In vitro experiments utilizing lentiviral RNA were conducted to silence TREM-1 and assess its effect on macrophage polarization.

Results: MR analysis demonstrated a significant association between OSAS and the progression of coronary AS ($P<0.001$), as well as atherosclerosis in other arterial territories ($P=0.003$). ScRNA-seq analysis revealed that OSAS-induced hypoxia did not significantly alter the cellular composition of lung tissue ($P>0.05$), whilst OSAS patients exhibited enhanced immune activity of CD14⁺ monocytes in peripheral blood. Macrophage subpopulations in AS tissues of non-OSAS patients showed elevated immune crosstalk with smooth muscle cells, with relatively low TREM-1 expression. In contrast, CIH mice exhibited significantly increased AS plaque area, accompanied by upregulated TREM-1 expression ($P<0.05$). Infiltrating macrophages in AS under CIH displayed a predominance of the M1 subpopulation. In vitro experiments using macrophages exposed to CIH showed elevated levels of IL-6, TNF- α , and TREM-1, as well as decreased IL-10 and VEGF ($P<0.05$). Silencing TREM-1 significantly reduced TNF- α expression and increased IL-10 and VEGF expression ($P<0.05$).

Conclusions: OSAS is genetically linked to aortic atherosclerosis. TREM-1 is involved in OSAS-related AS by influencing macrophage polarization towards M1 and may serve as a potential therapeutic target. OSAS can lead to more TREM-1⁺ monocytes in the blood, contributing to AS development. Targeting TREM-1 could be a promising approach for treating atherosclerosis.

The Safety of Oral Appliances for OSA: Ten Years of FDA Adverse Event Reports

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Introduction: Oral appliances (“OA’s”) are a leading treatment for OSA. Clinical practice guidelines advise on the risks of dental side effects, but do dental side effects result in adverse events? With the availability of pharmaceutical and surgical treatments for OSA, new learnings about CPAP, and the emergence of OAs, properly informing patients on the safety of treatment options is increasingly important.

Materials and methods: This investigation characterizes the safety profile for OA’s, based on adverse event reports submitted to the FDA over a 10-year period. The FDA MAUDE database was accessed on June 6, 2025.

The FDA MAUDE database documents serious adverse event reports, defined as undesirable medical device experiences when the patient outcome is: death, life-threatening, hospitalization, disability, permanent damage, requires a subsequent intervention, or other consequence that endangers the patient. The investigators searched for FDA product codes LRK (Anti-Snoring), PLC (Sleep Appliances with Patient Monitoring) and LQZ (Jaw Repositioning Devices).

OA’s were classified into three categories for post-hoc analysis: non-custom, semi-custom and precision-custom. Non-custom OA’s are prefabricated. Semi-custom OA’s are made from oral records but include prefabricated items. Precision-custom OA’s are 100% made from oral records for each patient without prefabricated components or modifications. This assessment was made by reviewing relevant device labelling.

Results: Our search queries for the three product codes returned 853 unique adverse event reports, after elimination of duplicates.

59% of records were categorized as OA device malfunctions. 41% as patient injuries.

Semi-custom, non-custom and custom precision OA’s accounted for 86%, 13% and 1% of records, respectively.

The ten most frequently cited patient problems comprise 87% of records. They are: No Clinical Signs (281), Hypersensitivity/Allergic Reaction (125), No Known Consequence (51), Insufficient Information (25), Pain (24) Reaction (20) No Information (14) Discomfort (12) Erythema (11) Inflammation (11) Swelling (11).

2% indicate dental related serious-adverse events. They are: Tooth Fracture (6), Sensitivity of Teeth (3),

Joint Dislocation (2), Break (1), Dry Mouth (1), Joint Disorder (1) and Lacerations (1).

The ten most frequently cited device problems comprise 90% of records. They are: Break (169), Detachment of Device Component (153), No Identified Problem (141), Insufficient Information (38), Biocompatibility (29), Fracture (29), Interaction Problem (14), Patient Incompatibility (13), Material Integrity Problem (12).

Conclusions: This investigation indicates that OA's are a relatively safe for OSA treatment. Applying conservative estimates for US OA prescriptions, adverse events remain well under 0.1% of total OA treatments.

Custom-precision OA's are associated with fewer adverse events than non-custom and semi-custom OA's, resulting in better health and safety, fewer emergency interventions, less time out of treatment for OA repairs and adjustments, and more efficiency for the healthcare provider and payers.

Stakeholders might be better served focusing on OA materials and design which account for the more frequently reported adverse events: Allergic Reactions, Biocompatibility, Inflammation, Swelling, and OA Component failures. Although patients should continue to be advised of dental side effects, the FDA MAUDE database results suggest that dental side effects rarely result in a serious adverse event.

The SHINE Survey: Uncovering Gender Differences in Psychosocial Burden of Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a serious, chronic sleep-related breathing disease in which the airway is obstructed during sleep causing disrupted breathing, sleep fragmentation, and reduced oxygenation. OSA may present differently by gender, potentially causing differential underdiagnosis and disease experience. The objective of this study was to assess the psychological and social impact of OSA by gender in U.S. adults with diagnosed OSA.

Materials and methods: The SHINE online patient survey, developed in consultation with patient advocates and OSA experts, was administered to 1,500 OSA patients in the U.S. Results were assessed via generalized linear models with binomial distribution and logit link function, adjusted for age group, BMI category, race, region, income level, comorbidities, and time since diagnosis. Outcomes of interest were whether patients experienced ≥ 2 negative OSA symptoms in the past 30 days, experienced ≥ 2 negative feelings with OSA in the past 30 days and agreed (6 or 7 on a 7-point Likert scale) with ≥ 2 statements of OSA negatively affecting relationships.

Results: Of 1,500 respondents, 755 were men and 745 were women, with mean ages (SD) 50.7 (14.5) and 41.2 (14.4) years, respectively. Of seven listed OSA symptoms (daytime sleepiness, fatigue, irritability, mood changes, loud snoring, morning headaches, inability to concentrate), women were 1.52 times more likely than men to report ≥ 2 symptoms in the past 30 days ($p=0.04$). When asked whether OSA negatively affected relationships (overall impact, impact on care for family/friends, ability to be present, and social engagement), women were 1.42 times more likely than men of agreeing with ≥ 2 of 5 statements ($p=0.01$). Of 13 listed negative feelings (hopeless, depressed, frustrated, misunderstood, anxious, irritable, angry, not dependable, isolated, ashamed, embarrassed, scared, and low self-esteem), women were 1.61 times more likely than men to experience ≥ 2 feelings in the past 30 days ($p=0.01$).

Conclusions: It is known that OSA manifests differently in women compared to men. Our study further supports gender differences in patient reported outcomes, with women experiencing a higher psychosocial burden and more severe lived experiences, even after adjusting for baseline characteristics. These findings underscore the critical need for gender-specific approaches in the screening, diagnosis and treatment of OSA.

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The theranostic value of gene signatures and molecular mechanisms between obstructive sleep apnea and heart failure derived by machine learning

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Introduction: A bidirectional relationship has been established between obstructive sleep apnea (OSA) and hear failure (HF). Considering that HF is a progressive and irreversible condition, it is crucial to identify potential biomarkers and elucidate the underlying mechanisms linking OSA and HF to facilitate early-stage personalized interventions.

Materials and methods: Training and validation datasets of OSA and HF were retrieved from the GEO database. The raw data was integrated to find common differentially expressed genes (DEGs). Three machine learning algorithms (RF, LASSO logistic regression, and SVM-RFE) were employed to screen candidate biomarkers from common genes. The enrichment analyses were conducted to elucidate the biological functions and pathways. The validation and diagnostic performance of candidate biomarkers was evaluated using nomogram model and receiver operating characteristic (ROC) curve analysis. Additionally, consensus clustering analysis and immune infiltration analysis were processed to identify molecular subtypes and uncover potential mechanism underlying OSA-related HF.

Results: A total of 19 DEGs were identified as overlapping between OSA and HF. Enrichment analysis indicated that these genes were predominantly enriched in pathways related to immune and inflammatory response. Utilizing three machine learning algorithms, nine core genes (BTN3A2, MAPK10, STEAP4, FCER1G, CD109, SAMHD1, LUM, SFRP4 and FRZB) were selected as candidate biomarkers, and a nomogram was developed. ROC analysis showed that the nomogram achieved an AUC exceeding 0.80 in both training and validation datasets. Furthermore, immune infiltration analysis explored that these core genes are significantly associated with several immunocytes and immune checkpoint, which potentially regulate metabolic dysfunction and cardiac remodelling in OSA-related HF.

Conclusions: OSA is a risk factor implicated in the pathogenesis and progression of HF. Our machine learning analysis investigated the potential mechanism underlying HF secondary to OSA, and identified novel candidate genes that may serve as diagnostic biomarkers and potential therapeutic targets.

The 'USA' System: A Novel Classification for Hypoglossal Nerve Stimulation Therapy Outcomes

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Introduction: Treatment effectiveness for obstructive sleep apnea (OSA) device therapy is traditionally defined by a binary (responder versus non-responder) assessment of the apnea-hypopnea index (AHI) and overlooks usage and symptom response. We sought to define a novel outcomes classification system within hypoglossal nerve stimulation (HGNS) patients to better capture the various multidimensional outcomes in clinical practice and to better guide therapy optimization efforts. The USA system combines metrics of therapy Usage (U), Symptom response (S), and reduction in Apnea burden (A); and is adaptable over time as novel metrics in these categories continue to evolve.

Materials and methods: The USA system was applied to the ADHERE registry, an international database of HGNS patients. Adequate *usage* (U) was defined as mean nightly use >4 h/night, *symptom* response (S) by a reduction of >2 in the Epworth Sleepiness Scale (ESS) or maintaining a baseline ESS <10 without postoperative increase, and adequate *apnea* burden reduction defined as a full-night treatment AHI <15 events/hour. USA Class I patients were successful in all three categories. Class II was characterized by favorable usage and variations of partial response. Class III had suboptimal therapy usage.

Results: We analyzed 1453 patients with complete data in all three categories. USA Class I patients met success criteria in all three outcome measures and comprised 45.5% of patients. USA Class II comprised 35.9%, also had favorable therapy usage, and were further categorized as IIA (symptom

control but residual AHI elevation, 25.1%), IIB (effective AHI reduction but residual symptoms, 5.6%), and IIC (residual AHI and symptoms, 5.2%). USA Class III comprised 18.7% of the group and were characterized by suboptimal usage.

Conclusions: Over 80% of HGNS patients are using therapy well with the majority of those (76.2%) meeting success criteria based on AHI or ESS or both. Almost half of the analyzed HGNS population met success criteria in all three dimensions. Targeted troubleshooting efforts for the other half could strengthen long-term HGNS outcomes. Compared to binary assessments of one metric, the USA classification system better captures the multidimensional outcomes of HGNS therapy and may focus future research efforts and guide therapy optimization strategies.

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Three-Year Results of Positive Airway Pressure Adherence in Children with Sleep Apnea Compared to Adults

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Introduction: Most pediatric patients with obstructive sleep apnea (OSA) are known to be treated with adenotonsillectomy (AT). However, in some of them, positive airway pressure (PAP) can be used for underlying diseases or in case of AT failure. However, studies on PAP adherence for children are relatively fewer than adults as PAP is less commonly used in children. Thus, 3-year PAP adherence and compliance were compared in pediatric OSA to adult OSA.

Materials and methods: A retrospective study was conducted on 17 children and 167 adults who had performed polysomnography (PSG) and were prescribed PAP and followed up for more than 3 months from July 2018 to January 2023. Adherence was defined as the percentage of patients continuing to use PAP after prescription and compliance was defined as an average of more than 4 hours per night usage of 70% of the monitoring days. A patient's underlying disease, PSG results, as well as PAP adherence and compliance for the 1st, 3rd, 6th, 9th, 12th, 18th, and 36th months were evaluated.

Results: There were 11 males (64.7%) in pediatric and 141 males (84.4%) in adult patients. The mean age was 8.0 years (6.50-12.50) in pediatric and 50.0 years (41.00-58.00) in adult patients. The mean body mass index showed significant differences in the pediatric and adult groups (17.86 vs 27.7) ($p=0.001$). The mean apnea hypopnea index (AHI) (37.0 vs 50.7) and Lowest O₂ saturation (79.4% vs 75.5%) did not show any differences in the 2 groups. Longest apnea showed considerable differences (25.9 sec vs 50.8 sec) ($p=0.000$). After 36 months of PAP usage, AHI dropped from 37.0 to 5.1 vs 50.7 to 2.6, adherence decreased from 94.1% to 41.2% vs 90.4% to 38.9% ($p=0.944$), compliance reduced from 64.7% to 28.9% vs 67.0% vs 29.3% ($p=0.268$) in pediatric and adults groups.

Conclusions: There were no significant differences in adherence and compliance with PAP in children compared to adults. Adherence and compliance decreased the most between 3 months and 6 months in children similar to adults. PAP was tolerated in 2/3 at 3rd month, and less than one third at three years in children.

Acknowledgments: not applicable

Time with increased intrathoracic pressure and nocturnal hypoxemia are independent predictors of mortality in patients with suspected obstructive sleep apnea

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Introduction: Severe obstructive sleep apnea, defined by an apnea/hypopnea index (AHI) >30, is associated with cardiovascular disease and high mortality rates. Exaggerated negative intrathoracic pressure and hypoxemia during obstructive apnea episodes represent important pathophysiological

mechanisms.

Hypothesis: Negative esophageal pressure (PES) and nocturnal mean oxygen saturation (mSpO₂) are separate independent predictors of mortality, and increased PES is associated with comorbid heart failure.

Materials and methods: Patients referred with suspected sleep apnea between 2003 and 2016 were examined by respiratory polygraphy including esophageal pressure measurement. We extracted time in bed (TiB), a surrogate for sleep time, with PES above 10 and above 60 cmH₂O, mSpO₂, AHI and body mass index from polygraphy recordings, and age, sex and comorbidities from medical records. Mortality status was retrieved from the Norwegian Death Registry up to June 2024 and analyzed with multivariable Cox regression models.

Results: We included 16,476 patients, of which 4,356 (26%) were females, and mean± SD age of 48±12 years. Median AHI was 9.7 (IQR 4.3–21.1) and 2,652 (16%) had AHI >30. Median mSpO₂ was 94% and median TiB was 239 minutes for PES above 10 cmH₂O and 0.8 minutes for PES above 60 cmH₂O. During a mean 14.7±3.7 years follow-up, 1,546 (9.4%) patients died. None-survivors were older and more frequently males. Compared to survivors, non-survivors had also higher AHI 16.3 (7.3–31) vs 9.3 (4.1–20), longer TiB-PES10 271 min (171–335) vs 235 (127–321), TiB-PES60 1.5 min (0.4–4) vs 0.8 (0.2–2.7), and lower mSpO₂ 93% (91%–94%) vs 94 (93%–95%). In a fully adjusted model with mSpO₂, log_TiB-PES60 and log AHI, there was no association between higher AHI values and increased risk of mortality (HR 0.99, 95% CI: 0.93–1.06, p=0.85), while higher levels of TiB-PES10 (HR 1.11, 95% CI: 1.05–1.17, p<0.001), and lower levels of mSpO₂ (HR 0.90, 95% CI: 0.88–0.91, p<0.001) was significantly associated with increased mortality risk. There was a significant association between TiB with increased PES and comorbid heart failure (OR 1.096, [95% CI: 1.029–1.167], p=0.004) for PES> 10 cmH₂O.

Conclusions: Lower mSpO₂ and prolonged TiB with increased PES, but not AHI, were independent predictors of mortality in patients with suspected OSA. AHI, as a treatment criterion for patients with sleep apnea, may not be the optimal metric to identify high-risk individuals. A potential link between sleep time with increased PES and heart failure should be further investigated.

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Tongue Function in Young Populations at High Risk for SDB: Age-Stratified Associations and Interaction Analysis

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Introduction: Sleep-disordered breathing (SDB) is increasingly recognized in both pediatric and adult populations. The tongue, as a primary pharyngeal dilator muscle, maintains upper airway patency and contributes to SDB. Few studies have simultaneously evaluated tongue function and stratified SDB risk across age groups. This study is to evaluate age-specific associations between tongue function traits and the risk of SDB in children and young adults using multivariate and interaction models.

Materials and methods: A cross-sectional study was conducted among 1,244 healthy participants, comprising 462 children aged 7.5 years (47.2% female) and 782 adults aged 21.0 years (67.4% female). Participants were defined as at risk for SDB as meeting any one of the following criteria: for children, Pediatric Sleep Questionnaire (PSQ ≥ 8), Epworth Sleepiness Scale (ESS > 10), or Snoring Severity Scale (SSS ≥ 7); for adults, Berlin Questionnaire (≥2 positive categories), ESS > 10, or SSS ≥ 7. Tongue function was assessed through resting posture (the Friedman tongue position), mobility (tongue range of motion ratio—TRMR), strength (measured via the Iowa Oral Performance Instrument), and the Orofacial Myofunctional Evaluation with Scores (OMES). Mouth opening during sleep (reflecting impaired tongue-palate contact and oral seal) and tonsillar hypertrophy (as a tongue-base-related anatomical constraint) were also evaluated. Logistic regression models were performed on the entire sample and stratified by age group. The final model included all variables retained at the last step, along with potential interaction terms. Statistical significance was set at p < .05.

Results: High-risk SDB was found in 26.8% of children, 12.0% of adults, and 17.5% overall. In children, improper tongue rest (OR = 1.69, p = .047) and regular mouth opening during sleep (OR = 2.69, p =

.033) increased the odds of SDB; anterior mobility showed a marginal association (OR = 1.69, $p = .063$). In adults, higher OMES score (OR = 0.80, $p = .020$) and posterior tongue strength (OR = 0.98, $p = .026$) were protective. In the total sample, older age (OR = 6.52, $p < .001$), reduced anterior mobility (OR = 0.98, $p = .014$), restricted posterior mobility (OR = 2.66, $p = .025$), tonsillar hypertrophy (OR = 3.51, $p = .02$), and regular mouth opening during sleep (OR = 2.52, $p = .046$) were significant. Interactions revealed that normal posterior mobility reduced the impact of tonsillar hypertrophy on SDB (OR = 0.53, $p = .010$), while the effect was stronger in children (OR = 2.06, $p = .005$). There were no significant interactions in age-stratified models.

Conclusions: Tongue function traits were differentially associated with SDB risk across age groups. Regular mouth opening during sleep (in children) vs restricted posterior tongue mobility and better general orofacial myofunction (in adults) were independently associated with higher odds of SDB. Older age, restricted mobility, tonsillar hypertrophy, and open mouth posture increased the odds across the entire sample. Age-specific patterns and anatomical–functional interactions should be considered in tongue function and SDB risk assessment strategies.

Toward Understanding How R-Oxybutynin Influences Upper Airway Muscle Tone in sleep apnea: Focus on the Genioglossus in Anesthetized Rats

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Introduction: Obstructive sleep apnea syndrome (OSA) is characterized by recurrent episodes of apnea and hypopnea due to upper airway collapse during sleep. Despite extensive research, no effective pharmacotherapy exists for this disease. While continuous positive airway pressure (CPAP) remains the standard treatment, its low adherence underscores the need for alternative oral medications. Reduced upper airway muscle tone and responsiveness play a central role in OSA pathophysiology, and a recent study (MARIPOSA study, [Am J Respir Crit Care Med, 2019](#)) reported that a combination of R-oxybutynin and atomoxetine improved these deficits. R-oxybutynin acts as a non-selective muscarinic receptor antagonist, but the specific subtype responsible for enhancing muscle activity remains unclear. This study aimed to develop a preclinical evaluation system for genioglossus (GG) muscle activity in rats and to identify the receptor subtype primarily responsible for the pharmacological effects of R-oxybutynin.

Materials and methods: Male rats were anesthetized with urethane (1.5 g/kg, i.p.), underwent bilateral vagotomy, and electromyogram (EMG) electrodes were implanted into the GG muscle. EMG signals were recorded using LabChart™ (ADInstruments), and phasic (peak), tonic (background), and integrated (total) GG activities were quantified. Baseline activity was calculated as the average over 5 minutes prior to drug administration. Rats received either vehicle (saline), R-oxybutynin (reference drug), non-selective antagonist scopolamine, or M2-selective antagonist compound A via subcutaneous injection. Drug effects were assessed by comparing the normalized average GG activity at 30 minutes after administration for R-oxybutynin and compound A, and at 15 minutes for scopolamine.

Results: R-oxybutynin showed dose-dependent enhancement of GG activity, specifically in tonic amplitude. Given known side effects linked to M1 and M3 receptor subtypes, compound A was designed as a selective antagonist for M2 receptor, with sufficient CNS exposure confirmed in rats. However, compound A failed to enhance either tonic or phasic GG activity. Similarly, scopolamine exhibited potentiation in GG activity at high doses, but not at lower doses. Analysis of free drug concentrations in the medulla and plasma suggested that neither selective M2 inhibition nor combined inhibition of M1, M2, and M3 receptors produced a significant increase in GG muscle activity.

Conclusions: These findings suggest that targeting the M2 receptor alone is insufficient to enhance GG muscle activity. Moreover, even broad muscarinic inhibition (M1 + M2 + M3) did not replicate the efficacy of R-oxybutynin, indicating the involvement of additional receptor subtypes or the need for a more balanced receptor profile. The specific muscarinic receptor subtype through which R-oxybutynin exerts its pharmacological effects could not be identified. Further investigation is necessary to elucidate the mechanisms underlying muscarinic modulation of upper airway motor tone.

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Transforming Rural Sleep Health Care: Establishing a Rural Sleep-Disordered Breathing Service in East Malaysia

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Introduction: Obstructive sleep apnea (OSA) remains a prevalent but underdiagnosed condition in rural Malaysia, where access to diagnostic and therapeutic services is often limited. In 2022, the Department of Otorhinolaryngology at Hospital Labuan—a rural secondary referral center—initiated a dedicated sleep service to improve the identification and management of sleep-disordered breathing (SDB).

Materials and methods: Between March 2022 and April 2024, 86 patients were evaluated through the newly established sleep clinic. Among them, 44 were diagnosed with severe OSA, 15 with moderate OSA, and 19 with mild OSA, based on AHI criteria and clinical findings. Most patients presented with moderate to severe OSA, with a high prevalence of comorbidities such as obesity, hypertension, and ischemic heart disease. Despite resource limitations, diagnostic PSGs were successfully conducted. Management was tailored to individual needs and preferences: 24 patients were initiated on CPAP therapy, while 11 patients underwent upper airway surgical interventions. The remaining patients were either managed conservatively or declined intervention.

Results: Between March 2022 and April 2024, 86 patients were evaluated through the newly established sleep clinic. Among them, 44 were diagnosed with severe OSA, 15 with moderate OSA, and 19 with mild OSA, based on AHI criteria and clinical findings. Most patients presented with moderate to severe OSA, with a high prevalence of comorbidities such as obesity, hypertension, and ischemic heart disease. Despite resource limitations, diagnostic PSGs were successfully conducted. Management was tailored to individual needs and preferences: 24 patients were initiated on CPAP therapy, while 11 patients underwent upper airway surgical interventions. The remaining patients were either managed conservatively or declined intervention.

Conclusions: Key challenges included limited patient awareness, delayed referrals, and issues with CPAP adherence, particularly among patients with lower health literacy or financial constraints. Nonetheless, early data show promising outcomes: patients with >70% compliance reported significant symptomatic relief, with mean AHI reduction to <5 events/hour. Customized education, follow-up, and equipment subsidies played a crucial role in improving adherence. This experience demonstrates that with structured planning, multidisciplinary coordination, and patient-centered care, effective sleep services can be successfully implemented even in rural settings. The Hospital Labuan model provides a replicable framework for other underserved regions aiming to address the growing burden of sleep disorders.

Trends and Associated Factors for Signs and Symptoms of Sleep-disordered Breathing in Children with Down Syndrome

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Introduction: Sleep-disordered breathing (SDB) is a prevalent disease in people with Down syndrome (DS). SDB is characterized by not only frequent mid-night arousal, fragmented sleep, and repetitive hypoxemia but also hypertension and daytime sleepiness. These might lead to cognitive impairment, impaired attention, and attention-deficit/hyperactivity disorder like behaviors, which are common in people with DS. Furthermore, snoring or choking are strongly associated with SDB and can be considered as “signs and symptoms of SDB”. Although such signs and symptoms would be important markers in management of SDB, their temporal trends and associated factors for “signs and symptoms of SDB” in children with DS are still unknown. This study, thus, sought age and sex-dependent changes or trends of “signs and symptoms of SDB” and associated factors for them in children with DS.

Materials and methods: This cross-sectional questionnaire-based study included the children with DS aged 1-5 years who were belonging to Japan Down Syndrome Society. This survey was answered by the children's caregivers. The questionnaire included demographic data (sex, age, body height and

weight), self-reported sleep time, and witnessed signs and symptoms of SDB (snore and apnea). The data was analyzed in each age level. The estimated SDB was defined as presence of witnessed frequent snoring (defined as ≥ 5 times/week) or apnea.

Results: In 212 children with DS, their body height and weight increased as they grew ($p < 0.001$; all), while the body mass index (BMI) did not significantly change not only with growing but also between boys and girls ($p = 0.95$ and $p = 0.55$, respectively). The mean subjective sleeping time in boys and girls of 1 year old were 9.8 ± 0.7 and 10.2 ± 0.8 hour, respectively. The self-reported sleeping time significantly decreased with growing in girls ($p = 0.04$) but only a tendency in boys ($p = 0.07$). The presence of snoring and apnea significantly increased with growing in boys ($p = 0.001$ and $p = 0.04$, respectively), but not in girls ($p = 0.39$ and $p = 0.52$, respectively). The age depending changes of the frequency of snore was not observed in both sexes, but the estimated SDB suggested by frequent snore and/or apnea increased only in boys ($p = 0.04$) not in girls ($p = 0.47$). Growing was a significant associated factor for presence of snore, apnea, and estimated SDB, only in boys and high BMI was only a significant associated factor for presence of snoring in girls.

Conclusions: This study shows that the age dependent trends and predictors for estimated SDB and its' signs and symptoms are different between boys and girls with DS. In the low age generation, development or growing related anatomical changes might be more associated with SDB related signs and symptoms in boys than girls. Especially increase in body weight might be more related to SDB related signs and symptoms in girls. We should keep in mind this sexually different trends for management and follow up of SDB in the children with DS.

Ultrasound-Guided Tongue Base Thickness as a Screening Tool for Assessing Severity among patients with symptoms of Obstructive Sleep Apnea (OSA) at the Lung Center of the Philippines

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Introduction: Obstructive Sleep Apnea is a sleep-related breathing disorder causing cessation of breathing for short periods of time and radiographic modalities such as ultrasound have been applied to assess the upper airway anatomy in OSA patients. This study aimed to determine if ultrasound-guided tongue base thickness can be used as a screening tool for assessing severity in patients who presented with symptoms of obstructive sleep apnea.

Materials and methods: This research was a single-center, analytical study conducted at the Lung Center of the Philippines. Study subjects included patients seen at the Sleep lab and Sleep disorders clinic from March to May 2024. Data was gathered from patients with sleep-related symptoms and tongue base thickness was measured via ultrasound. Subsequently, gold-standard polysomnography was done and subjects were classified according to apnea-hypopnea index (AHI) and OSA severity

Results: Of 143 patients who took part of the study, 98 were included in this study, 13 patients classified as non-severe OSA (mild and moderate OSA), and 85 patients as severe OSA. Those with severe OSA were found to be predominantly male, significantly increased weight and BMI, had a lower baseline awake oxygen saturation, higher STOP-BANG score of 5, lower oxygen saturation nadir during the sleep study, and higher Apnea-Hypopnea Index (AHI). Ultrasound guided tongue base thickness was significantly increased in the severe OSA group. After multivariate analysis, oxygen saturation of $\leq 97\%$ (OR 5.996 CI 1.23-29.13), and tongue-base thickness of $\geq 5.75\text{cm}$ (OR 7.7529 CI 1.68-35.8) was associated with an increased likelihood of having severe OSA. On the other hand, having a symptom of difficulty falling asleep (OR 0.0859 CI 0.02-0.43) was less likely to have severe OSA. Ultrasound guided tongue-base thickness was positively correlated with the apnea-hypopnea index on PSG ($r = 0.4683$). Area Under the Receiver Operating Characteristics (ROC) curve of tongue-base thickness to discriminate severe OSA was at 0.77 which means that there is 77% chance that ultrasound-guided tongue base thickness can correctly classify patients with severe OSA. This is corroborated by the measured sensitivity (70.59%) and specificity (69.23%) of ultrasound guided tongue-base thickness. After considering a cut-off tongue-base thickness of $\geq 5.75\text{cm}$, the probability of having severe OSA increases to 93.75% (PPV 93.75%). On the other hand, tongue-base thickness of $< 5.75\text{cm}$ lowers the probability of having severe OSA to 26.47% (NPV 26.47%). The accuracy of ultrasound guided tongue-base thickness was 70.41% which represents the overall proportion of patients who were correctly classified as severe and non-severe OSA based on our study.

Conclusions: Those with severe OSA were predominantly male, obese, had lower baseline awake oxygen saturation, higher STOP-BANG score, lower oxygen saturation nadir during the sleep study, higher Apnea-Hypopnea Index (AHI), and higher ultrasound guided tongue base thickness measurement. After multivariate analysis, oxygen saturation of $\leq 97\%$ and tongue-base thickness of $\geq 5.75\text{cm}$ was independently associated with severe OSA. Tongue-base thickness was positively correlated to the apnea-hypopnea index (AHI) with severe OSA cut-off at $\geq 5.75\text{cm}$. This is a good screening test for classifying severe OSA and can be utilized in combination with existing screening tools used by clinicians.

Ultrasound Tongue Tracking for Intraoperative Assessment of Neurostimulation Implant Placement for Obstructive Sleep Apnea

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Introduction: Hypoglossal nerve (HGN) stimulation is a treatment option for obstructive sleep apnea (OSA). Recently, percutaneous electrode placement near distal arborizing branches of the nerve under ultrasound guidance has been developed to reduce surgical invasiveness. To confirm optimal placement in the absence of airflow measurements, nasoendoscopy and nerve integrity monitor (NIM) systems can be used to assess upper airway responses to stimulation. Here, we propose that an ultrasound-based method to track and quantify tongue morphology can improve intraoperative decision-making for HGN stimulation devices.

Materials and methods: A deep learning model, comprising a segmentation network (encoder-decoder) and a discriminator network, was developed to track anatomical features from midsagittal ultrasound views of the tongue. A selection of 1,574 midsagittal ultrasound tongue images was extracted from UltraSuite, an open repository of ultrasound datasets for speech disorders. Selected images included a wide distribution of tongue morphologies from 25 subjects performing various speech tasks. Images were acquired using different curvilinear probes with a field of view of 90-140 degrees, a frequency of 3-5 MHz, and a depth of 70-90 mm. Images were annotated with 14 anatomical landmarks, including 11 points along the tongue surface, 1 point on the hyoid bone, and 2 points on the mandible (base and insertion point of genioglossus muscle fibers). To address the challenge of heterogeneous datasets, unsupervised domain adaptation was incorporated into the deep learning framework to enable alignment of feature distributions between labeled source domains (open speech data) and unlabeled target domains (clinical sleep data).

Results: The model achieved a mean sum of distances of 0.443 pixels and a mean intersection over union of 53.64%, indicating robust tongue surface tracking and hyoid-mandible detection. It can also be used to output real-time predictions from a continuous stream of ultrasound images used as inputs. In addition, modified components of the Dorsum Excursion Index (DEI) and Tongue Constraint Position Index (TCPI), two measures used in speech pathology research, were identified as possible correlates of airway patency. These new measures quantify the spatial relationship between the predicted tongue surface and the predicted positions of the hyoid bone and mandible.

Conclusions: The proposed method remains to be clinically validated in future studies involving HGN stimulation devices for patients with OSA. If validated as a reliable complement or alternative to nasoendoscopy and NIM systems, it has the potential to reduce procedure risks, while simplify operating room setup and minimizing personnel needs, thereby lowering costs. It could also be used for therapy optimization at the physician's office or in sleep laboratories to provide a quick assessment of the effectiveness of different stimulation strategies.

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Unmasking Obstructive Sleep Apnea: Estimated Prevalence and Impact in the United States

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Introduction: Obstructive sleep apnea (OSA) is a serious, chronic sleep-related breathing disease, characterized by repeated upper airway obstructions during sleep, leading to episodes of disrupted breathing, sleep fragmentation, and reduced oxygen saturation. Adjusting for obesity as a major risk factor, we aimed to estimate the up-to-date prevalence of OSA in United States (US) adults in 2024.

Materials and methods: We conducted a literature-based analysis to identify studies of OSA prevalence in the general or community adult population, using the AHI₄ criteria (all apneas plus hypopneas with $\geq 4\%$ oxygen desaturation) from polysomnography or home sleep apnea test. OSA was defined as having an AHI₄ ≥ 5 events/hour. For the total prevalence, we estimated age- and gender-specific rates based on eligible studies and extrapolated missing data (e.g., age-group) from studies where data were available. The base-year estimation for 2004 was calculated by averaging age-specific total OSA prevalence data from these studies, accounting for methodological and population differences, to establish a foundational baseline for further adjustments. We calculated the obesity population attributable fraction (PAF) which was applied to base year estimates to project OSA prevalence in year 2024 adjusting for obesity and extrapolated to the US Census population data. The AHI distribution of mild (5 – <15), moderate (15 – <30) and severe (≥ 30 events/h) were also estimated.

Results: Total of 80.6 million individuals were estimated to be living with OSA in the US in 2024, of whom 47,623,848 (59%) were males and 32,967,117 (41%) females. This translates to 32.2% overall prevalence in the US among adults aged 20 years and older, with 39% males and 25.8% females, adjusting for obesity. The AHI severity distribution was estimated to be 61% mild, 24% moderate, and 15% severe.

Conclusions: Our findings indicate that OSA is highly prevalent among US adults. Despite its substantial prevalence, OSA remains largely undiagnosed, highlighting the urgent need for improved screening and diagnosis as well as greater awareness about the chronic and serious complications of untreated OSA.

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Unmasking OSA: Predisposing Factors in Asian and Non-Caucasian Populations in Australia

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Introduction: Obstructive sleep apnoea (OSA) is a common condition associated with obesity, excessive daytime sleepiness, cardiovascular disease, type 2 diabetes (T2DM), and increased risk of accidents. Understanding whether traditional OSA risk factors differ between Caucasian and non-Caucasian populations is critical for equitable clinical care. However, data on non-Caucasian Australians (including the Asian and Australian First Nation populations) remains limited, despite known disparities in cardiometabolic health. Importantly, emerging evidence suggests that OSA pathophysiology in this group may involve factors beyond obesity alone. This study compares conventional OSA predictors and their clinical relevance in Caucasian and non-Caucasians within our local health service, aiming to inform more tailored screening and intervention strategies.

Materials and methods: We undertook a retrospective analysis of medical records of all adults (≥ 18 years) undergoing a diagnostic sleep study in 2022-2023 at Gold Coast Hospital and Health Service (Queensland, Australia) and MySleep Upper Mount Gravatt (Queensland, Australia). Medical records were evaluated to compile data set. Linear regression was used to determine the association between traditional OSA predictors and AHI (Apnoea-Hypopnoea Index). BMI (body mass index) thresholds for moderate-to-severe OSA in Caucasians and non-Caucasians were estimated using Youden's Indices.

Results: A total of 2,181 patients were included in the study, of which 77% (n=1866) had OSA. Amongst these, 31% had mild, 23% moderate, and 32% severe OSA. The median age was 50 (IQR 39-61) years, with 60% being males. BMI was a significant predictor of OSA in both Caucasian and non-Caucasian groups ($p < 0.001$), with data suggesting trend towards strongest association between BMI and AHI in the Asian subgroup (1.8 AHI units per BMI point; $p < 0.001$). The BMI threshold for moderate-to-severe OSA was relatively lower in non-Caucasians (28kg/m²). Whereas a greater

proportion of patients with moderate-to-severe OSA were obese in the Caucasian group (76%) compared to the Asian subgroup (38%). Neck circumference, independent of BMI, was also a significant predictor of OSA in Caucasian, non-Caucasian, and Asian populations ($p < 0.001$). Male gender and hypertension were also linked to higher AHI in both Caucasian and non-Caucasian groups ($p < 0.001$), with a trend suggestive of gender having a greater impact on AHI in the non-Caucasian cohort.

Conclusions: OSA screening tools are derived from data that is predominantly taken from the Caucasian population. Our findings underscore the importance of considering ethnic variability in OSA risk profiling. Specifically, a lower BMI threshold may be warranted for OSA screening in the Asian population, which may be more sensitive to BMI increases. Male gender and hypertension also appear to be stronger predictors of OSA severity in non-Caucasians. Our results highlight potential ethnic differences in OSA burden and BMI sensitivity, reinforcing the need for ethnicity-specific screening and risk assessment strategies to improve early detection and targeted management of OSA. Future research should evaluate the performance of tools like STOP-BANG and Epworth Sleepiness Scale in Asian population to improve diagnostic accuracy and equity of OSA screening.

Unveiling Predictive Factors for CPAP Adherence: A Pilot Cohort Study on Real-World Use in OSA

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Introduction: Obstructive sleep apnea (OSA) is a modifiable risk factor for cardiovascular and cerebrovascular diseases. Continuous positive airway pressure (CPAP) remains the first-line treatment; however, adherence is often suboptimal. This study aimed to explore clinical and polysomnographic factors associated with CPAP adherence in a real-world setting.

Materials and methods: We conducted a prospective cohort study enrolling 10 participants diagnosed with OSA by in-lab polysomnography (PSG). All underwent overnight CPAP titration and were then offered home CPAP use for 30 or 90 days at their discretion, without a required minimum usage, to reflect natural adherence. We collected: 1. Demographics (age, sex, BMI, Epworth Sleepiness Scale score), 2. Baseline PSG data (AHI, minimum SpO₂, arousal index [AI], sleep efficiency [SE]), 3. CPAP titration data (residual AHI, SpO₂, AI, SE, optimal pressure), 4. Differences between baseline and titration parameters, 5. Daily CPAP usage metrics (residual AHI, pressure, and leak).

Good CPAP adherence was defined as using CPAP for more than 50% of total days at home, with both mean and median nightly usage ≥ 6 hours. Collinearity was assessed using Pearson correlation matrices. Group comparisons, univariate logistic regression, and multivariate regression were performed.

Results: The mean age was 50.2 ± 10.4 years, BMI 29.4 ± 5.7 , and baseline AHI 49.4 ± 24.3 . Older age was correlated with lower baseline sleep efficiency ($r = -0.82$). Higher baseline AHI was associated with a higher arousal index ($r = 0.79$), but also with greater improvement in arousal index ($r = 0.73$) and AHI ($r = 0.99$) during titration. Higher AHI was also associated with the need for higher daily pressure ($r = 0.72$).

Participants with good adherence had significantly lower optimal titration pressure (6.6 vs. 11.8 cmH₂O, $p = 0.03$), lower residual AHI during titration (2.7 vs. 8.1, $p = 0.04$), and lower daily CPAP pressure (7.5 vs. 9.3 cmH₂O, $p = 0.04$). These associations were statistically significant in univariate analysis. However, in multivariate analysis including these predictors, none remained statistical significance due to small sample size and co-linearity among pressure-related variables.

Conclusions: This pilot study suggests that individuals with higher AHI not only exhibit more disrupted sleep but also derive greater benefit from CPAP in terms of AHI and arousal reduction. Importantly, lower pressure requirements, both during titration and in daily use, along with effective titration (lower residual AHI), were associated with better CPAP adherence. Although significance was not retained in multivariate analysis, consistent trends support the importance of optimizing pressure settings for comfort and effectiveness. Larger studies are warranted to confirm these findings and to inform pressure adjustment strategies that promote long-term adherence.

Unveiling the circHDAC9/miR-138-5p/SIRT1 Axis: A Novel Mechanism Linking Obstructive Sleep Apnea-Hypopnea Syndrome to Cognitive Impairment through Senescence-Associated Neuronal Autophagy

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Introduction: To investigate the circHDAC9/miR-138-5p/SIRT1 pathway in Intermittent Hypoxia (IH)-induced cognitive impairment for Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) complication diagnosis and therapies.

Materials and methods: Ten 3-month-old male C57 mice were randomly divided into a control group (normoxic environment) and a model group (IH: 4.6-4.8% O₂ for 60 seconds followed by 20% O₂ for 30 seconds cyclically, 8 h/day). Cognitive function was assessed using the Morris water maze test. Hippocampal tissues were analyzed for histopathology, apoptosis, senescence, autophagy, mitochondrial structure, protein expression, and gene/protein levels via HE staining, TUNEL staining, β -gal staining, transmission electron microscopy, immunofluorescence, and Real Time PCR/Western blotting. In vitro experiments used HEK293T cells to validate miR-138-5p targeting SIRT1 and circHDAC9 via dual luciferase assays, and HT22 cells to confirm circHDAC9 expression and its interaction with SIRT1 using FISH and RIP.

Results: Model group mice exhibited significantly impaired cognitive function ($p < 0.05$), increased hippocampal neuron aging, apoptosis, and autophagy ($p < 0.0001$), upregulated miR-138-5p, and downregulated circHDAC9 and SIRT1 ($p < 0.001$). Aging-related molecules and autophagy-related proteins were upregulated ($p < 0.001$), pro-apoptotic Bax increased, anti-apoptotic Bcl2 decreased ($p < 0.001$), and telomere length shortened ($p < 0.0001$). Cell experiments confirmed miR-138-5p directly targets SIRT1 and circHDAC9, reducing luciferase activity ($p < 0.0001$), and revealed an interaction between circHDAC9 and SIRT1.

Conclusions: OSAHS triggers cognitive decline through a "senescence-autophagy-apoptosis" cycle via circHDAC9/miR-138-5p/SIRT1 axis disruption. CircHDAC9's dual regulation (sponging miR-138-5p and interacting with SIRT1) reveals therapeutic targets.

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Validation of Ambulatory Polysomnography for Measuring Sleep and Detecting Obstructive Sleep Apnea in Patients with Rapid Eye Movement Sleep Behaviour Disorder

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Introduction: Rapid eye movement sleep behaviour disorder (RBD) is often associated with obstructive sleep apnea (OSA). The standard method for assessing sleep disorders is in-laboratory polysomnography (lab PSG). However, ambulatory polysomnography conducted in home setting (home PSG) has become increasingly utilised in clinical settings due to its convenience and ease of administration. Despite this, the agreement between home PSG and lab PSG in evaluating OSA in RBD patients remains insufficiently validated. This study aimed to compare the consistency of home PSG and lab PSG in measuring the key sleep structure parameters (such as sleep latency, sleep efficiency, etc.) as well as the OSA severity.

Materials and methods: This study included 35 patients (mean age 66.7 years, 25.7% female) who were diagnosed as suffering from RBD with standard attended lab v-PSG. Each participant underwent both home and standard PSG, with a mean time interval of 63.7 days (range 12 to 113 days). AHI thresholds of ≥ 5 , ≥ 15 , and ≥ 30 , and ODI thresholds of ≥ 5 and ≥ 15 were applied, and the sensitivity, specificity,

positive predictive value (PPV), negative predictive value (NPV), and accuracy of home PSG in detecting OSA were calculated for both AHI and ODI. The correlation between home PSG and lab PSG in various sleep parameters, including AHI, ODI, sleep latency, sleep efficiency, wake after sleep onset (WASO), REM latency, stages percentages, and arousal index, was compared using correlation analysis.

Results: There was a strong correlation between home PSG and lab PSG for most sleep parameters, with the highest correlation coefficients being for ODI ($r = 0.85$), followed by AHI ($r = 0.81$) and N3 sleep ($r = 0.78$). However, the correlation for REM sleep ($r = 0.24$) and arousal index ($r = -0.02$) was low. Regarding the OSA severity and diagnosis, 23% of the patients ($N = 8$) had $AHI \geq 15$ as diagnosed by lab PSG. The sensitivity of home PSG was 0.75, specificity was 1.00, PPV was 1.00, NPV was 0.93, and accuracy was 0.94. In contrast, the sensitivity in the $AHI \geq 5$ group ($N = 17$, 48.5%) was lower (0.53), while for severe OSA ($AHI \geq 30$; $N = 4$, 11.4%), despite a specificity and PPV of 1.00, the sensitivity was only 0.25. For ODI, in the $ODI \geq 5$ group ($N = 10$), home PSG had a sensitivity of 0.60, specificity of 0.88, PPV of 0.67, NPV of 0.85, and accuracy of 0.80. In comparison, for the $ODI \geq 15$ group ($N = 3$), sensitivity improved to 1.00, with higher specificity (0.94) and accuracy (0.94), but lower PPV (0.60).

Conclusions: Home PSG shows good diagnostic agreement with lab PSG in assessing OSA severity, particularly for $AHI \geq 15$ and $ODI \geq 15$ in RBD patients. However, home PSG has lower sensitivity in detecting mild OSA, leading to a potential risk of underdiagnosis. Nevertheless, home PSG can serve as an effective screening tool especially when lab PSG is not feasible.

Vasomotor Intracranial Blood Vessels in Obstructive Sleep Apnea Patients

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Introduction: Obstructive Sleep Apnea (OSA) is characterized by episodes of complete or partial airway collapse accompanied by decreased oxygen saturation or awakening from sleep. OSA is an independent factor for stroke. The initial sign of vascular abnormalities in OSA is vascular endothelial dysfunction. Cerebral vascular endothelial dysfunctions in OSA can be detected by Transcranial Doppler (TCD) examination by assessing cerebral vasomotor reactivity (RVS). Assessing RVS can be done through the Breath Holding test procedure by assessing the Breath Holding Index (BHI). Currently, there are no specific assessments objectively to predict stroke in OSA patients, so this study is expected to be the basis for objective initial screening in assessing stroke risk.

Materials and methods: In this study, OSA patients were screened using a STOP-BANG questionnaire of more than 1 point. Then, 46 subjects were grouped into non-OSA ($N = 8$) and OSA ($N = 38$) based on the results of the polysomnography (PSG) examination. Mean flow velocity (MFV) and BHI were measured in the middle cerebral artery (MCA) using a TCD device. BHI values above 0.69 are considered normal and MFV MCA values less than 120 cm/sec are considered normal. Screening for comorbidities and other risk stroke (smoking, physical activity) was evaluated.

Results: In this study, there was a significant difference in BHI score values between the OSA and non-OSA groups (0.76 ± 0.62 vs 1.27 ± 0.70 ; $p = 0.04$) and a higher trend in MFV MCA values in the OSA group. There was a negative correlation between AHI and BHI values ($r = -0.381$, $p = 0.009$). There was a correlation between smoking and BHI values ($p = 0.115$). Then continued into multivariate linear regression analysis, but only the AHI value was significant ($p = 0.029$).

Conclusions: As the degree of OSA increases, the vasomotor function of intracranial blood vessels is disrupted. This shows that the more severe the degree of OSA, the more cerebral endothelial dysfunction has occurred.

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Sleep Health

A comparison of coblation and modified monopolar tonsillectomy in adults

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Introduction: Objective: To compare the intraoperative records and postoperative clinical outcomes of adults who underwent coblation and modified monopolar tonsillectomy tonsillectomies.

Materials and methods: Material and Methods: Adult patients with tonsillectomy were randomly divided into the coblation and modified monopolar tonsillectomy groups. The estimated blood loss, postoperative pain score, operation time, post-tonsillectomy hemorrhage (PTH), and cost of disposable equipment were compared.

Results: Results: Pain intensity in the coblation and monopolar groups was similar on postoperative days 3 and 7. However, the mean maximum pain score in the monopolar group was significantly higher compared to the coblation group on postoperative days 1 ($P < 0.01$) and 2 ($P < 0.05$). Secondary PTH occurred in 7.1% (23/326) of patients in the coblation group and 2.8% (9/327) of patients in the monopolar group ($P < 0.05$).

Conclusions: Conclusion: Although pain was significantly increased on postoperative days 1 and 2 in the modified monopolar tonsillectomy group, the operation time, secondary PTH, and medical costs were significantly decreased compared to the coblation technique group.

Adult Attachment, Sleep Hygiene and Sleep Quality, a Cross-Sectional Mediation Analysis

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Introduction: Insecure attachment dimensions have been associated with decreased sleep quality and reduced health behaviors. The current study aimed to expand the literature by testing whether sleep hygiene might mediate the relationship between adult attachment dimensions and sleep quality.

Materials and methods: Adult participants from an international sample ($N = 221$) were recruited through opportunity sampling using an online participant platform and were asked to fill in a online questionnaire containing sections on attachment dimensions, sleep quality, mood, fatigue, and sleep hygiene. Multiple regressions were conducted to determine the associations between attachment dimensions (anxious and avoidant) and sleep hygiene, as well as to assess whether sleep hygiene mediated the relationship between attachment dimensions and sleep quality, while controlling for age, gender, mood, and fatigue.

Results: The mediation diagrams indicate a partial mediation effect of sleep hygiene; individuals scoring higher on both insecure attachment scales also reported lower sleep hygiene scores and poorer sleep quality.

Conclusions: Previous literature has revealed relationships between insecure attachment styles and decreased sleep quality. Our results suggest that sleep hygiene may be contributing to this relationship through partial mediation as insecure attachment appears to have a negative effect on sleep hygiene which in turn appears associated with decreased sleep quality. Future sleep interventions should consider incorporating attachment based strategies as individuals' may benefit from an interpersonal approach in terms of their sleep hygiene and sleep quality.

An 8-week mindfulness programme for sleep and well-being among informal caregivers of children with neurodevelopmental disorders: a mixed-methods feasibility case series

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Introduction: Poor sleep and mental health are common among parents of children with neurodevelopmental disorders, including autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). However, the existing options and evidence regarding psychosocial mental health interventions for this specific group remain limited. Mindfulness-based interventions have shown promise in improving mental health outcomes across different populations, including those with subclinical conditions and busy schedules. The unique practical challenges faced by parents of children with neurodevelopmental disorders highlight the importance of adapting psychological interventions to meet their specific needs. The objective of this mixed-methods feasibility case series study was to evaluate the feasibility and acceptability of a mindfulness-based programme with an abridged adaptation in informal caregivers of children with neurodevelopmental disorders.

Materials and methods: Parents of children with neurodevelopmental disorders were recruited via a local non-governmental organisation (NGO) in Hong Kong and were invited to participate in an 8-week mindfulness programme. Participating parents first underwent a clinical interview and were subsequently asked to complete a set of questionnaires that assessed depression, anxiety, insomnia, stress, and mindfulness before and after the programme. Additionally, participants' experiences in the intervention were evaluated by a post-programme survey and an individual qualitative interview.

Results: Seven participants were recruited (mean age: 47 years, range 35 - 53 years; 86% female; 71% married; and 29% in full-time employment). Two participants dropped out by session 4 and did not complete the follow-up assessment because of their family commitments. The mean number of attended sessions in the follow-up sample was 7 sessions (5 - 8 sessions). Of the completed participants (n=5), 4 reported reduced depression, 2 reported reduced anxiety, 3 reported reduced insomnia symptoms, 4 reported reduced perceived stress, and 2 reported improved mindfulness. Qualitative findings revealed four key themes. Firstly, participants expressed expectations for the programme (e.g., learning mindfulness, improving well-being). Secondly, positive intervention experiences were highlighted, such as good quality of teaching and guidance, as well as reported improvements in sleep and daily functioning. Third, negative intervention experiences were also identified, such as distractions during practice, a lack of energy, and challenges related to travel time. Lastly, participants offered some suggestions for improvement (e.g., adopting a hybrid format to facilitate participation).

Conclusions: The preliminary findings showed that an 8-week mindfulness programme is feasible and well-accepted by parents of children with neurodevelopmental disorders to improve their psychological well-being and sleep. There is a need to explore ways to address the barriers reported by the participants to improve their engagement in the future implementation of the programme in this population.

Anaerobic Airborne Bacteria Dominate Bedroom Environments of Individuals with High Sleep Apnea Risk

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Introduction: Sleep disorders such as obstructive sleep apnea (OSA) may be influenced by environmental exposures like air pollution, temperature, humidity and season. The role of indoor microbial communities and endotoxins, especially in bedroom, remains poorly understood. Our aim was to examine the association between the composition and the load of indoor airborne bacteria and endotoxins in bedroom and a clinical indicator of OSA risk in a well-defined general population sample from five Nordic centers.

Materials and methods: Participants in five Nordic centers (Aarhus, Bergen, Uppsala, Reykjavik and Tartu) in the ECRHS III study (<https://www.ecrhs.org>) were asked to collect dust samples for two weeks from their bedrooms (For details see: PMID: 37523308). They used electrostatic dust fall collectors (EDCs) and the extracted dust was later analysed for bacterial and endotoxin load (qPCR, LAL

assay) and bacterial community composition (16S rRNA sequencing). While these microbial data have previously been used to characterize environmental determinants of indoor bacterial exposures, this study is the first to assess their relationship with sleep health.

The multivariable apnoea prediction (MAP) index (sensitivity 88% and specificity 55%) was used to identify subjects with a high risk of OSA using scores above 0.5 and 0.7 to determine a high risk of OSA. We assessed the relationship between bedroom microbial exposures and the MAP index using both continuous scores and clinically relevant categorical cutoffs (MAP > 0.5 and >0.7). Linear regression models were adjusted for centre, window opening, pets in the bedroom, number of residents, house age, season, and cleaning frequency.

Results: Altogether 801 (M 362, F 439) participants mean age (SD) 50 years (± 7) returned usable EDCs after two weeks. In total 127 (15.8%) had MAP index <0.5. Majority was males (110). Bacterial composition differed significantly between MAP risk groups at both 0.5 and 0.7 thresholds (ANOSIM R = 0.085–0.116, $p < 0.05$). Participants with MAP > 0.7 had significantly higher bedroom bacterial load ($p = 0.016$). In total, 35 bacterial genera were significantly associated with MAP index scores. Genera positively associated with higher MAP scores were predominantly anaerobic and human-associated (oral or gut), such as *Blautia*, *Porphyromonas*, and *Murdochella*. In contrast, genera negatively associated with MAP were primarily aerobic and environmental, including *Marmoricola* and *Nakamurella*.

Conclusions: Participants with high risk for OSA in a multi-center epidemiological study on general populations showed bedroom airborne bacterial exposures with a microbial profile dominated by human-associated anaerobic taxa. These findings indicate a relevance of the bedroom microbiome in sleep-related conditions and indicate the importance of further studies to evaluate environmental indicators of sleep health risk.

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Analysis of the Characteristics and Influencing Factors of Working Memory Impairment in Middle-aged and Young Patients with Obstructive Sleep Apnea-Hypopnea Complicated by Nocturia

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Introduction: Lower urinary tract symptoms are a major public health issue worldwide that affect patients' quality of life. Among these, nocturia is evaluated as the most common condition associated with various diseases, such as sleep disorders and/or obstructive sleep apnea syndrome (OSAS). Although the long-recognized association between nocturia and OSAS exists, cognitive impairment in patients with OSAS complicated by nocturia has yet to be explored. This study investigates the incidence of nocturia in middle-aged and young patients with obstructive sleep apnea-hypopnea and examines the characteristics of their working memory impairment.

Materials and methods: This study recruited patients diagnosed with OSA due to snoring at the Sleep Center of The Second Affiliated Hospital of Soochow University from September 2021 to September 2022. According to inclusion and exclusion criteria, a total of 102 patients were enrolled. Cognitive function was thoroughly assessed, and all patients' clinical data and polysomnography (PSG) parameters were collected. Based on whether patients woke to urinate due to the urge at night ≥ 2 times, they were divided into the OSA group and the OSA + nocturia group. Collected indicators were compared between the two groups, and characteristics of cognitive impairment in OSA patients with nocturia were analyzed. Additionally, partial correlation analysis was used to explore factors influencing working memory impairment in these patients.

Results:

1. Among the 102 OSA patients included in the study, 44.12% (45/102) had nocturia. Compared with the OSA group, the OSA + nocturia group had higher age, Epworth Sleepiness Scale scores, a higher proportion of nocturnal awakenings due to urgency, a higher prevalence of hypertension, and higher arousal index (Arl) (all $P < 0.05$); no statistically significant differences were found in other aspects (all $P > 0.05$).

2. There was no statistically significant difference in overall cognitive function between the OSA group and the OSA + nocturia group. However, in terms of working memory, the OSA + nocturia group had significantly lower correct rates of delayed paired associate recall (PRM) than the OSA group ($P < 0.05$).
3. After adjusting for age, BMI, and years of education by partial correlation analysis, the results showed that the correct rate of delayed PRM in OSA patients with nocturia was negatively correlated with the longest apnea duration ($P < 0.05$).

Conclusions: Among middle-aged and young patients with OSA, those with nocturia exhibited more significant working memory impairment than those without nocturia, characterized by decreased object working memory, and the degree of impairment was negatively correlated with the longest apnea duration.

A national study and public mandate for sleep health policy reform

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Introduction: Unlike established campaigns on mental health, diet, and physical activity, Scotland lacks a public health sleep strategy, with sleep not formally recognized in national health frameworks. In 2023, the World Sleep Society identified sleep as a global public health concern. Countries such as Finland, Japan, and Australia have implemented national strategies including school education, workplace reform, and public campaigns. Scotland has yet to follow. The aim of this study was to examine sleep patterns in the Scottish population, explore public perceptions of sleep, identify barriers to healthy sleep, and assess support for integrating sleep into national policy.

Materials and methods: *Scotland Speaks* is a mixed-methods study, one component being a cross-sectional online national survey, launched on World Sleep Day. Adults (16+) in Scotland completed questions on sleep habits, insomnia symptoms, occupational and societal influences, and awareness of sleep-related policy. Caregivers reported children's sleep using the Children's Sleep Habits Questionnaire (CSHQ). Wearable users submitted weekly sleep duration and quality. Quantitative data were analyzed descriptively and statistically (ANOVA, correlation, linear regression), adjusting for age, gender, employment, sleep-aid use, and formal diagnosis. Open-text responses were thematically analyzed.

Results: Participants included 5,039 adults (53.2% male, most aged 25-44 (44.6%), employed full-time (67.1%)) from all 32 Scottish regions. Shorter sleep (<7 hours) was common on weekdays (77.4%) and weekends (35.6%), with women reporting significantly less than men ($p < 0.001$). Moderate-to-severe insomnia affected 46.8%, more prevalent in males ($p < 0.001$), yet only 10.8% reported a formal sleep disorder diagnosis. Over a third (36.0%) used sleep-aids; 41.5% of which used alcohol 3+ times a week. Participants felt sleep was less prioritized by government and employers than diet (75.2%), physical activity (76.4%), mental (71.5%), and physical health (72.8%). High support existed for identifying sleep as a core health pillar (96.8%) and embedding it in community programs (97.2%), workplace policies (91.3%), school education (92.0%), medical training (93.4%), and a national sleep strategy (87.4%). Among caregivers ($n=2,473$), 50.3% of children met the CSHQ threshold for sleep problems (mean= 31.0 ± 17.5). Primary barriers included inconsistent routines (90.1%), screens (84.4%), homework (81.4%), early school times (81.4%), and mental health (67.3%). Adjusted regression analyses indicated that poorer CSHQ scores were significantly associated with caregivers who were younger ($\beta = -2.46, CI[95\%] = -2.89, -2.04, p < .001$), had shorter sleep ($\beta = -2.73, CI[95\%] = -3.23, -2.24, p < .001$), had more severe insomnia ($\beta = .85, CI[95\%] = .77, .95, p < .001$), had a sleep disorder ($\beta = 10.99, CI[95\%] = 9.47, 12.52, p < .001$), or did not view sleep as a public health concern ($\beta = -1.42, CI[95\%] = -1.70, -1.14, p < .001$). Thematic analysis revealed public support for a societal approach to sleep health, prioritizing school-based education, expanded NHS services (sleep clinics, CBT-I), workplace reforms (flexible working, right to disconnect), addressing environmental barriers (noise, light pollution), and campaigns to shift cultural attitudes undervaluing sleep.

Conclusions: *Scotland Speaks* highlights widespread sleep disruption, limited policy awareness, and strong public demand for change. A disconnect exists between public recognition of sleep as essential and its absence in national strategy. With clear support for integrating sleep into schools, workplaces,

healthcare, and public health promotion, Scotland faces an urgent policy opportunity. The case for a national sleep strategy is not only evidence-based, but also publicly driven.

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A peer-influence approach to reduce night-time use of interactive devices and social media among adolescents: CLOCK OFF intervention development and feasibility study

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Introduction: Poor sleep among adolescents poses significant risks to their health and wellbeing. A key contributor to delayed bedtimes and disrupted sleep is prolonged night-time use of interactive electronic devices (IED), including social media use. The aim of this study was to develop and assess the feasibility and acceptability of CLOCK OFF, a 10-week school-based intervention combining teacher-led lessons and peer-nominated students trained as Peer Supporters (PS) to promote healthy sleep habits and reduce IED use.

Materials and methods: CLOCK OFF was implemented with all students in S1 (11-12 years) in four high schools across Scotland during 2024. Fifty-eight PS and sixteen teachers were trained by a sleep charity. Semi-structured interviews and focus groups were conducted with PS ($n = 18$), non-PS ($n = 9$), teachers ($n = 8$), parents ($n = 8$), and trainers ($n = 3$). Data underwent thematic analysis, with 50% independently double-coded.

Results: Key strengths of CLOCK OFF included the peer nomination process (representative, fair), engaging peer training and teacher-led lessons (useful and comprehensive, engaging materials and activities), benefits of the PS role (improved confidence, expanded social networks, improved sleep and wellbeing). Challenges included teacher time constraints (study set up, training, lesson delivery), perceived role of PS (sharing peer messages, gap in digital strategies, prevalence of IED use), engagement (training materials, parental involvement), researcher challenges (school coordination, obtaining consent).

Conclusions: CLOCK OFF is feasible and refinements for an effectiveness study will consider duration of teacher training, dose of PS training, session content and materials, inclusion of digital strategies, and parental engagement. Adaptions to theory of change will include increased focused on IED behaviour change and delivery to an older adolescent population (12 - 13 years). These modifications aim to enhance the impact and scalability of CLOCK OFF.

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A Proposal on a Formula for Calculating Optimal Sleep Duration Based on Self-Reported Survey Data

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Introduction: Many adolescents have sleep debt. Individuals who sleep for their optimal sleep duration (OSD) are expected to experience no sleepiness. Therefore, it is important to recognize one's OSD to reduce sleep debt. However, there is no simple method for determining individual OSD. Since body mass index (BMI) and sleep duration exhibit a U-shaped association, it is expected that person sleeping

for his/her OSD would show no marked deviation from the mean BMI value for the population. This study aimed to estimate individual OSD using self-reported sleepiness and BMI.

Materials and methods: Data from 2,540 students in grades 5–11 were used. Written informed consent from each pupil's parent was obtained. Students who reported no sleepiness during class and had a gender- and grade-standardized BMI within ± 1.5 were termed ideal students (id-St). The differences in sleep duration between id-St and non-id-St were added to the habitual sleep duration (HSD) of each non-id-St to obtain the assumed OSD. A multiple regression line to predict the assumed OSD was calculated using the least squares method. This cross-sectional study was approved by the Committee for Medical Research Ethics of author's institute.

Results: A total of 666 ideal students (id-St) were identified. Their average weekly sleep durations were higher than those of non-ideal students (non-id-St): 62.0 hours in elementary school (61.2 hours), 55.6 hours in junior high school (54.1 hours), and 50.1 hours in senior high school (48.6 hours), exceeding the 49 hours assumed appropriate for children aged 6 to 17 years by the National Sleep Foundation. Two key issues were confirmed: the sleep duration of id-St fell within the appropriate range, and id-St slept longer than non-id-St. Then, the habitual sleep duration (HSD) of each id-St was considered their "assumed daily OSD." The differences in average daily sleep duration between the id-St group (8.49 hours) and the 11 groups of non-id-St ranged from 0.04 hours to 1.92 hours. The "assumed daily OSD" for each non-id-St was then determined by adding these differences to the HSD of each non-id-St individual. Multiple regression analysis was conducted using bedtime (on schooldays and non-schooldays), wake time (on schooldays and non-schooldays), BMI, grade, gender, self-reported academic performance, after-school activity (hours/week), breakfast frequency score, defecation frequency score, physical activity (days/week), and screen time (on schooldays and non-schooldays) as independent variables, with "assumed OSD" as the dependent variable. A significant linear formula for estimating OSD was derived (adjusted $R^2 = 0.996$, $p < 0.001$): $23.375 - 0.710 * (\text{bedtime before schooldays}) - 0.286 * (\text{bedtime before non-schooldays}) + 0.714 * (\text{wake time on schooldays}) + 0.281 * (\text{wake time on non-schooldays}) + 0.513 * (\text{sleepiness score; from 1 = never to 4 = always}) + 0.009 * [\text{gender (male: 1; female: 2)}] + 0.003 * (\text{BMI})$. Times were measured in hours; Bedtimes (23:45 as 23.75, 3:15 as 27.25), Waking times (6:00 as 6.00, 11:30 as 11.5).

Conclusions: Although further studies are needed, this formula offers a simple method for estimating individual OSD based on easily obtainable parameters.

References: Children 2025, 12, 566.

A Python-Based Analysis of Sleep-Related Projects Funded by the U.S. National Science Foundation

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Introduction: To analyze the funding status of sleep-related research projects supported by the U.S. National Science Foundation, in order to provide references for the advancement of sleep medicine in China.

Materials and methods: Python-based web scraping and the Latent Dirichlet Allocation (LDA) model were used to collect, preprocess, and analyze sleep-related project data from the U.S. National Science Foundation.

Results: A total of 193 sleep-related research projects funded by the U.S. National Science Foundation were included in this study. Covering the period from 1987 to 2024, both the number of projects and the overall funding amount demonstrated a steadily increasing trend. A total of 4,728 unique terms were extracted from the project data. Using the Latent Dirichlet Allocation (LDA) model, these projects were clustered into nine thematic areas: (1) sleep and technological development, (2) sleep and circadian health, (3) sleep and cognitive-emotional development, (4) sleep and circadian behavior, (5) circadian modeling and activity, (6) sleep environment and physical activity, (7) sleep deprivation and neural networks, (8) sleep and gene regulation, and (9) sleep-related respiratory monitoring and devices. These topics collectively reflect a broad and multi-dimensional research landscape in the field of sleep science, with each theme characterized by distinct high-frequency terms. The results highlight research progress and practical applications across multiple layers, including the influence of sleep on circadian rhythms and cognitive functions, the neural consequences of sleep deprivation, and

technological advancements in sleep monitoring and respiratory assessment. Together, the findings underscore the diverse directions of sleep-related research at the intersection of life sciences, technology, and public health.

Conclusions: By applying new data analysis techniques to explore research trends and methodologies in the field of nursing, researchers can further investigate the development prospects of nursing in China in light of the national context.

A Scoping Review of Sleep Patterns and Circadian Rhythm Disturbances in Critically Ill Pediatric Patients

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Introduction: To conduct a scoping review of research on sleep and circadian rhythms in critically ill children. The aim is to provide guidance for the early diagnosis, treatment, and intervention of sleep disorders in critically ill pediatric patients.

Materials and methods: Following the methodology of a scoping review, relevant literature on sleep and circadian rhythms in critically ill pediatric patients was retrieved from five English-language databases (PubMed, Embase, CINAHL, Ovid, and Web of Science) and three Chinese databases (CNKI, Wanfang, and VIP Information Services Platform). The search covered all available literature up to July 15, 2024. Two researchers independently screened the literature and extracted key study characteristics, including author, publication year, year of data collection, country of sample collection, study type, study objective, study population, sample size, assessment tools or methods, and main findings.

Results: A total of 1,801 articles were retrieved, and 42 studies were ultimately included. Among them, 32 were in English and 10 in Chinese, with publication years ranging from 2014 to 2024. The studies were mainly categorized into observational studies (n = 24) and interventional studies (n = 17), along with one consensus study. The analysis indicated that sleep disorders are common among critically ill children and are associated with significant adverse outcomes. A total of nine assessment tools or methods were identified, including seven structured questionnaires. Commonly used instruments included the Pittsburgh Sleep Quality Index (PSQI), Brief Infant Sleep Questionnaire (BISQ), Brief Infant Sleep Questionnaire-Revised-Short Form (BISQ-R-SF), Children's Sleep Habits Questionnaire (CSHQ), Sleep Disturbance Scale for Children (SDSC), Adolescent Sleep-Wake Scale (ASWS), and the Richards-Campbell Sleep Questionnaire (RCSQ). Factors influencing sleep disorders in critically ill children were grouped into three categories: sociodemographic factors, disease- and environment-related factors, and psychological and behavioral characteristics. Interventions for sleep disorders were classified into four types: pharmacological, physical, cognitive-behavioral, and nursing care interventions. However, existing studies on prevention and intervention remain limited.

Conclusions: Sleep disorders are highly prevalent among critically ill children and are associated with significant adverse outcomes. Current research demonstrates limited awareness and understanding of sleep disturbances in this population. The contributing factors to sleep disorders in critically ill children are complex and multifaceted.

Association between cyclic alternating pattern during sleep and incident dementia

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Introduction: Cyclic Alternating Pattern (CAP) is a sleep physiological rhythm observed during non-rapid eye movement (NREM) stage, characterized by alternating phases of transient events (A1–A3 phase) and background activity (B phase). Particularly, subtype A1 is almost exclusively composed of slow waves, which promote cognitive processing, memory consolidation and the restoration of hippocampal learning. In addition, reduced slow-wave sleep has been linked to impaired clearance of

amyloid-beta, which is one of the most common pathogenesises of Alzheimer's dementia. However, the potential role of CAP for dementia remains unknown.

Materials and methods: We conducted a prospective cohort study involving 2,586 dementia-free participants from the Osteoporotic Fractures in Men Sleep Study (MrOS) who underwent overnight polysomnography (PSG) at baseline. A high-performance automated CAP detection system was applied for CAP scoring from electroencephalogram (EEG), and CAP rate, CAP index, A index subtypes, number of CAP sequences, and CAP sequence duration were calculated. Dementia was identified by self-reported physician-diagnosed dementia and dementia medication use during follow-up. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: During 9.0 ± 3.1 years of follow-up, 175 participants developed incident dementia. Participants in the lowest tertile of A2 index exhibited an increased risk of developing dementia compared to those in the highest tertile (HR 2.04, 95% CI: 1.41, 2.96) after adjustment for age, ethnicity, education, BMI, smoking status, alcohol intake, prevalence of hypertension and diabetes, and total sleep time (TST). Further, a lower combined A2+A3 index and shorter CAP sequence duration were associated with higher risk of dementia in the fully adjusted model ($P < 0.05$).

Conclusions: These findings suggest that specific features of CAP may serve as useful markers to identify those at risk of dementia.

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Association Between Daily Step Count and Sleep Health: Findings from a National Survey in China

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Introduction: Sleep health is closely linked to chronic disease prevention, cognitive function, and overall quality of life. With the growing use of wearable devices, daily step count has become a widely used measure of physical activity. Its relationship with sleep duration, sleep quality, insomnia, and obstructive sleep apnea (OSA) has gained increasing attention. This study, based on a large-scale 2024 national survey, aims to examine the association between daily step count and various sleep health indicators.

Materials and methods: Data were collected from 93,640 participants. Subsamples who completed the Pittsburgh Sleep Quality Index (PSQI), the Athens Insomnia Scale (AIS), and the Stop-Bang questionnaire were analysed after excluding those with missing data, extreme step counts ($> 50,000$), implausible sleep durations (< 3 or > 13 hours), or incomplete questionnaires. Mean sleep duration across multiple days was calculated. Associations between step count and sleep measures were assessed using Spearman correlation. Participants were grouped by average daily steps ($\leq 4k$, 4-8k, 8-12k, $> 12k$), and group differences were compared using Kruskal-Wallis H tests with post hoc analysis. Sleep quality (PSQI), insomnia risk (AIS), and OSA risk (Stop-Bang) were categorized, and group differences in these classifications were analyzed using Chi-square tests.

Results: Step count showed a weak negative correlation with sleep duration ($r = -0.117$, $P < 0.001$). The $> 12,000$ -step group had significantly shorter sleep duration (6.27 ± 1.44 hours) than the $\leq 4,000$ -

step group (6.81 ± 1.76 hours, $P < 0.001$). Higher step counts significantly associated with better sleep quality ($r = -0.141$, $P < 0.001$), with peak improvement around 8,000 steps/day; improvements plateaued thereafter ($P = 0.240$). Higher step counts were associated with a greater proportion of participants classified as having good sleep quality ($\chi^2 = 138.351$, $P < 0.001$). Step count was also inversely correlated with insomnia risk ($r = -0.109$, $P < 0.01$), with significant differences between the 4,000–8,000 and 8,000–12,000 step groups ($P = 0.014$). Participants with higher step counts were more likely to be in the non-insomnia group ($\chi^2 = 12.499$, $P = 0.006$). For OSA risk, the correlation was weak ($r = 0.044$, $P = 0.013$), and group differences based on Stop-Bang scores (>2 indicating high risk, ≤ 2 indicating low risk) were not statistically significant ($\chi^2 = 7.461$, $P = 0.059$).

Conclusions: Higher daily step count is significantly associated with improved sleep quality and reduced insomnia risk, with 8,000 steps/day representing a potential optimal threshold. The inverse association with sleep duration may suggest a complex relationship between physical activity and sleep health. Future longitudinal and objective sleep measurement studies are warranted to clarify causality. Moderate physical activity—such as walking 8,000 steps per day—is an potentially effective strategy for improving population sleep health.

Association Between Multidimensional Sleep Health and Psychological Distress in Japanese Community Residents

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Introduction: To investigate the association between multidimensional sleep health (MDSH) and psychological distress among Japanese community residents.

Materials and methods: A self-administered questionnaire survey was conducted from December 2022 to February 2023 among Kyoto City residents aged 40 years or older. MDSH was assessed using the RU_SATED, which evaluates six sleep health dimensions (regularity, satisfaction, arousal, timing, efficiency, and sleep duration) and generates a total score. Psychological distress was measured using the Kessler 6 (K6) scale. This study was approved by the Ethics Committee of Kyoto University.

Results: Among 661 respondents (57.9% female, mean age 64.9 years, 68.4% urban residents), the prevalence of K6-5 distress, K6-13 distress was 28.9%, and 3.0%. Spearman correlation analysis showed that K6 scores were negatively correlated with total RU_SATED scores ($r_s = -0.25$, $P < 0.001$). Each 1-point increase in the RU_SATED score corresponded to a -0.325-point decrease in the K6 score. Multiple logistic regression analysis showed that K6-5 distress was associated with all six dimensions (odds ratio [OR] = 0.309–0.671), whereas K6-13 distress was associated with satisfaction (OR = 0.176).

Conclusions: This study found that total RU_SATED scores were negatively associated with psychological distress, with each sleep dimension showing a distinct relationship. Further research is needed to explore these relationships in diverse populations.

Association Between Ophthalmic Diseases and Sleep Duration: A Nationwide Cross-Sectional Study

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Introduction: To investigate the relationship between specific ophthalmic diseases—diabetic retinopathy (DMR), age-related macular degeneration (AMD), epiretinal membrane (EM), and glaucoma—and sleep duration in a nationwide, population-based sample, focusing on whether individuals with these conditions experience altered sleep duration compared to those without.

Materials and methods: This cross-sectional study analyzed data from the 2019 and 2020 Korea National Health and Nutrition Examination Survey. Ophthalmic diseases were diagnosed through fundoscopy, and sleep duration on weekdays and weekends was self-reported. The study included 8,395 participants aged 40 and older who underwent fundoscopy. Multistage, stratified, clustered sampling ensured population-wide representation. Statistical models adjusted for demographic and clinical covariates, including age, sex, BMI, and comorbidities.

Results: Patients with DMR and EM experienced significantly reduced sleep duration, with reductions of 0.3 to 0.5 hours on both weekdays and weekends compared to individuals without these conditions. No significant differences in sleep duration were observed for AMD or glaucoma. After adjusting for covariates, the association between shorter sleep duration and DMR or EM remained significant, while no significant differences were found for AMD or glaucoma.

Conclusions: This study highlights that DMR and EM are associated with reduced sleep duration, while AMD and glaucoma do not show a significant impact. These findings emphasize the need for targeted sleep interventions for patients with certain ophthalmic conditions. Further research is warranted to elucidate the mechanisms linking ophthalmic diseases and sleep disturbances and to develop tailored clinical strategies.

Association Between Screen Time Exposure and Sleep Duration among U.S. Adolescents and Young Adults: An exploratory analysis of NHANES 2011–2016 cohorts

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Introduction:

Digital addiction is an emerging public health concern associated with various comorbidities, mental health issues, sleep disturbances, and even mortality. Previous research has examined the impact of screen time exposure on sleep health, particularly sleep latency, continuity, and duration, with inconsistent findings. These were mainly observational studies, primarily conducted in adults and using unrepresentative samples, often without adequate adjustment for confounders.

In the present study, we aimed to explore the association between high daily screen exposure and sleep duration among youth, using pooled, nationally representative cross-sectional data.

Materials and methods: We analysed pooled cross-sectional data from the U.S. National Health and Nutrition Examination Survey (NHANES) cycles 2011–2016, including participants aged 16–20 years. Self-reported sleep duration served as the primary dependent variable, whereas screen exposure was the main independent variable. Sleep loss was defined as fewer than 7 hours of sleep per night. A univariate logistic regression analysis was conducted to assess the crude association between sleep loss and high screen time (≥ 3 hours/day). A multivariate logistic regression model was then adjusted for race/ethnicity, gender, age, body mass index (BMI), household poverty index, physical activity, depressive symptoms (assessed via the nine-item Patient Health Questionnaire, PHQ-9), and other health conditions.

Results:

The final sample included 2,227 participants. High screen time was significantly associated with increased odds of sleep loss (OR 1.40, 95% CI: 1.08–1.81, $p < 0.05$). After adjustment, the association remained significant (aOR 1.66, 95% CI: 1.13–2.46, $p < 0.05$). Other covariates independently associated with sleep loss in the final model included older age (aOR 1.22, 95% CI: 1.11–1.33, $p < 0.001$), non-Hispanic Black ethnicity (aOR 1.80, 95% CI: 1.26–2.56, $p < 0.01$), and severe depression (aOR 3.33, 95% CI: 1.15–9.66, $p < 0.05$).

Conclusions:

High daily screen exposure is independently associated with increased odds of sleep loss among U.S. adolescents and young adults, as demonstrated in a pooled 6-year nationally representative sample. Our findings, based on a large cohort and adjusted for key confounders, align with parts of the existing literature and a recent systematic review. Moreover, the significant associations between sleep loss, race/ethnicity, and mental health symptoms highlight the multifactorial nature of sleep health and reinforce the need for multidisciplinary approaches in clinical care. Prospective and controlled trials are warranted to determine safe thresholds for screen exposure duration and content in relation to sleep, given the growing relevance of this issue as a major public health concern in the digital age.

Association between Sleep Disturbances and Stages of Parkinson's Disease: A Cross-Sectional Study

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Introduction: Various studies and research show that People with Parkinson's Disease (PwPD), apart from motor issues also suffer with various non-motor symptoms such as sleep issues (insomnia, obstructive sleep apnea, circadian rhythm sleep disorders and so on) orthostatic hypotension, psychological difficulties and many more. Sleep disturbances are one of the most common and frequently encountered issues. These issues need further attention. Sleep disturbances have been associated with decreased quality of life (QOL) and can lead to many serious health issues. The objective of this study was to identify sleep disturbances among (PwP) and to investigate the association between sleep disturbances and stages of PD.

Materials and methods: A cross-sectional study design with convenient sampling method was used for this study. Study was conducted at the Malaysian Parkinson's Disease Association (MPDA), Malaysia. The Parkinson's Disease Sleep Scale 2 (PDSS-2) and Hoehn and Yahr scale were used in the study.

Results: A total of 33 (PwPD) participated in this study. Altogether 63.6% (n=21) of the participants were found to have some form of sleep disturbances. Nocturia, with a prevalence of 72.7%, has been found the most prevalent sleep disturbance, followed by psychosis, then issues with sleep refreshment and others. Prevalence of sleep disturbances among the patients in the later stages (stage 2- 81.8%, stage 3- 57.1%, stage 4- 100.0%, and stage 5- 100.0%) was higher than the prevalence of sleep disturbances in the lower stage (stage 1- 0.0%).

Conclusions: This study found that there is a considerably high prevalence of sleep disturbances among (PwPD) and an association was also found between sleep disturbances and stages Parkinson's disease. Larger sample size, with further subjective and objective assessment of sleep and confounding factors that may impact sleep should be assessed further. A physiotherapist can be instrumental in making an early diagnosis, methods such as positioning, inspiratory muscle training, oropharyngeal exercise and various intensity exercises can also help in managing a few of the issues. An awareness, knowledge and attitude towards the sleep problem can improve the quality of life of the (PwPD) and may prevent from consequences of poor sleep. Knowledge of the application of chronobiology in the context of timing of exercise with medication or standalone method can also be explored further in the management of circadian rhythms sleep disorders in (PwPD).

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Association between Sleep Duration and Cancer-Specific Mortality among community-based population: A Systematic Review and Meta-Analysis

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Introduction: Cancer has emerged as a significant challenge in global public health, imposing a substantial burden on individuals, healthcare systems, and societies worldwide. Abnormal sleep duration may influence cancer mortality, but evidence for U-shaped/J-shaped relationships and daytime napping with cancer-specific mortality remains inconsistent. Thus, the current study aimed to conduct a systematic review and meta-analysis of the association between sleep duration (nighttime, 24-hour, daytime napping) and all-cancer and site-specific cancer mortality.

Materials and methods: We conducted a systematic search of PubMed, Embase, and the Cochrane Library databases up to March 19, 2025 without language restrictions, following PRISMA guidelines (PROSPERO: CRD420251009205). Observational studies reporting risk estimates for cancer-specific mortality associated with sleep duration in community-based populations were included. Data were extracted independently by two reviewers, and study quality was assessed using the Newcastle-Ottawa Scale (NOS). Random-effects models were used to pool relative risks (RRs) with 95% confidence intervals (CIs). Heterogeneity, publication bias, and sensitivity analyses were performed.

Results: Of the 7,326 screened studies, 32 studies (622,133 participants; 25,244 deaths) were included. All-cancer-specific mortality showed U-shaped associations: short sleep (RR=1.04, 95% CI 1.01–1.08; $I^2=23.4\%$) and long sleep (RR=1.13, 1.08–1.19; $I^2=51.1\%$) vs. 7–8h. Lung cancer-specific mortality increased with short (RR=1.14, 1.01–1.29) and long (RR=1.22, 1.02–1.45) sleep. No associations were found for digestive system, breast, or prostate cancers. Daytime napping slightly increased the risk of all-cancer-specific mortality (RR=1.06, 1.02–1.10). Subgroup analyses revealed 24-hour short sleep (RR=1.07, 1.03–1.12), but not nighttime short sleep (RR=1.01, 0.98–1.04), was significant. The association of long sleep was stronger in Asian populations and studies with ≤ 10 -year follow-up.

Conclusions: A U-shaped relationship exists between sleep duration and all-cancer-specific mortality in community-based populations, with both short and long sleep durations, as well as daytime napping, associated to increased risk.

Association between Sleep Problems and Social Frailty Among U.S. Older Adults

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Introduction: Sleep problems can negatively impact various aspects of social functioning, potentially increasing the risk of social frailty in older adults. While sleep quality and duration have been previously linked to social frailty, other dimensions of sleep remain understudied. This study examined the association between multidimensional sleep problems and social frailty among older adults, including differences by sex.

Materials and methods: We analyzed cross-sectional data from 2,318 community-dwelling adults aged 65 and older from the 2013–2014 waves of the National Health and Aging Trends Study. Sleep health was assessed across five dimensions (satisfaction, alertness, timing, efficiency, and duration) using the SATED framework. Social frailty was measured using the Makizako Index, classifying participants as socially robust (0 components), pre-frail (1), or frail (≥ 2). Multinomial logistic regression models examined associations between sleep problems and social frailty status, adjusting for socio-demographics, depressive symptoms, and chronic conditions including hypertension, diabetes, cardiovascular diseases, stroke, lung disease, arthritis, osteoporosis, dementia, and cancer.

Results: Older adults with sleep problems had a significantly higher risk of being socially pre-frail (RR = 1.15, 95% CI: 1.03–1.29) and socially frail (RR = 1.46, 95% CI: 1.27–1.67) after adjusting for covariates. The association between sleep problems and social frailty was more pronounced among older men compared to women (interaction $p < 0.05$). Among individual sleep domains, dissatisfaction with sleep (RR = 2.53, 95% CI: 1.74–3.69), poor daytime alertness (RR = 1.66, 95% CI: 1.15–2.37), and suboptimal sleep efficiency (RR = 2.53, 95% CI: 1.78–3.58) were significantly associated with increased risk of social frailty. No significant associations were observed for sleep timing or sleep duration.

Conclusions: Multidimensional sleep problems are associated with a higher risk of social frailty in older adults, particularly among men. Interventions that improve sleep health, especially targeting sleep satisfaction, alertness, and efficiency, may help reduce the burden of social frailty in this population.

Association between snoring and in vitro fertilization outcomes among infertile women

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Introduction: Snoring is well known to increase risk of metabolic and cardiovascular consequences in general population, with limited attention to reproductive health. The study aim to explore the association between snoring and in vitro fertilization (IVF) outcomes in infertile women, focusing on embryological parameters and pregnancy outcomes.

Materials and methods: 632 infertile women, aged 24 to 45 years, undergoing their first IVF treatment, were continuously recruited at the Reproductive Center of Peking University People's Hospital from January 2018 to Nov 2021. All patients with their husbands' assistance completed a questionnaire including snoring status and frequency before ovulation induction (OI). Embryology parameters were observed during the first IVF cycle, with subsequent follow-up to assess pregnancy outcomes.

Results: Results: Of the 579 subjects, 33.5% reported occasional snoring, and 8.8% reported frequent snoring. A multiple linear regression model adjusted for confounding factors, indicated that frequent snorers had higher β -coefficients for the number of blastocysts and available embryos compared to non-snorers (both $P < 0.05$). Among 551 subjects who completed the first embryo transfer, 6.2% suffered biochemical pregnancy loss, Frequent snorers had a higher likelihood of biochemical pregnancy loss compared to non-snorers and occasional snorers (5.7% vs. 14.6%, $P = 0.033$; 4.8% vs. 14.6%, $P = 0.026$). Multivariable analysis revealed that frequent snoring (adjusted odds ratio, aOR: 2.95, 95% confidence interval, CI: 1.06-8.24, $P = 0.039$) was a risk factor for biochemical pregnancy loss, while high-density lipoprotein cholesterol (HDL-C) level (aOR: 0.21, 95% CI: 0.05-0.92, $P = 0.038$) was found to be a protective factor after IVF.

Conclusions: Frequent snoring is associated with a reduced number of available oocytes and is a risk factor for biochemical pregnancy loss after IVF. However, this observed association should be interpreted with caution, as the potential effects of undiagnosed obstructive sleep apnea (OSA) have not been excluded.

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Association between Work Engagement and Psychomotor Vigilance among Physicians in a Japanese University Hospital: Stratified Analysis by Age Group and Medical Specialty

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Introduction: Work engagement is a positive and fulfilling psychological state related to one's work, often considered the opposite of burnout. In clinical settings, higher work engagement among physicians has been associated with better patient care and lower turnover rates. Since the COVID-19 pandemic, there has been growing concern about the work environment and mental health of healthcare professionals. This study aimed to examine age- and specialty-related differences in work

engagement and its association with psychomotor vigilance, an objective indicator of sleep debt, among physicians at a Japanese university hospital.

Materials and methods: Among 836 physicians, 391 (response rate: 46.8%) completed a questionnaire and underwent a 3-minute brief Psychomotor Vigilance Test (PVT-B) after work. The total score of the Utrecht Work Engagement Scale (UWES-17) was used as the dependent variable. Independent variables included depressive symptoms (Center for Epidemiologic Studies Depression Scale: CES-D) and PVT performance (lapse355), with sex, BMI, age group (20s, 30s, 40s, ≥ 50 s), and sleep duration (< 5 h or ≥ 5 h) as covariates. Stratified analyses were performed by age group and by specialty (medical vs. surgical). Statistical significance was defined as $p < 0.05$. Statistical analyses were conducted by SAS version 9.4 software (SAS Institute Inc., Cary, NC).

Results: Stratified analyses were performed by age group and by specialty (medical vs. surgical). Statistical significance was defined as $p < 0.05$. UWES scores were significantly lower in the 20s ($\beta = -13.8$, $p < 0.01$) and 30s ($\beta = -10.1$, $p < 0.01$) compared to ≥ 50 s. Lapse355 was negatively associated with UWES ($\beta = -0.3$, $p < 0.01$), and CES-D showed a marginal association ($\beta = -3.9$, $p = 0.08$). In adjusted models that substituted objective PVT measures for subjective sleepiness, model fit improved ($\Delta R^2 = 0.018$, $\Delta F = 7.58$, $p < 0.01$). In age- and specialty stratified analyses, the association was more evident among physicians with a surgical specialty in their 20s.

Conclusions: The results from present study suggest that work engagement is associated with PVT performance, an objective indicator of sleep debt, especially among young physicians at a Japanese university hospital.

These findings highlight the need for early intervention in cognitive and mental fatigue among early-career physicians.

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Association of Accelerometer-measured Daily Steps and Sleep Disorders: A Prospective Cohort Study

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Introduction: Sleep medicine is a vital component of psychiatry. As one of the most common mental disorders, sleep disorders have raised a global concern. Emerging evidence suggests that physical activity may help alleviate sleep disturbances. Tracking daily steps is a simple and popular way of physical activity, but its impact on sleep quality remains unclear.

Materials and methods: This prospective cohort study analyzed UK Biobank data collected from February 2013 to November 2021, with a median follow-up of 6.94 years. Several potential confounders were considered in this study, including demographic factors, socioeconomic indicators, lifestyle variables, health conditions, environmental exposure, medication history, accelerometer wearing season and duration. We employed Cox proportional hazards regression and restricted cubic spline analyses to examine the relationship between accelerator-measured step count and the incidence of sleep disorders.

Results: Among 83,578 participants with valid step measurements, 913 developed sleep disorders. An inverse dose-response relationship was observed between daily step count and intensity with the risk of developing sleep disorders. Risk reduction plateaued after 4,800 steps/day and 100 steps/min for purposeful steps and peak-30 cadence, respectively. Compared with low volume of total daily steps, moderate and high volumes of total daily steps were significantly associated with a 17% (HR = 0.83, 95%CI = 0.70-0.99) and 26% (HR = 0.74, 95%CI = 0.61-0.90) reduction in the risk of developing sleep disorders, respectively. For purposeful steps, only high daily steps were associated with 31% (HR = 0.69, 95%CI = 0.56-0.85) reduction in risk. Regarding peak-30 cadence, only moderate intensity was associated with a 25% (HR = 0.75, 95%CI = 0.62-0.89) reduction in risk of developing sleep disorders.

Conclusions: Higher step count and intensity, as measured by accelerometers, are associated with a lower risk of sleep disorders. These findings suggest that daily steps management could be a valuable strategy in public health interventions aimed at improving sleep quality.

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Association of Longitudinal Changes in Rapid Eye Movement Sleep with Mortality in Older Men

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Introduction: Decreased rapid eye movement (REM) sleep has been linked to an increased risk of mortality. However, existing research has focused on sleep stages at a single point in time, leaving a gap in understanding how longitudinal changes in REM sleep influence mortality. The aim of this study is to evaluate the relationship between longitudinal changes in REM sleep and mortality in older men.

Materials and methods: This study included 871 community-dwelling older men who participated in the first (2003-2005) and second (2009-2012) sleep ancillary study visits of the Osteoporotic Fractures in Men Study (MrOS). We utilized polysomnographic data from the two sleep visits, along with data on the occurrence and timing of mortality during the follow-up period. Participants who had two measures of REM sleep were included in the analysis. Participants showed a decline in mean REM sleep percentage from 19.83% at sleep visit 1 to 19.12% at sleep visit 2, corresponding to an annual reduction of 0.11% per year. Cox models were used to adjust for multiple sociodemographic and lifestyle factors, depression, comorbidities, and other clinical characteristics.

Results: During a median follow-up of 9.4 (interquartile range, 5.5-12.5) years, a total of 620 all-cause deaths, 243 cardiovascular disease (CVD) deaths, and 112 cancer deaths were recorded. After adjustment for multiple sociodemographic and lifestyle factors, depression, comorbidities, and other clinical characteristics, men with a more rapid decline (tertile 1) change in REM sleep had an elevated risk of all-cause (hazard ratio, 1.25; 95% CI, 1.02-1.54; P = 0.03) and CVD-specific mortality (hazard ratio, 1.50; 95% CI, 1.07-2.10; P = 0.02) as compared to those with an increased change (tertile 3) in REM sleep. However, no significant association was found between changes in REM sleep and the risk of cancer-specific mortality and other non-CVD/non-cancer mortality.

Conclusions: Our results suggested that reduction in REM sleep was associated with a greater risk of all-cause and cardiovascular disease-specific mortality. These findings may help identify older men at increased risk for mortality.

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Association of Sleep Quality and Mental Health Among Students : A College Based Study From Bilaspur District of Himachal Pradesh (North India)

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Introduction: Sleep is necessary for maintenance of physical and mental health. Sleep disorders among young adults have emerged as a significant global health issue, ranking as second most common mental health problem. Varying degree of environmental and academic challenges causes inappropriate sleep hygiene practice among young adults leading to circadian rhythm disturbances. Poor sleep quality can lead to host negative consequences, including physical Health Risks and mental health Issues like elevated risk of depression, anxiety, cognitive impairment and impaired academic achievements and absenteeism. Hence to better manage these problems in college students, it is important to determine prevalence poor sleep quality, and its potential risk factors. This study was conducted with objectives. 1. to assess the sleep hygiene practice (SHP), sleep quality (SQ) and mental health; 2. To determine prevalence of poor sleep quality and mental health problems among medical and non medical students; 3. To find association between these.

Materials and methods: The cross sectional observation study was conducted on 638 students (17-25 years of age) from medical institute and degree college of Bilaspur, HP. Data was collected using online questionnaire. Students having chronic disease, current or past history of neurological disorders, taking neuro-psychotic medications were excluded from study. Questionnaire consisted of items of Pittsburgh Sleep Quality Index (PSQI) & Sleep Hygiene practice and Awareness Scale (SHAPS) and Depression, Anxiety Stress Scale²¹(DASS 21). Time for distribution of questionnaire was chosen carefully paying attention to exams schedule of students such that they will not be having exam over one month before and after filling out questionnaire. After collecting data and eliminating defective questionnaires, properly completed questionnaires were scored as per the scale provided in questionnaires. Appropriate statistical analysis was performed using SPSS.

Results: Total of 638 students including medical 314(49.21%) and nonmedical (324(50.78%) students, participated in study . Mean age of all participants was 22.95 ±2.59. Median of PSQI score was 7.71 significantly higher among medical students (7.91). Males (7.24) were having significantly higher PSQI score than females (7.11). Total Median score of SHA and SHP were :21 and 11 respectively. Mild to moderate level depression, anxiety and stress was observed in 468 (73.35%) students with no significant difference between two groups.

Significant association was observed between SHP and sleep quality in both groups; between sleep quality and all three components of mental health. Poor SHP and Poor sleep quality have shown significant association with academic year in medical groups of students, being statistically higher among first and final year medical students.

Sleep efficiency, sleep latency, and daytime dysfunction were found as main predictor of these mental health problems.

Conclusions: Poor sleep quality and mental health problems are prevalent among students more in medical students. Study's findings emphasize the need for targeted interventions and given the potential negative impact of poor sleep on mental health of this vulnerable group, it's crucial to implement strategies to address this issue. Educational institutions should consider implementing sleep awareness programs and providing accessible mental health resources and creating a supportive learning environment that prioritizes student well-being.

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Associations between multidimensional sleep health domains and brain structure, cognition, emotion and body composition in middle-aged adults

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Introduction: Sleep health has been recognised as a multidimensional construct encompassing domains including duration, continuity, and regularity, which in turn relate to cognitive, physical and mental well-being. Midlife represents a pivotal period in the life course, during which health and well-being can shape later-life outcomes. To date, few studies have systematically examined how multiple sleep domains relate to diverse health outcomes in midlife. Our study addressed this gap by testing whether and how different sleep components differentially relate to brain structure, cognition, emotion, and body composition in community-dwelling middle-aged adults.

Materials and methods: We studied 140 healthy middle-aged adults (age=52.0±6.7 years, 51 males) who completed brain MRI, body composition, neurocognitive and emotion assessments. Participants additionally wore an Oura Ring and completed cognitive tasks (via the Z4IP app) daily for four weeks prior to MRI. Principal components analysis was performed on 22 Oura Ring-derived sleep measures (comprising means and standard deviations (SDs) of 11 metrics across the tracking period: efficiency, wake after sleep onset (WASO), wake after sleep offset (WASF), sleep fragmentation index (SFI), time-in-bed (TIB), total-sleep-time (TST), sleep onset latency (SOL), wake count, durations of light, rapid eye movement (REM) and deep sleep). We then conducted Pearson correlations between sleep component scores and various health outcomes (body composition, cognition, emotion and cortical thickness measures), after regressing out age, sex, education, handedness and total intracranial volumes (for cortical thickness).

Results: We identified three principal components corresponding to sleep continuity (high positive loadings in mean efficiency, high negative loadings in mean WASO and SFI), duration (high positive loadings in mean TIB, TST, SOL, light and REM sleep durations) and variability (high positive loadings in SD across most metrics), which exhibited differential associations with health outcomes in middle-aged adults. Specifically, sleep variability- and continuity-related components were both associated with body fat measures, with higher sleep variability-related component score linked to higher waist-hip ratio, and higher sleep continuity-related component score linked to lower body mass index, waist-hip ratio and visceral fat area ($r_s=0.188-0.227$, $p_{\text{false discovery rate (FDR)-adjusted}}<0.05$).

In contrast, higher sleep duration-related component score related to better performance in daily app-based cognitive assessments including faster reaction time in the symbol search task, better performance in the dot memory task, and less reaction time variability in the psychomotor vigilance task ($r_s=0.191-0.252$, $p_{\text{FDR-adjusted}}<0.05$).

Of the three components, only higher sleep continuity-related component score was associated with higher cortical thickness in specific regions including the left fusiform gyrus, left pars orbitalis, right entorhinal cortex and right precuneus ($r_s=0.265-0.341$, $p_{\text{FDR-adjusted}}<0.05$). No associations with emotion measures and neurocognitive assessment scores were found.

Conclusions: Our findings reveal distinct associations of sleep continuity-, variability- and duration-related components with cognitive, brain, and physical health in middle-aged adults. Our study underscores the importance of multidimensional sleep health for brain, cognitive, and metabolic vulnerability in midlife, and suggest that targeted sleep interventions may offer promising avenues for promoting healthy ageing.

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Associations between obesity, a composite risk score for long COVID, and sleep problems in SARS-CoV-2 vaccinated individuals

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Introduction: Preliminary data suggests that obesity might hasten the decline in mRNA vaccine-induced immunity against SARS-CoV-2. However, whether this renders individuals with obesity more susceptible to long COVID symptoms post-vaccination remains uncertain. Given sleep's critical role in immunity, exploring the associations between obesity, probable long COVID symptoms, and sleep disturbances is essential.

Materials and methods: We analyzed data from a survey of 5919 adults aged 18 to 89, all of whom received two SARS-CoV-2 mRNA vaccinations. Participants were categorized into normal weight, overweight, and obesity groups based on ethnicity-specific BMI cutoffs. The probability of long COVID was evaluated using the Post-Acute Sequelae of SARS-CoV-2 (PASC) score, as our survey did not permit confirmation of acute SARS-CoV-2 infection through methods such as antibody testing. Additionally, sleep patterns were assessed through questionnaires.

Results: Participants with obesity exhibited a significantly higher adjusted odds ratio (OR) of having a PASC score of 12 or higher, indicative of probable long COVID in our study, compared to those with normal weight (OR: 1.55, 95% CI: 1.05, 2.28). No significant difference was observed for overweight individuals (OR: 0.92 [95% CI: 0.63, 1.33]). Both obesity and probable long COVID were associated with increased odds of experiencing a heightened sleep burden, such as the presence of obstructive sleep apnea or insomnia ($P < 0.001$). However, no significant interaction between BMI and probable long COVID status was found.

Conclusions: Even post-vaccination, individuals with obesity may encounter a heightened risk of experiencing prolonged COVID-19 symptoms. However, confirming our observations necessitates comprehensive studies incorporating rigorous COVID infection testing, such as antibody assays - unavailable in our anonymous survey. Additionally, it is noteworthy that the correlation between probable long COVID and sleep disturbances appears to be independent of BMI.

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Associations Between Sleep Health and Gut Microbiota: A Metagenomic Analysis in a Community-Based Sample in Hong Kong

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Introduction: The gut-brain axis plays a pivotal role in health and disease. Previous studies have shown that sleep problems disrupt gut microbiota composition, which have been linked to inflammation, metabolic dysregulation, and cognitive impairments. However, evidence of sleep-gut microbiota relationships in community-dwelling populations is limited, with most studies relying on subjective sleep assessments and 16S sequencing microbiome analyses. This study addresses these gaps by employing both validated subjective and objective actigraphy-based sleep assessments, combined with high-resolution shotgun metagenomic profiling with the aim to investigate the associations between gut microbiota diversity and composition with sleep health.

Materials and methods: This cross-sectional study recruited participants from community in Hong Kong. A total of 645 participants (mean age: 53 ± 14 years; 64% female) provided stool samples for shotgun metagenomic profiling and completed sleep questionnaires assessing sleep related parameters including sleep-wake pattern, insomnia severity index and excessive daytime sleepiness. Actigraphy

data (Actiwatch Spectrum PRO, Philips Respironics) was available for 567 participants meeting wear-time criteria (≥ 3 valid days with $< 33.3\%$ missing data/day). Sleep parameters included total sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency (SE) and sleep fragmentation index (SFI) were generated from actigraphy. Multivariable linear models adjusted for age, sex, BMI, education, smoking and alcohol drinking habits, chronic disease history, depression and COVID-19 infection history were used to assess associations between gut microbiota diversity and sleep parameters. Species-level associations were identified using MaAsLin2, with false discovery rate correction.

Results: Gut microbiota alpha diversity indices were significantly reduced in individual with SE $< 80\%$ (adjusted beta [95% CI]: richness: -24.76 [-39.24, -10.28], $P < 0.001$; Shannon index: -0.13 [-0.23, -0.04], $P = 0.008$). PERMANOVA tests revealed that SE and SFI significantly influenced gut microbiota composition (SE $< 80\%$: $R^2 = 0.003$, $P = 0.018$; SFI: $R^2 = 0.003$, $P = 0.031$). In contrast, subjective sleep assessments were not associated with either alpha or beta diversity of the gut microbiota. MaAsLin2 identified 13 species significantly associated with SE $< 80\%$ and SFI. For example, *Coprobacillus cateniformis* and *Clostridium scindens* were positively associated with SFI (Coef = 0.0006, $P < 0.001$, $Q = 0.192$; Coef = 0.0002, $P = 0.007$, $Q = 0.322$). *Odoribacter splanchnicus* and *Phocaeicola plebeius* were reduced in individual with SE $< 80\%$ (Coef = -0.0002, $P = 0.008$, $Q = 0.348$; Coef = -0.004, $P = 0.024$, $Q = 0.469$). Elevated *P. plebeius* abundance was associated with increased TST (Coef = 0.004, $P = 0.028$, $Q = 0.517$). Increased *C. scindens* abundance was also associated with higher WASO (Coef = 0.0001, $P = 0.004$, $Q = 0.283$).

Conclusions: Our findings demonstrate that gut microbiota diversity and specific bacterial taxa are strongly associated with actigraphy-measured sleep parameters, particularly with sleep efficiency and fragmentation, in a community-based adult population. Notably, no significant associations were observed between gut microbiota and subjectively measured sleep parameters. These results highlight the potential for microbiota-targeted interventions to improve sleep health. Future studies are needed to confirm these findings, explore underlying mechanisms, and evaluate the causality in longitudinal and interventional studies.

Associations Between Sleep Quality, Sleep Duration, and Cognitive Function Among Older Adults in India: Evidence From the WHO-SAGE Study

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Introduction: Sleep is fundamental to human health and well-being, significantly influencing various cognitive functions such as attention, memory, and executive functioning. This study aimed to investigate the relationship between sleep quality, sleep duration, and cognitive performance among older adults in India.

Materials and methods: The data were drawn from the second wave of the World Health Organization's Study on Global AGEing and Adult Health (WHO-SAGE), conducted in 2015 across six selected states in India, representing different regions of the country. The sample consisted of 6,396 adults aged 50 years and older. Multivariable linear regression models were employed to assess the associations between sleep quality, sleep duration, and cognitive function separately for older men and women.

Results: Older men and women who experienced poor sleep quality or short sleep duration had lower average cognitive scores compared to their counterparts with good sleep quality and adequate sleep duration. Among older men, both poor sleep (adjusted coefficient [aCoef]: -5.09, 95% CI: -8.66 to -1.51) and short sleep duration (aCoef: -5.43, 95% CI: -7.77 to -3.10) were significantly associated with poorer cognitive functioning, and these associations remained significant even after adjusting for a wide range of socio-demographic, health, and behavioral factors (poor sleep aCoef: -2.39, 95% CI: -3.78 to -1.00; short sleep duration aCoef: -4.39, 95% CI: -6.46 to -2.31). Similarly, poor sleep (aCoef: -3.15, 95% CI: -5.79 to -0.52) and short sleep duration (aCoef: -2.72, 95% CI: -4.64 to -0.81) were associated with lower cognitive functioning among older women; however, these associations were not statistically significant after adjusting for potential confounders.

Conclusions: This study highlights a significant link between sleep health and cognitive functioning among older adults in India, particularly among older men, indicating that poor sleep quality and inadequate sleep duration may negatively impact cognitive health. It is recommended that healthcare

providers regularly assess sleep quality and ensure age-appropriate sleep duration in older patients, while also incorporating sex- and gender-sensitive sleep interventions into cognitive health management strategies.

Associations between thyroid hormone regulation and sleep phenotypes

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Introduction: Our study aims to assess the causal relationships between thyroid hormone regulation (including thyroid stimulating hormone (TSH), free thyroxine (FT4) levels, hypothyroidism, and hyperthyroidism) and sleep traits such as Apnea-Hypopnea Index (AHI)/Respiratory event index (REI), obstructive sleep apnea (OSA), snoring, excessive daytime sleepiness (EDS), insomnia as well as sleep duration.

Materials and methods: We obtained summary statistics from published genome-wide association studies (GWAS) on thyroid hormone regulation and sleep traits. Subsequently, we performed bidirectional Mendelian Randomization (MR) analyses to estimate the causal directions and effects between them. The inverse variance weighting (IVW) approach was used as the primary method, with multiple methods serving as alternative sensitivity analyses.

Results: We revealed that insomnia has a negative causal influence on TSH levels ($\beta = -0.192$, 95%CI = [-0.383, -0.002], $p = 0.048$). We also observed that OSA has a positive causal influence on FT4 levels ($\beta = 0.098$, 95%CI = [0.022, 0.175], $p = 0.012$). Sleep duration was found to have a negative causal effect on FT4 levels ($\beta = -0.187$, 95%CI = [-0.314, -0.060], $p = 0.004$). Conversely, TSH levels showed a positive causal impact on OSA ($\beta = 0.079$, 95%CI = [0.025, 0.132], $p = 0.004$). Further validation analyses based on heterogeneity and pleiotropy status were consistent with the causal direction of the above initial results.

Conclusions: Our results indicated suggestive causations from insomnia to TSH levels, from OSA and sleep duration to FT4 levels as well as from TSH levels to OSA, providing valuable insights into clinical strategies for regulating thyroid function and preventing sleep problems.

Associations between waking activities and sleep, morning/evening preference and perceived barriers to sleep in first-year undergraduate students

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Introduction: Sleep is typically studied in isolation or in relation to bedtime routines; however, research shows that how we spend our waking hours influences our sleep. This holds true for both the broad structure of daily obligations (e.g., daytime class/work schedules) and individual activities with direct effects on sleep architecture (e.g., exercise influences NREM/REM ratio). In this study, we characterize incoming university students based on daily time use data to identify common patterns of waking activities and how they affect students' sleep and what are perceived as barriers to sleep.

Materials and methods: 505 incoming National University of Singapore undergraduate students provided daily 24-hour time use data for the first two weeks of term. Latent class analysis (LCA) was used to identify days sharing similar activity profiles. Fuzzy k-means clustering was then used to group participants based on the proportion of days belonging to each activity profile. These groups were then compared on objective measures of sleep (Oura ring), the Insomnia Severity Index (ISI), morning/evening preference and perceived barriers to sleep.

Results: Eight daily activity profiles were identified by LCA, and participants were grouped into six clusters. Each cluster was characterized by a particular combination of time use profiles. There were three Study clusters, comprising students who had a greater proportion of activity profiles involving studying. There was one Digital Leisure cluster, including students who engaged in more late-night digital leisure activities; and two hybrid Social clusters (Social and Digital Leisure, and Social and Co-Curricular Activities).

Objective sleep measures indicated earlier sleep timing and longer sleep duration for students in the Study clusters than the other clusters (mean Study bedtimes: 00:32, 01:03, 00:55; mean non-Study bedtimes: 02:49, 02:23, 01:59; mean Study sleep duration (hrs): 6:39, 6:26, 6:44; mean non-Study sleep duration (hrs): 6:14, 6:28, 6:10). ISI scores for the Study clusters were lower than those for the other groups, indicating fewer insomnia symptoms. Both the Digital Leisure and the Social and Digital Leisure groups, which displayed the latest sleep timing, reported a stronger evening preference.

The Digital Leisure and hybrid Social groups reported social activities and digital entertainment as more significant barriers to sleep than the Study groups. Study load and academic worries were rated similarly across most groups, although the Afternoon Study group perceived them as higher barriers.

Conclusions: In this study, we reveal underlying patterns of daily time use exhibited by incoming university students, and how they co-occur within individuals. Students who showed different combinations of daily time use profiles also showed different sleep patterns, morning/evening preference and perceived barriers to sleep. These results illustrate how waking activities influence sleep in concert with intrinsic sleep regulation mechanisms.

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Associations Between Weather Variables and Sleep Architecture: A Large-Scale Analysis Using Consumer Sleep Data

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Introduction: Environmental conditions such as temperature, humidity, and sunlight exposure have been shown to influence sleep, yet large-scale studies linking objective sleep data with weather patterns remain limited. This study aimed to examine the effects of daily weather variables on sleep architecture and assess how these associations vary depending on the severity of suspected sleep-disordered breathing.

Materials and methods: Sleep data were collected from 1,067 users in South Korea who used the SleepRoutine mobile application at least once monthly between December 1, 2023, and November 30, 2024. After applying exclusion criteria based on extreme or implausible values, 236,115 nights of data were included. Weather variables included daily mean temperature, humidity, and sunshine duration in Seoul, Korea.

Results: A total of 1,067 individuals used the app at least once per month, and 236,115 nights were included in the analysis. Higher temperature was significantly associated with reduced sleep efficiency (SE), total sleep time (TST), and deep sleep ratio (SE: $\beta = -0.041$, $p < 0.001$; TST: $\beta = -0.274$, $p < 0.001$; Deep: $\beta = -0.035$, $p < 0.001$), and with increased sleep latency (SL), wake after sleep onset (WASO) and light sleep ratio (SL: $\beta = 0.022$, $p = 0.008$; WASO: $\beta = 0.123$, $p < 0.001$; Light: $\beta = 0.008$, $p = 0.031$). Increased humidity was associated to decreased SE and light sleep ratio (SE: $\beta = -0.009$, $p < 0.001$; Light: $\beta = -0.006$, $p = 0.004$), and prolonged SL and WASO (SL: $\beta = 0.011$, $p = 0.018$; WASO: $\beta = 0.023$, $p = 0.002$). Longer sunshine duration was associated with decreased light sleep ratio ($\beta = -0.021$, $p = 0.001$) but increased TST and REM sleep ratio (TST: $\beta = 0.156$, $p < 0.001$; REM: $\beta = 0.020$, $p < 0.001$). Seasonal comparisons showed that summer was associated with poorer sleep quality than spring, while autumn and winter exhibited mixed effects on sleep parameters. Notably, interactions between weather variables and Apnea-Hypopnea Index (AHI) groups revealed that temperature and sunshine duration had differential effects on SE, SL, and WASO depending on AHI severity. Significant seasonal interactions with AHI group were also found sleep stages.

Conclusions: Daily weather conditions, particularly temperature, humidity, and sunshine duration, exert significant influence on sleep structure. These effects may be less pronounced in individuals with sleep-disordered breathing.

Associations of Lifestyle Habits with Sleep Quality

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Introduction: Sleep is a fundamental biological process crucial for overall health and well-being. However, poor sleep quality is a widespread public health concern. Numerous factors are believed to influence sleep, with lifestyle habits playing a prominent role. While these associations are often discussed, a comprehensive understanding of their independent contributions to sleep quality remains essential for developing effective public health strategies. Therefore, this study aimed to investigate the relationship between these multiple lifestyle habits—smoking, alcohol consumption, daily mobile phone use duration, eating before bed, and caffeine intake—and sleep quality.

Materials and methods: Demographic information and lifestyle habit data were collected using questionnaires. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), where a total PSQI score greater than 5 was defined as poor sleep quality. We used a multivariate logistic regression model, adjusting for covariates such as demographic factors (e.g., body mass index (BMI), age, gender, marital status, education level, occupation type, region, area type, number of bed partners, income level) and the lifestyle habits under investigation (smoking, alcohol consumption, daily mobile phone use, eating before bed, caffeine intake). Data analysis was conducted using R statistical software (version 4.4.2), with statistical significance set at $P < 0.05$.

Results: From 19,680 collected data, 13,407 complete questionnaires were included after data cleaning. Drinking alcohol before bed was significantly associated with poorer sleep quality. Compared to non-drinkers, individuals who consumed alcohol before bed had an odds ratio (OR) of 2.100 (95% Confidence Interval [CI]: 1.277-3.700) for poor sleep quality. Compared to non-smokers, daily smokers had an OR of 1.521 (95% CI: 1.353-1.712) for poor sleep quality. Smoking fewer than 5 cigarettes daily showed no significant difference from non-smokers, but sleep quality significantly declined for those smoking 5 or more cigarettes daily. Individuals smoking more than 20 cigarettes daily had an OR of 1.793 (95% CI: 1.415-2.295). Compared to using a phone for less than 2 hours daily, the ORs for poor sleep quality were 1.225 (95% CI: 1.019-1.470) for 2-5 hours, 1.472 (95% CI: 1.219-1.776) for 5-8 hours, and 1.860 (95% CI: 1.521-2.263) for more than 8 hours of use. Compared to those who never ate before bed, the ORs for poor sleep quality were 1.417 (95% CI: 1.264-1.588) for occasional eaters, 2.023 (95% CI: 1.750-2.339) for sometimes eaters, and 2.270 (95% CI: 1.921-2.688) for frequent eaters before bed. Compared to those who never consumed caffeine, the ORs for poor sleep quality were 1.223 (95% CI: 1.112-1.345) for consuming caffeine less than 3 times per week, 1.383 (95% CI: 1.212-1.579) for 3-7 times per week, and 1.459 (95% CI: 1.239-1.721) for more than 7 times per week.

Conclusions: Drinking alcohol before bed, smoking, prolonged mobile phone use, eating before bed, and high-frequency caffeine intake are all significantly associated with poorer sleep quality. These findings underscore the importance of modifying these lifestyle habits to improve sleep health and provide a scientific basis for developing targeted health interventions.

Associations of microarousals-related ventricular repolarization lability during sleep with long-term cardiovascular disease and mortality

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Introduction: Sleep plays a critical role in regulating autonomic nervous system activity. Even brief arousals during sleep can significantly impact cardiac autonomic modulation, as reflected in changes of heart rate variability (HRV) after arousals. Microarousals (MAs) are defined as brief (3- to 15-s-long) wake intrusions during sleep, which are clinical markers for various sleep disorders. Previous studies have established a link between MAs and the incidence of cardiovascular diseases (CVD), but the underlying mechanisms remain unclear. Cardiac ventricular repolarization lability is a measure of the instability in the ventricular repolarization process, which can be quantified using various ECG-based metrics and is clinically significant for assessing CVD risk. However, whether MAs-associated changes in ventricular repolarization lability are associated with the risks of CVD and mortality remains unclear. We hypothesize that MAs-related cardiac ventricular repolarization lability could predict long-term CVD risk and mortality.

Materials and methods: We analyzed overnight polysomnography (PSG) data from two large independent cohorts, the Sleep Heart Health Study (SHHS) and Osteoporotic Fractures in Men (MrOS), comprising a total of 8,702 participants. A deep learning algorithm was developed to accurately detect the MAs for each subject. Cardiac ventricular repolarization lability was assessed by the short-term variability of the QT interval (STVQT) before and after these MAs. The importance of STVQT in predicting CVD risk was evaluated by the Cox regression model and the Shapley Additive Explanations (SHAP) method.

Results: During 11.0 ± 2.8 years of follow-up in SHHS, 729 participants had incident CVD and 192 participants died due to CVD. During 15.5 ± 4.4 years of follow-up in MrOS, 427 participants had incident CVD, and 391 died due to CVD. In multivariable Cox regression models, elevated STVQT during MAs was associated with an increased risk of chronic heart failure (SHHS: hazard ratios [HR]: 1.34; 95% confidence interval [CI]: 1.02 - 1.75; $p = 0.034$; MrOS: HR: 1.89; 95% CI: 1.15 - 3.10; $p = 0.012$), CVD (SHHS: HR: 1.33; 95% CI: 1.10 - 1.62; $p = 0.003$; MrOS: HR: 1.45; 95% CI: 1.14 - 1.86, $p = 0.003$), and CVD mortality (SHHS: HR: 1.67; 95% CI: 1.21 - 2.31; $p = 0.002$; MrOS: HR: 1.50; 95% CI: 1.13 - 1.98; $p = 0.005$) after adjusting for covariates. Additionally, SHAP_Values indicated that MAs-related STVQT was a more important predictor of CVD risk compared to conventional HRV metrics.

Conclusions: Our results suggest that MAs-related ventricular repolarization lability may be a useful metric to identify those at increased risk for CVD and CVD mortality.

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Associations of Pre-Sleep Arousal and Dysfunctional Sleep Belief with Depression in Youths with Eveningness

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Introduction: Youths with eveningness are vulnerable to developing sleep disturbances and mood related psychopathology. Psychological and arousal related factors may contribute to both insomnia and depression. Although previous research has investigated the association between insomnia, chronotype and depression, there has been limited research to explore insomnia-related cognitive and physiological factors specifically in youths with eveningness, especially in the context of depression.

Materials and methods: A total of 112 youths with eveningness (mean age = 18.3 ± 1.7 ; 69.6% female), as defined by a Morningness-Eveningness Questionnaire (MEQ) score of ≤ 41 , were recruited. Participants were classified into depressed (DA group: $n = 59$, mean age = 18.2 ± 1.8 , 76.3% female) and non-depressed groups (Control group: $n = 53$, mean age = 18.5 ± 1.7 , 62.3% female), based on the presence of depressive disorders by DSM-IV criteria as confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) psychiatric interview. Insomnia

severity (Insomnia Severity Index, ISI), dysfunctional sleep beliefs (Dysfunctional Beliefs and Attitudes about Sleep Scale, DBAS-16), and pre-sleep arousal (Pre-Sleep Arousal Scale, PSAS) were assessed.

Results: Depressed participants, as compared to non-depressed participants reported significantly higher levels of insomnia severity (ISI: DA:15.0 vs. Control:1.76, $t = 22.90$, $p < .001$), more dysfunctional sleep beliefs (DBAS: DA 97.2 vs. Control 71.5, $t = 4.36$, $p < .001$), and heightened pre-sleep arousal (PSAS: DA 40.0 vs. Control 30.2, $t = -4.14$, $p < .001$). Linear regression analysis demonstrated that depression was significantly associated with more severe insomnia (ISI: $\beta = 0.77$, $p < .001$), and elevated pre-sleep arousal (PSAS-C: $\beta = 0.24$, $p = 0.02$), after controlling for education level.

Conclusions: These findings highlight a significant association between depression and insomnia among youths with eveningness. In addition, pre-sleep cognitive arousal was elevated in depressed adolescents with eveningness. The findings underscore the importance in attending to insomnia-related factors in assessing depression in adolescents with eveningness. Interventions that address cognitive hyperarousal, alongside mood symptoms may be needed for this vulnerable group.

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Associations of sleep characteristics with all-cause, cardiovascular, and non-cardiovascular mortality among rural Chinese older adults: A cohort study

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Introduction: The longitudinal associations of sleep timing and time in bed (TIB) with all-cause, cardiovascular, and non-cardiovascular mortality are unclear in Chinese rural populations.

Materials and methods: This population-based cohort study included 2468 participants who were aged ≥ 60 years and residing in rural communities in western Shandong Province. Sleep timing and TIB were assessed using standard questionnaires at baseline in 2014. Mid-sleep time was defined as the halfway point between the bedtime and wake-up time. Vital status until December 2022 and causes of death for all participants were ascertained via death registry plus interviews with informants. Data were analyzed using restricted cubic splines (RCS) and Cox proportional-hazards models.

Results: During the mean follow-up of 7.36 (SD=2.03) years, 657 participants died. The RCS analysis showed non-linear relationships of sleep duration and mid-sleep time at baseline with all-cause and non-cardiovascular mortality. Specifically, when baseline sleep characteristics were categorized into tertiles, the multivariable-adjusted hazard ratio (HR) for all-cause mortality were higher for long sleep duration (>8 vs. 7-8 hours; HR=1.27; 95% CI=1.06-1.53), long TIB (>9 vs. <8 h hours; 1.63; 1.27-2.08), early bedtime (before 9 p.m. vs. 10 p.m. or later; 1.58; 1.00-2.49), and early mid-sleep time (before 1 a.m. vs. 1 a.m.-1.5 a.m.; 1.45; 1.20-1.76). Long TIB was associated with multivariable-adjusted HR of 1.61 (1.15-2.27) for cardiovascular mortality and 1.64 (1.09-2.47) for non-cardiovascular mortality.

Conclusions: Long sleep duration and early sleep timing may be associated with increased risk of all-cause and cardiovascular mortality in rural Chinese older adults. In addition, long TIB was also linked to increased risk of all-cause, cardiovascular, and non-cardiovascular mortality.

Balancing sleep, work, and care: A comparative study of factors associated with wellbeing of caregivers in Japan and New Zealand

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Introduction: Caregivers provide support to people (often family members) with a variety of health needs. Sleep problems can be common due to awakenings of the care recipient, providing 'around the clock' care, and mood disturbances. Circumstances highlighted as particularly challenging include those when the care recipient has complex needs as well as situations when the caregiver is under-supported

or over-committed, such as reconciling work with care responsibilities. However, factors related to sleep as well as work and caregiving also vary cross-culturally. This research aims to better understand and represent such variations between New Zealand (NZ) and Japanese (JPN) contexts.

Materials and methods: Self-reported sleep duration (per 24-hours) and satisfaction (on a 5-point Likert scale) as well as self-reported fatigue or exhaustion and symptoms of depression (CES-D10) were explored amongst older (≥ 50 years) caregivers who were also working in NZ and JPN. Data included a stratified sample from the NZ Health Work and Retirement (HWR) cohort and a Japanese online survey (including relevant matched and translated items from the HWR study). Binary logistic regression analyses were used to explore the relationship between sleep (amongst demographic, caregiving, and health factors) with likelihood of depression and fatigue/ exhaustion between cultures.

Results: The NZ sample (N=517, 68% female) reported spending a median 38 hours per week working and 8 hours caregiving. They had a median sleep duration of 7 hours and 32% reported being dissatisfied or very dissatisfied with their sleep. The JPN sample (N=590, 51% female) reported spending a median 35 hours per week working and 10 hours caregiving. They had a median sleep duration 6 hours and 60% reported being dissatisfied or very dissatisfied with their sleep. Scores on the CES-D10 revealed that 25% of the NZ sample and 62% of the JPN sample were within range for high depressive symptoms. Furthermore, 25% of the NZ sample and 74% of the JPN sample reported experiencing severe fatigue or exhaustion. Sleep dissatisfaction was independently related to depression for both the NZ (OR 0.51, 95%CI 0.41-0.64) and JPN samples (OR 0.54, 95%CI 0.44-0.66) alongside increased job stress (NZ) and negative carer affect (JPN) as well as lower exercise (both). Sleep dissatisfaction was independently related to severe fatigue/exhaustion for both the NZ (OR 0.63, 95%CI 0.51-0.78) and JPN samples (OR 0.56, 95%CI 0.45-0.69) alongside increased negative carer affect (JPN) as well as younger age, lower income, and lower exercise (both).

Conclusions: These analyses illustrate the differing contexts and wellbeing of older working carers in NZ and JPN. Sleep dissatisfaction was a key independent predictor of depression and fatigue or exhaustion across both contexts. With stress related to work and caregiving also being significant for NZ and JPN samples respectively. Together, this demonstrates the cross-cultural needs of older adults' balancing paid employment and family care. Strategies to support sleep and wellbeing require unique context-dependent considerations.

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Barriers to Sleep Apnea Diagnosis and Treatment in Shelter Settings: A Qualitative Study of Experiences and Compassionate Care Pathways

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Introduction: Sleep apnea is a prevalent but underdiagnosed condition among individuals experiencing homelessness (IEH), significantly impacting their physical and mental health. In Ontario, Canada, access to diagnosis and treatment for obstructive sleep apnea (OSA) is hindered by rigid healthcare policies and systemic barriers, particularly affecting shelter residents. Despite assumptions of disinterest or non-adherence, prior pilot data suggested strong engagement with OSA care when services are contextually adapted. This study explores individual and systemic barriers to sleep apnea diagnosis and treatment in shelters, identifying critical themes for more equitable and compassionate care.

Materials and methods: A grounded theory methodology guided this qualitative study, integrating trauma-informed and equity-oriented frameworks. Semi-structured interviews were conducted with 20 shelter residents and 5 shelter staff across three Toronto shelter sites between January 2024 and February 2025. Participants were recruited through onsite information sessions and interviewed in private or semi-private settings. Interviews explored barriers to OSA engagement, diagnosis, and treatment, as well as experiences with compassionate care. Transcripts were coded iteratively using Excel-based thematic analysis and constant comparison. Themes were organized across three analytical levels (Engagement, Diagnosis, and Treatment) reflecting the continuum of care and systemic influence.

Results: Across all stages, participants identified profound material, psychological, and institutional barriers. At the Engagement level, barriers included lack of awareness of OSA, mistrust in health

systems, and diminished motivation due to trauma and survival priorities. At the Diagnosis level, logistical obstacles (e.g., lack of transportation, absence of primary care), fear of institutional settings, and cultural and communication mismatches obstructed access. At the Treatment level, standard therapies such as CPAP and oral appliances were often impractical due to shelter conditions, lack of infrastructure, and unmet dental or mental health needs. The misalignment between clinical expectations and shelter realities consistently limited adherence. Across all levels, compassionate care, defined as dignity-based, empathetic, and context-responsive support, emerged as a foundational condition for participation. Residents emphasized that being treated without judgment, with trust and flexibility, was essential to engage with and sustain care.

Conclusions: This study demonstrates that individuals experiencing homelessness are not inherently disinterested in managing sleep apnea but face complex, intersecting barriers at each stage of care. Compassionate care, operationalized through trauma-informed communication, flexible delivery models, and cultural safety, is essential for building trust and fostering health equity. Current diagnostic and treatment pathways are largely misaligned with shelter environments and must be reimaged to account for instability, stigma, and survival pressures. The findings call for co-designed, low-barrier, and system-integrated interventions that prioritize relational engagement and contextual fit. To reduce sleep health disparities in shelter populations, structural reforms in policy, infrastructure, and service design are urgently needed. This research offers actionable insights to inform policy, clinical practice, and future community-based sleep health interventions.

Bedtime at Midnight: Actigraphy-Measured Sleep Dimensions and Socioeconomic Predictors among Toddlers in Dhaka, Bangladesh

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Introduction: Healthy sleep in early childhood supports healthy neurodevelopment and growth, and protects against obesity. Data on children's sleep health and the guidelines that flow from it originate in high-income countries, which may not be relevant to conditions in low- and middle-income settings. Recently, the WHO released 24-hour movement guidelines (sleep, physical activity, and screen time) for children under five, but objective sleep data from LMICs remain sparse. To fill this gap, we measured sleep health dimensions and their predictors among toddlers in Dhaka, Bangladesh, a rapidly urbanizing lower-middle-income context now facing persistent stunting and emerging childhood obesity.

Materials and methods: Data for the present analysis came from 140 healthy toddlers (21 ± 3.65 months) recruited in a prospective cohort study from diverse neighborhoods of Dhaka city. We measured objective sleep using wrist actigraphy. Children wore a Philips Actiwatch 2 for a median of 6 days (interquartile range 5-7). Parent-reported sleep was collected using the Brief Infant Sleep Questionnaire–Short Form (BISQ-SF). Data on socioeconomic predictors, maternal depression, and parenting stress were collected using a study-specific questionnaire, the Edinburgh Postnatal Depression Scale, and the Parenting Stress Index-SF, respectively. Actigraphy data were processed in Philips Actiware and manually rescored to derive sleep dimensions. We used multiple linear regression models to examine socioeconomic and psychosocial predictors of sleep, adjusting for toddler age and sex.

Results: Mean bedtime was 11:50 pm (Standard Deviation, SD 1.2 hours). Nighttime sleep averaged 9.5 hours (SD 1.2), daytime sleep 2.0 hours (SD 0.54), yielding 24-h total sleep of 11.6 hours (SD 0.9). 21.4% of toddlers slept less than 11 hours, below WHO guidelines (11-14 hours) for this age group. Night-to-night variability was high, with an SD of bedtime of 0.8 hours and an SD of night sleep duration of 1.1 hours. Toddler bedtime shifted later with rising household income (p-trend < 0.05). Compared to a household income of 40000 taka/ month, children in 100000-taka and 200000-taka households went to bed 77 (95 % Confidence Interval, CI: 7.5, 126) and 123 (CI: 8.8, 238) minutes later, respectively. Compared to children of fathers with less than 10th grade education, children with fathers with higher-secondary (HSC) and professional (MD/engineer) education were associated with 90 (CI: 24,155) and 77 (CI: 11, 144) minutes longer nighttime sleep. Toddlers of fathers with flexible

work schedules went to bed an hour earlier ($p=0.03$) than those of fathers with fixed schedules. Toddlers in nuclear families slept 38 minutes ($p=0.04$) longer at night and napped 20 minutes ($p=0.08$) less than toddlers in joint families. Maternal education and maternal depression were not significantly associated with toddler sleep dimensions.

Conclusions: Toddlers in Dhaka go to bed late, display considerable night-to-night variability, and nearly one-fifth fail to meet WHO sleep recommendations. Later bedtimes and shorter nighttime sleep were linked with higher household income, joint living arrangements, lower paternal education, patterns that differ from high-income countries, and highlight context-specific predictors. Qualitative studies are needed to understand cultural practices (e.g., late meals, co-sleeping) mediating these associations to inform sleep-promotion strategies suitable for a densely populated South-Asian context.

Bedtime Stories: Sleep Health Education for Pediatric Providers in Community-Based Healthcare Centers

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Introduction: Pediatric providers are often the first line of defense in promoting healthy sleep practices. However, many receive limited training on implementing foundational sleep health practices. Moreover, anticipatory guidance on sleep for school-aged children remains sparse, potentially contributing to sleep health inequities in communities disproportionately affected by poor sleep. This study aimed to develop and evaluate a sleep health education course for pediatric providers by examining changes in their knowledge and clinical practices.

Materials and methods: Pediatric providers, residents, and nurse practitioners were recruited from two hospital-affiliated centers in Boston. Participants received a personalized link to enroll in the self-paced online course which included six required modules (Basics of Sleep, Sleep and Development, Sleep Health, Consequences of Insufficient Sleep, Sleep Health Disparities, Screening and Referral) and one optional module (Melatonin). All participants completed a course evaluation, a retrospective pretest-posttest survey examining knowledge and intent to change practice by indicating their level of agreement with each statement before and after the course using a five-point Likert scale (1-strongly disagree; 5-strongly agree). Participants received continuing medical education credit and a gift card.

Results: Data collected (December 2024 to May 2025) include 34 consented participants, of which: 11 are in-progress, 1 has not started, and 22 have completed the course. Course completers (18 MDs, 4 nurse practitioners) were on average 35.9 years of age (range= 26-34 years), primarily female (90.9%), majority white (79%) non-Hispanic (90%) with an average of 8.6 years (range= 0.5 – 30 years) of experience. An overwhelming majority (14, 88%) said this course changed their practice. Topics providers rated most highly were basics of sleep and sleep and development. Aspects of the program that learners rated most helpful were text, clinical pearls, and videos. The majority (81.3%) either agreed or strongly agreed that the program was relevant to their practice and found the program interesting and easy to complete. The retrospective pre-test indicators revealed that participants experienced a positive change in knowledge with the overall mean for the six knowledge areas increased from 2.8 (before) to 4.1 (after) ($p<0.001$). The Kruskal-Wallis test results indicate no statistically significant differences between groups based on healthcare profession (all p -values > 0.05).

Conclusions: The results suggest that knowledge among pediatric professionals could be improved through a short educational course. This improvement not only highlights the course's effectiveness but also suggests that similar educational interventions could play a crucial role in enhancing pediatric sleep practices on a wider scale. Through pilot data from this study, we will use the feedback we collect to improve the program. We also hope to assess the efficacy of the program in a large, multiple arm trial with other pediatric professionals.

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Bedtime Stress and Prefrontal Cortex Hemodynamics During Sleep: A Pilot Study Using Wearable fNIRS and Salivary Biomarkers

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Introduction: Psychological stress is a well-known disruptor of sleep quality, yet little is known about how stress modulates brain activity during sleep. While neuroimaging studies have advanced our understanding of stress responses during wakefulness, technical and methodological barriers have hindered investigation of stress-related neural dynamics during sleep. This pilot study aimed to explore whether bedtime stress is reflected in cortical hemodynamics during the first sleep cycle. We further examined which signal features and prefrontal subregions are most sensitive to stress indicators.

Materials and methods: A longitudinal N-of-1 design was conducted with a healthy adult male over 15 consecutive nights. Stress was assessed using three complementary indicators: salivary cortisol (mean = 3.4 nmol/L), secretory immunoglobulin A (sIgA; mean = 295.3 µg/mL), and subjective perceived stress scores (range 2–8; mean = 4). Sleep-related hemodynamics were recorded using a wireless, wearable 27-channel functional near-infrared spectroscopy (fNIRS) system (Brite 24) targeting the prefrontal cortex. Supplementary physiological data (heart rate, respiratory rate, and sleep timing) were collected using Fitbit Sense. fNIRS signals were preprocessed to remove physiological artifacts, and time-, frequency-, and nonlinear-domain features were extracted from both oxyhemoglobin (ΔO_2Hb) and deoxyhemoglobin (ΔHHb) signals. An ensemble feature-ranking algorithm, integrating six machine learning and statistical methods, was used to identify stress-related signal features and channels.

Results: Cortisol was most strongly associated with time-domain features—particularly signal mean at channel 16 (left rostral lateral prefrontal cortex, RLPFC)—with correlation coefficients reaching $|r| = 0.74$. Sample entropy of ΔHHb at channel 26 also showed strong negative associations ($r = -0.70$). sIgA was moderately associated with Hurst exponent and Poincaré plot asymmetry at channels 21 and 26 ($r = 0.53$ – 0.61). Perceived stress showed robust correlations with nonlinear features such as crest factor (ΔHHb , channel 16; $r = 0.68$) and skewness (ΔO_2Hb , channel 16; $r = -0.65$). While each indicator related to distinct feature sets, channel 16 emerged as a common site associated with all three stress measures. Additional associations were observed in the mid- and caudal dorsolateral prefrontal cortex (channels 3 and 20). The ventrolateral PFC showed no significant relationships with any stress markers.

Conclusions: This study introduces a novel, ecologically valid framework for assessing how stress manifests in the sleeping brain. Our findings highlight the relevance of the RLPFC and DLPFC in processing stress during early sleep, extending known wake-state functions of these regions into the nocturnal domain. The integration of wearable fNIRS, real-world biomarker tracking, and personalized analysis (via an N-of-1 design) provides a powerful methodology for sleep neuroscience. These results lay the groundwork for future multi-night, multi-participant studies and demonstrate the potential for next-generation stress monitoring and personalized sleep medicine. As stress increasingly contributes to sleep disorders, tools that noninvasively reveal how the brain processes stress during sleep could support earlier interventions, self-tracking, and more precise behavioral and clinical guidance.

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Beyond Manual Scoring: What an EEG-based Sleep Staging Model Learns Compared to AASM Guidelines

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Introduction: Deep neural networks (DNNs) have demonstrated high accuracy in automatic sleep staging. However, their decision processes—particularly regarding spectral information—remain poorly understood, which represents a barrier to clinical application. Post hoc explainable AI (XAI) methods can help address this gap by providing insights into the “importance” of specific input segments for a DNN’s decision. However, for time series data, most of these methods operate in the time domain and do not provide information regarding the frequency domain. To overcome this limitation, we extended the established XAI method Integrated Gradients (IG) to enable attribution scoring in the frequency

domain. This allows for the direct identification of spectral EEG features relevant to a DNN's prediction.

Materials and methods: An adapted dense recurrent convolutional neural network (DRCNN) was trained to predict all five AASM sleep stages (Wake, N1, N2, N3, R) from single-channel EEG. The architecture combines dense convolutional feature extraction and a bidirectional LSTM, followed by a softmax output layer. For model development, 4055 randomly selected C3/A2 and C4/A1 EEG recordings from the Sleep Heart Health Study (SHHS) were assigned to the training set, with 20% of these used for validation. An additional 1738 recordings were reserved for testing. All EEG signals were preprocessed by resampling to 100 Hz, amplitude and root mean square normalization, and moving average filtering. The trained model was then used for XAI analysis. We implemented a dedicated frequency processing layer consisting of a Real Fast Fourier Transform (RFFT) on the 30-second EEG segment, followed by an inverse RFFT prepended to the trained DNN. IG was applied to compute frequency-domain attribution scores for 339 EEG recordings, restricted to correctly classified (true positive) samples for all AASM-defined sleep stages. Attribution scores were then averaged across all recordings, yielding stage-wise frequency-domain attribution profiles.

Results: In N3 sleep, a pronounced attribution score peak of 0.0019 at 2 Hz was observed, vastly exceeding all other peaks across sleep stages (all others ≤ 0.0005). N2 was mainly characterized by a negative attribution peak of 0.0005 at 2 Hz. In N1, positive and negative attribution peaks with absolute values ≤ 0.0003 were found between 1.5 and 8 Hz. Across all stages, delta and theta bands (0.5 – 8 Hz) consistently exhibited greater relevance than higher frequency ranges. Additionally, small attribution peaks (≤ 0.0002) were detected around 38 Hz in N1 and wake stages.

Conclusions: Averaged results demonstrate that the frequency-domain XAI method reliably identified established sleep EEG markers, such as low delta activity in N3 and theta band relevance in N1, supporting the physiological validity of the decisions of this particular DNN. The observed peak around 38 Hz in wake and N1 may indicate either noise artifacts or previously unrecognized features. This novel XAI approach enhances the interpretability of DNN-based sleep staging models and may facilitate their integration into clinical workflows.

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Bi-directional associations between physical activity and sleep in school-age children: differences across times of day

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Introduction: Adequate sleep and physical activity, essential to children's development, have a bidirectional relationship. However, most prior research only considered total daily activity and overlooked the potential contribution of the timing and intensity of physical activity to sleep and the impact of sleep on physical activity at different times of day. In adults, exercise timing has shown mixed effects on sleep, and similar investigations in children are limited. Also, structured school schedules may shape weekday-weekend differences in sleep-activity patterns in children. This study examined (1) weekday-weekend differences in sleep and physical activity, and (2) the bidirectional associations between sleep and physical activity at different times of day, stratified by intensity, in school-age children.

Materials and methods: Wrist-worn accelerometers and sleep diaries measured sleep and physical activity in 129 school-age children (mean age $\pm$ SD = 9.65 $\pm$ 1.37 years; 64 boys) over at least 7 days during the school term. Sleep metrics—time in bed (TIB), total sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO), and sleep efficiency—were derived alongside physical activity duration (sedentary behaviour [SED], light physical activity [LPA], and moderate-to-vigorous physical activity [MVPA]). Activity was quantified for early morning (wake–08:59), late morning (09:00–11:59), early afternoon (12:00–14:59), late afternoon (15:00–17:59), early evening (18:00–20:59) and evening (21:00–sleep onset). Paired-samples t tests were used to examine weekday-weekend differences.

Generalised linear mixed models were used to investigate the bidirectional associations between physical activity and sleep, adjusting for age and sex.

Results: Compared to weekdays, children had longer TIB (mean $\pm$ SD: 36.45 $\pm$ 2.00 min) and TST (34.19 $\pm$ 15.00 min, p <0.01) on weekends. Since children woke up later on weekends (mean $\pm$ SD: 36.45 $\pm$ 2.00 min), weekend early mornings showed significantly lower activity levels across all intensities (MVPA: -4.27 $\pm$ 1.82 min; LPA: -24.28 $\pm$ 2.25; SED: -42.46 $\pm$ 25.48, p <0.01). In contrast, late afternoon activity levels were higher on weekends: MVPA increased by 2.69 $\pm$ 3.53 min and LPA by 7.26 $\pm$ 6.74 min, while SED decreased by 6.63 $\pm$ 6.26 min (p <0.02). The bidirectional associations between physical activity and sleep differed across times of day. Early morning activity, regardless of intensity, was associated with greater sleep efficiency that night (p <0.01), while higher sleep efficiency predicted increased SED (p =0.01) and reduced LPA and MVPA (p < 0.01) the next late morning. Early afternoon MVPA was linked to reduced WASO that night (p =0.01), whereas higher WASO predicted increased afternoon MVPA the following day (p =0.03). Late evening activity, regardless of intensity, was consistently associated with shorter TIB, TST, and SOL (p <0.01). In contrast, both TIB and TST were positively associated with MVPA (p <0.04) during the early evening of the following day.

Conclusions: In school-age children, weekday-weekend differences in sleep and physical activity are prominent, and the bidirectional relationships between them are not uniform across times of day. Our findings highlight the importance of considering not just the quantity but the timing of physical activity in its relationship with sleep.

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BP fluctuations during REM sleep as indicator to cardiovascular risk

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Introduction: Beat to beat Blood pressure fluctuations during REM sleep

We developed the "Circul VS" monitoring system, that consists of FDA cleared BP watch and FDA cleared Pulse Oximeter Ring that work in tandem through the night to produce beat-to-beat BP and SpO2 graphs. In the BP graphs we combine static BP measurements every hour with continuous Dynamic BP estimation from the ring. By providing around 30,000 measurements of BP and SpO2 (every second) we discovered high spikes of BP appearing as bursts during REM sleep in some of the patients. As we will explain later, we see these bursts of high spikes (e.g. from 100 mmHg to 160-200 mmHg) as indicator to Endothelial Dysfunction in controlling the BP and need for treating the endothelial function by lifestyle or medication.

Materials and methods: We used our "Circul VS" system that included BP watch with inflatable bladder and multiple wavelength optical sensors that was spring loaded to ensure constant pressure in the skin. The ring also includes AI algorithms for estimation Dynamic BP from PPG.

Results: Young healthy subjects hardly showed significant fluctuations. As age increased, older adults showed higher and higher fluctuations. Higher Fluctuations were demonstrated during Sleep Apnea events, and their size was correlated to the depth of the Oxygen desaturations.

In the end of the night, a report is automatically generated. The report which appears both on the Circul VS display and also sent to the hospital/clinic EHR system, with Dashboard for the sleep report physician.

The report uses Generative AI to generate text that explains to the physician what s/he can see in the graphs, what is the clinical significance of the finding looking at all graphs simultaneously and ever recommendations for next steps.

This report can be edited by the physician and then signed for reimbursement purposes.

Conclusions: Our hypothesis is that size and spectral content of these spikes bursts during REM indicate deterioration of the Endothelial Function and correlates with the CVD risk, even for patients that are normotensive. This open a new paradigm of assessing hypertension and CVD risk

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Bridging the Guideline Gap: Clinically Tested Casein Tryptic Hydrolysate (CTH) and the Combination of CTH-Theanine as First-Line Therapy for Mild to Moderate Insomnia

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Introduction: Cognitive-behavioural therapy for insomnia (CBT-I) is recommended as the first-line treatment for chronic insomnia in adult patients of all ages, including those with comorbidities. When the CBT-I approach is not effective, pharmacological intervention can be offered as a short-term (≤ 4 weeks) approach, prescribing benzodiazepines, benzodiazepine receptor agonists, daridorexant, and low-dose sedating antidepressants; a longer-term approach (up to 3 months) with orexin receptor antagonists or prolonged-release melatonin, considering their advantages and disadvantages.

Materials and methods: Antihistamines, antipsychotics, fast-release melatonin, ramelteon, and phytotherapeutics are not recommended for insomnia, as indicated by the recent European Insomnia Guideline. This guideline leaves a significant gap in safe, effective, and well-tolerated options. Bridging that gap, casein tryptic hydrolysate (CTH), a milk-derived protein hydrolysate rich in bioactive peptides such as α -caseozepine, has demonstrated promising anxiolytic and sleep-enhancing effects by modulating the GABAergic system, akin to conventional anxiolytics.

Results: In three randomised, placebo-controlled trials involving 144 participants, oral administration of 150–600 mg/day of CTH for 2 to 4 weeks produced statistically significant improvements in overall sleep quality and sleep latency. Additionally, three more trials involving 84 subjects given the combination of CTH (150–600 mg/day) and theanine (an amino acid derived from green tea; 50–204 mg/day) over 4 to 8 weeks demonstrated a significant reduction in sleep latency in common, while two of the trials showed a significant enhancement in total sleep duration, sleep efficiency, and daytime dysfunction—without causing sedation or dependency.

Conclusions: In contrast to many pharmacological options, both CTH and CTH-theanine formulations consistently exhibit favourable safety profiles, positioning them as compelling candidates for first-line therapy when CBT-I is inadequate. Larger, multinational trials are warranted to further validate these findings and support broader clinical adoption.

Can extending the time between last meal of the day and bedtime improve sleep regularity? A pilot study in Australian adults

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Introduction: Sleep regularity is important for health and wellbeing. Food intake close to bedtime negatively impacts sleep regularity by lengthening sleep onset and reducing sleep duration. Extending the time between the last meal of the day and bedtime could improve sleep regularity. This pilot study investigated, for the first time, whether extending the time between last meal and sleep onset through time-restricting eating (TRE) is feasible for Australian adults and if it impacts sleep regularity.

Materials and methods: Adults ($n=6$, 18–38 y, 5 female) completed 2-weeks baseline with usual eating timing followed by 6-weeks of TRE (10-hours between first and last meal, with last meal by 8pm), and a daily sleep diary. The standard deviations of sleep onset and sleep duration were calculated to indicate sleep regularity. Interviews were conducted to understand lived experience of TRE and sleep regularity.

Results: A one-way ANOVA revealed differences in time between last meal of the day ($p=0.04$), with 2.04 hours between last meal and sleep onset during baseline and 4.00 hours during TRE. There were no significant differences in sleep variables between baseline, 3-weeks TRE, and 6-weeks TRE (onset $p=0.54$; duration $p=0.85$). Participants reported positive experiences of TRE on sleep, commenting that TRE is “TRE helps me be consistent...because if I finish eating at a certain time, then I tend to go to bed at a set time.”

Conclusions: A 10hour TRE was feasible for Australian adults. While there were no significant improvements to sleep regularity after TRE, participants found it easier to have a consistent sleep routine when there was a longer time between eating and sleep. The next step is to build on these findings with objective sleep measures

Causal Relationship Between Metabolites and Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) Based on Two-Sample Mendelian Randomization Analysis

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Introduction:

Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS), a sleep-related breathing disorder, affects nearly one-fifth of adults worldwide. Identifying the pathogenesis associated with OSAHS is crucial. OSAHS patients exhibit metabolic alterations, which reflect the underlying biochemical activities and states of cells and tissues, directly linking to pathophysiology. Fatty acids, carbohydrates, and amino acids are common metabolites involved in cellular physiological processes, maintenance of cell structure, signal transduction, and cellular activity. Changes in these metabolites may serve as novel biomarkers, providing substantial insights into disease development.

Mendelian randomization (MR) analysis, a key epidemiological method, uses genetic variants as instrumental variables (IVs) to infer causal relationships between exposure factors and outcomes. Compared with traditional observational studies and randomized controlled trials, this approach avoids confounding factors and overcomes challenges such as high research costs and lengthy cycles. This study employed bidirectional two-sample MR analysis to further explore the causal relationship between metabolites and OSAHS.

Materials and methods: Metabolic disorder data and OSAHS data were obtained from OpenGWAS (<https://gwas.mrcieu.ac.uk>). MR analysis utilizes single-nucleotide polymorphisms (SNPs) strongly associated with exposure factors as instrumental variables (IVs). MR analyses were conducted in R (version 4.3.3) using the TwoSampleMR package. The inverse variance weighting (IVW) method served as the primary analysis, supplemented by alternative methods: MR-Egger regression, simple mode, weighted mode, and weighted median. Cochran's Q test assessed statistical heterogeneity among SNPs; MR-Egger regression intercepts analyzed horizontal pleiotropy. Sensitivity analysis was performed using leave-one-out methods. Funnel plots were generated to investigate potential influencing factors. A causal association was inferred if the IVW result had $P < 0.05$ and the causal effect directions of multiple methods were consistent with IVW.

Results: A total of 34,843 SNPs highly correlated with metabolism (all $F > 10$) were included from 1,400 metabolites. From the outcome data, 9,752 SNPs highly associated with exposure were extracted as instrumental variables. In IVW analysis, results with $P < 0.05$ were considered statistically significant. After excluding instrumental variables (IVs) with trends inconsistent with the inverse variance weighting (IVW) method across the remaining four MR analysis approaches, removing IVs with pleiotropy, and performing false discovery rate (FDR) correction, 45 metabolism-related SNPs were finally included, representing two metabolites or metabolite ratios: 2-palmitoyl-GPC (16:0) levels ($OR > 1$) and phosphate to threonine ratio ($OR < 1$).

Conclusions: This study used MR to investigate the causal relationships between 1,440 metabolites and OSAHS. As MR relies on the random allocation of genes during meiosis, it effectively avoids confounding factors and reverse causality compared with traditional observational studies. We found a positive association between 2-palmitoyl-GPC (16:0) levels and OSAHS, and a negative association with the phosphate to threonine ratio. Further validation using clinical samples is needed to confirm these intriguing findings.

Cerebral Metabolic Abnormalities and Disrupted Gut Microbiota in Adolescents with Major Depressive Disorder and Comorbid Insomnia Symptoms: A Proton Magnetic Resonance Spectroscopy Study

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Introduction: Adolescents are at an elevated risk of developing major depressive disorder (MDD), which is frequently accompanied by insomnia symptoms (IS). This study aims to elucidate the

mechanisms underlying this comorbidity, focusing on the gut-brain axis by evaluating cerebral metabolism and gut microbiota in adolescent patients with MDD and comorbid IS.

Materials and methods: A total of 102 adolescents diagnosed with MDD were recruited for this study, comprising 68 individuals with comorbid with IS (MDD-IS), 36 individuals without insomnia (MDD-nIS), and 35 healthy controls (HCs). Proton magnetic resonance spectroscopy (^1H -MRS) was employed to measure levels of N-acetylaspartate (NAA), choline-containing compounds (Cho), and creatine (Cr) in the prefrontal white matter (PWM), anterior cingulate cortex (ACC), basal ganglia (BG), thalamus, and cerebellum. Additionally, gut microbiota was analyzed using 16S rRNA gene sequencing of fecal samples.

Results: Compared to HCs, the MDD-IS group demonstrated decreased NAA/Cr ratios in the bilateral PWM and left ACC, as well as decreased Cho/Cr ratios in the right cerebellum. The MDD-nIS group showed decreased NAA/Cr ratios in the right PWM and left ACC. In comparison to the two patient groups, the MDD-IS group exhibited increased NAA/Cr ratio in the left ACC relative to the MDD-nIS group. LEfSe analysis at the genus level revealed an enrichment of *Escherichia*, *Shuttleworthia*, *Enterobacter*, and *Klebsiella*, and other genera in the MDD-IS, while *Fusobacterium*, *Desulfovibrio*, *Erysipelothrix*, and additional genera were more abundant in the MDD-nIS group. Differential analysis indicated that both MDD-IS and MDD-nIS groups exhibited a significantly higher abundance of the *Escherichia* genus compared to HCs, whereas the MDD-nIS group showed a lower abundance of the *Shuttleworthia* genus than HCs. Furthermore, the MDD-IS group had a significantly higher abundance of the *Shuttleworthia* genus compared to the MDD-nIS group. Correlation analyses demonstrated a significant positive correlation between the NAA/Cr ratio in the left ACC and the abundance of *Desulfovibrio* in the MDD-nIS group.

Conclusions: These findings suggest that sleep disturbances in adolescents with MDD may be associated with abnormal metabolism in the prefrontal cortex and cerebellum, as well as dysbiosis of the gut microbiota.

Changes in long-term circadian sleep parameters (365 days) after liver transplantation

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Introduction: The state of sleep in patients on the waiting list for liver transplantation has been little studied and is not considered a routine intervention necessary for maintaining their health. The aim of the study was to determine whether undergoing liver transplantation, without further intervention on sleep health, leads to an improvement in sleep-related parameters.

Materials and methods: Sleep-related parameters were monitored using a Kronowise K6 wrist device and the data were analysed using Kronowise 100 software (both from Kronohealth, Murcia, Spain). Patients wore the device on their non-dominant wrist for at least 7 days at two points in time: before the transplant (PRE), at the time of recruitment for this study, and one year after receiving the transplant. Up to 27 parameters related to sleep quality were calculated: Lights off and on (hh:mm), sleep onset and end time (hh:mm), sleep latency (min), total sleep time (min), WASO (min), number of awakenings/hour, sleep efficiency (%), actual sleep time (min), nap duration (min) and nap frequency, light received 2 hours before, during sleep and 2 hours after sleep; blue light received 2 hours before, during sleep and 2 hours after sleep, average activity 2 hours before, during and 2 hours after sleep and total time in bed.

Results: The parameters in which differences were found were average activity before sleep (preTX= 6.9 ± 0.7 vs 1Y= 7.4 ± 0.6 $p < 0.001$), average activity 2 hours after sleep (preTX= 11.8 ± 1.1 vs 1Y= 14.1 ± 1.1 ; $p < 0.001$), total light (PreTx= 549.7 ± 302 vs 1Y= 312.6 ± 165.1 $p < 0.001$) and blue light (PreTx= 263.2 ± 170 vs 1Y= 158.2 ± 67.7 ; $p < 0.001$) during the 2 hours after sleep, and nap frequency (PreTx= 1.1 ± 0.1 vs 1Y= 1.2 ± 0.1 ; $p = 0.005$). Trends towards differences were also found for lights off (hh:mm) ($p = 0.09$), total time in bed (min) ($p = 0.068$) and WASO (min) ($p = 0.092$).

Conclusions: Most parameters related to sleep quality do not change after transplantation, although there is a reduction in light received during the first two hours of sleep, an increase in activity during

the two hours before and after sleep, and an increase in the frequency of naps and awakenings. This means that, although overall health improves and chronic liver disease disappears, patients do not change their sleep habits. In this case, the absence of intervention and the lack of differences show the need for professional intervention on the quality of sleep of patients before and after transplantation.

Changes in short-term circadian sleep parameters (30 days) after liver transplantation

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Results: Differences were found in: sleep latency (PreTx= 17.7±2.9 vs 1M=10.6±0.9; p=0.027); Average Temperature during sleep (PreTx= 33.8±0.2 vs 1M=33.1±0.2; p=0.001), Light received during sleep in lux (PreTx=606.1±276 vs 1M= 271±145.8; p=0.014) and blue light received during sleep (PreTx=280±151 vs 1M=95.6±49.6; p=0.022). A latency higher than 20 minutes is considered as pathological; in the pre-transplant period, up to 24.5% of patients had a latency of more than 20 minutes, while one month post-transplant only 1.9% of them did (p=0.016).

Conclusions: There are short-term changes in sleep parameters following liver transplantation. Sleep onset improves; the percentage of patients with insomnia decreases significantly and screen use habits improve significantly.

Changes in the expression of clock genes after liver transplantation

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Introduction: Circadian biological rhythms are governed by a central clock and various oscillators in the organs. The maintenance of these rhythms depends on the expression of certain clock genes, which are either inducible, such as CLOCK or ARNTL, or repressive, such as CRY1, CRY2, PER1, PER2 and others such as RORA. Given that chronic liver disease causes certain sleep disturbances, this study sought to determine the gene expression of these genes before and after liver transplantation.

Materials and methods: Fifteen patients on the waiting list for liver transplants were recruited to participate in the CRONORGAN 21 project, which studied sleep disorders in patients with chronic liver disease. This study investigated the gene expression of these genes in blood mononuclear cells in patients at the time of inclusion on the waiting list, after transplantation in the hospital (1, 3 and 7 days

PT) and 30, 90, 180 and 365 days PT. A q-PCR was performed using beta-actin to perform relative quantification using the method of Livack et al (2001).

Results: Patients show a post-transplant increase in the expression of the inducer genes ARNTL and CLOCK and the repressors CRY1, PER1 and PER2. However, the CRY2 and RORA genes do not change their gene expression. When a linear regression was performed between gene expression and the days after transplantation, it was significant for the expression of RORA ($R=0.285$; $p=0.003$), ARNTL ($R=0.264$, $p=0.003$), CLOCK ($R=0.355$, $p<0.001$) and CRY1 ($R=0.254$, $p=0.005$). However, it was not significant for PER1, PER2 and CRY2. After a significant increase in all genes after transplantation, there is a decrease on days 3 and 7, followed by a progressive increase in gene expression in the genes that increase. RORA clearly shows a different dynamics from the other genes; there is less gene expression after transplantation and it returns to pre-transplantation values from day 30 onwards. CRY2 shows a drop on the third day after transplantation, while none of the other expressions differ from those prior to transplantation. The molecular mechanism that regulates the circadian clock is connected to other pathways such as metabolism, cell growth, DNA regulation and repair, angiogenesis, inflammation, and immune response.

Conclusions: An alteration in the expression of clock genes has previously been observed in animal models of liver disease and in cirrhotic patients. In the future, the gene expression of these genes could be used as an additional indicator of disease severity.

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Characteristics and influencing factors of sleep quality in newly employed nurses: a latent profile analysis study

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Introduction:

Sleep deprivation is a known risk factor for multiple chronic conditions, including hypertension, cardiovascular disease, and diabetes. Nurses, especially those newly employed, often experience irregular work schedules and rotating shifts, which can disrupt their sleep patterns. These disruptions may negatively impact both physical and mental health, as well as the quality of patient care. Previous studies have shown that poor sleep quality among nurses is associated with reduced attention, increased risk of errors, and occupational burnout. In China, one study reported an average Pittsburgh Sleep Quality Index (PSQI) score of 7.26 ± 3.56 among nurses, with 42.9% experiencing some degree of sleep disturbance. This study aims to investigate the distribution of sleep disorders among newly employed registered nurses, identify the potential profiles of sleep disorders, and explore the associated influencing factors.

Materials and methods: This cross-sectional study was conducted from September to October 2024 at the First Affiliated Hospital of Soochow University. A total of 362 nurses were surveyed using paper-based questionnaires through face-to-face interviews. Research instruments included the general demographic questionnaire, the Pittsburgh Sleep Quality Index (PSQI), the Transition Shock of Newly Graduated Nurses Scale (TSNGS), the Connor-Davidson Resilience Scale (CD-RISC), and the Simplified Coping Style Questionnaire (SCSQ). Latent profile analysis (LPA) was performed using Mplus 8.3, and multiple logistic regression analysis was conducted using SPSS 25.0. This study aims to investigate the distribution of sleep disorders among newly employed registered nurses, identify the potential profiles of sleep disorders, and explore the associated influencing factors.

Results: Four latent profiles of sleep disorders were identified: the 'Good Sleep Quality Group' (63.9%), the 'Poor Sleep Quality–Insomnia Group' (22.0%), the 'Poor Sleep Quality–Medication-Dependent Group' (7.7%), and the 'Moderate Sleep Quality Group' (6.3%). Logistic regression analysis showed that older nurses were more likely to be classified into the Poor Sleep Quality–Insomnia Group ($OR=1.386$, 95% CI : 1.093–1.759). Nurses with higher levels of transition shock were more likely to fall into the Insomnia Group ($OR=1.035$, 95% CI : 1.013–1.058) and the Medication-Dependent Group ($OR=1.034$,

95% CI: 1.001–1.068). Nurses with more than one year of work experience were more likely to be in the Medication-Dependent Group (OR=0.171, 95% CI: 0.049–0.599) and the Moderate Sleep Quality Group (OR=0.236, 95% CI: 0.068–0.814). Nurses with negative coping styles were more likely to be in the Moderate Sleep Quality Group (OR = 0.297, 95% CI: 0.093–0.945).

Conclusions: Newly employed nurses exhibit significant individual differences in their sleep disorder profiles. Older age, longer employment duration, and higher levels of transition shock are associated with more severe sleep disturbances, while positive coping strategies help alleviate these issues. Future efforts should focus on facilitating transition adaptation among new nurses and enhancing their coping skills to improve sleep quality and occupational health.

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Chronotype-Specific Associations Between Lifestyle Factors and Daytime Sleepiness in Japanese Elementary School Children: Focus on Japanese-Style Bathing

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Introduction: Daytime sleepiness in children has been associated with various lifestyle, sleep, and psychological factors. Among these, pre-sleep bathing has been suggested to promote sleep, and Japanese-style bathing (JSB)—a cultural practice involving soaking in a warm-water bathtub almost every evening—is one such example. Chronotype, or individual preference for morningness or eveningness, may also influence these associations. However, few studies have examined whether the factors associated with daytime sleepiness differ by chronotype in school-aged children. This study aimed to identify lifestyle factors, including JSB, associated with daytime sleepiness by chronotype in Japanese elementary school children.

Materials and methods: A web-based survey was conducted in November 2023, targeting 2,400 pairs of Japanese elementary school children and their parents. After excluding participants using sleep medication or providing incomplete responses, 1,042 pairs were included in the final analysis. Children completed the Pediatric Daytime Sleepiness Scale (PDSS), while parents responded to questions on demographic variables, sleep duration, screen time after 5:00 p.m., JSB-related habits (e.g., frequency of soaking in a warm bath), and the Strengths and Difficulties Questionnaire (SDQ). Chronotype was classified into morning-type, intermediate-type, and evening-type based on the Children's Chronotype Questionnaire (CCTQ). Multiple linear regression analyses were conducted separately within each chronotype group to identify factors associated with daytime sleepiness. This study was approved by the ethics committees of the affiliated institutions.

Results: Among the participants, 214 children were classified as morning-type, 666 as intermediate-type, and 162 as evening-type. Chronotype distribution differed significantly by grade, with the proportion of evening-type children increasing in higher grades ($p < .0001$). Mean PDSS scores differed significantly by chronotype, with morning-type scoring 5.7 ± 4.5 , intermediate-type 9.8 ± 4.7 , and evening-type 14.9 ± 4.9 ($p < .0001$, one-way ANOVA), indicating a significant increasing trend in daytime sleepiness from morning to evening types.

In the morning-type group, PDSS scores were significantly associated with SDQ total difficulties score, screen time after 5:00 p.m., sleep duration, and social jetlag (all $p < .05$; adjusted $R^2 = 0.116$). In the intermediate-type group, SDQ scores, screen time after 5:00 p.m., social jetlag, and frequency of bathtub soaking were significantly associated with PDSS ($p < .05$; adjusted $R^2 = 0.115$). In the evening-type group, only the SDQ score was a significant predictor ($p < .05$; adjusted $R^2 = 0.158$).

Conclusions: The results suggest that psychological, social, and behavioral factors associated with daytime sleepiness differ by chronotype in children. Morning- and intermediate-type children showed greater associations with multiple lifestyle and psychological variables, whereas for evening-type children, only psychological difficulties were linked to sleepiness. Tailored interventions that consider chronotype may be effective for improving daytime functioning in school-aged children.

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Clusters of sleep disturbance in people with systemic lupus erythematosus and associated factors

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Introduction: Systemic lupus erythematosus (SLE) is a debilitating chronic autoimmune disease. Individuals with SLE often suffer from sleep disturbance, affecting quality of life and even disease progression. Sleep disturbance in people with SLE is very complex and exhibits heterogeneity, posing challenges to the development of personalized interventions. The aim of this study was to investigate heterogeneous clusters of sleep disturbance and associated factors in people with SLE.

Materials and methods: A cross-sectional design was used and 434 people with SLE in China were recruited from an online Community for SLE Outpatient Support. Data were collected via electronic questionnaires. Sleep disturbance was evaluated by the Pittsburgh Sleep Quality Index (PSQI). Other information, such as disease activity, pain, fatigue, depression, and anxiety was also collected using validated instruments, including Systemic Lupus Erythematosus Disease Activity Index 2000, Visual Analogue Score of Pain, Fatigue Severity Scale, Patient Health Questionnaire-9, and Generalized Anxiety Disorder-7. Latent profile analysis was performed to reveal the distinct clusters of sleep disturbance. Multiple logistic regression analysis was performed to investigate factors associated with the clusters.

Results: Participant mean age was 32.9 years and 92.6% were females. All had sleep disturbance (PSQI>5) and their mean PSQI was 8.8 (SD=2.9). Three distinct clusters were identified: mild sleep disturbance with poor sleep quality, adequate sleep duration, and good daytime functioning (50.7%), mild sleep disturbance with poor sleep quality, adequate sleep duration, and poor daytime functioning (30.9%), and moderate sleep disturbance with poor sleep quality, inadequate sleep duration, and impaired daytime functioning (18.4%). There are both overlaps and unique aspects in terms of factors associated with each cluster of sleep disturbance, including age, BMI status, cardiovascular system damage, musculoskeletal system damage, depression, and anxiety. Overall, patients who were overweight, having musculoskeletal system damage or anxiety were more likely to have mild sleep disturbance with daytime functioning significantly impaired. Increasing age, depression, and musculoskeletal system damage could predispose patients to moderate sleep disturbance.

Conclusions: Sleep disturbance in patients with SLE showed three distinct clusters. In clinical practice, healthcare professionals (e.g., nurses) are recommended to prioritize assessment and interventions to those at-risk subgroups. They could also use the above information to develop and provide targeted interventions to address the unique needs of each cluster of sleep disturbance.

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Co-Designing Sleep Education for Primary Schools: Insights from Australian and Canadian Teachers

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Introduction: Sleep problems affect one in five school-aged children, and poor sleep has been linked to academic difficulties, emotional dysregulation, and long-term health risks. While several school-based sleep programs have been developed, the vast majority (~85%) target high school students, leaving a gap in resources tailored for younger children. Embedding sleep education earlier, during the formative years when lifelong habits are shaped, is essential. However, for sleep education to be effective and sustainable in primary schools, it must be aligned with classroom needs, developmentally appropriate, and integrated into existing educational priorities. The aim of the current research was to utilise a qualitative co-design approach with primary school teachers to inform development of a school-based sleep education program for primary school teachers.

Materials and methods: In Australia, twelve primary school teachers (75% female) participated in six online focus groups after reviewing the *Healthy Sleep for Healthy Schools* (HS4HS) high school program.

In Canada, nine primary school teachers (100% female) participated in individual virtual interviews after viewing the *ABCs of SLEEPING* storybook video. Teachers were asked to provide qualitative feedback on the content and presentation of each resource, the types of teaching and parent resources needed, and potential barriers and facilitators to implementing sleep education in the classroom. Reflexive thematic analyses were undertaken.

Results: In the Australian focus groups, teachers suggested that the content on healthy sleep practices be provided upfront, as this was the most practical and useful information for presenting to young children. A microlearning approach was preferred over longer, structured lessons, with participants recommending more visuals and short videos to support engagement. Age-appropriate resources were considered essential, with teachers highlighting the need for different materials for younger and older primary-aged students. Story-based learning emerged as a top recommendation, and participants also expressed the need for accompanying resources for parents. A key barrier identified was the overcrowded curriculum, but participants offered suggestions such as integrating sleep into existing wellbeing programs and aligning content with Australian curriculum requirements.

In the Canadian interviews, all teachers acknowledged the need for sleep education in the classroom and reported a lack of available sleep resources. The *ABCs of SLEEPING* storybook was viewed as a credible and evidence-based resource. Most teachers found the content to be relevant to their students, particularly messages related to electronics use, and appreciated its engaging illustrations and classroom-appropriate layout. The majority recommended involving parents or caregivers in the education process.

Conclusions: Findings from both co-design studies highlight the need for a short, online teacher learning module paired with supplementary age-appropriate classroom materials to support effective sleep education in primary school settings. Teachers consistently emphasised the importance of aligning content with curriculum and involving families to reinforce sleep messages at home. The *ABCs of SLEEPING* storybook was positively received and offers a strong foundation for developing story-based learning resources. These findings will directly inform the development of a primary school version of *HS4HS*, with a usability and pilot study scheduled in Australia and Canada for 2026.

Comparative Efficacy of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) versus SSRIs for Sleep Improvement in Depression: An 8-Week Randomized Controlled Trial

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Introduction: Depression is typically accompanied by considerable sleep disorders, which often remain even after treatment. Transcutaneous auricular vagus nerve stimulation (taVNS), a non-invasive neuromodulation therapy, has showed potential in treating depressive symptoms. Some research reveals that taVNS may alter sleep regulation via its effects on the autonomic nervous system and sleep-wake cycle modulation. However, its comparative efficacy with first-line selective serotonin reuptake inhibitors (SSRIs) for improving sleep symptoms in depression remains unclear. This study aims to compare the efficacy of 8 weeks of taVNS treatment with SSRI drug treatment in improving sleep disorders in patients with depression.

Materials and methods: This study included 43 adult patients with depression meeting DSM-5 diagnostic criteria. Participants were randomly assigned to the taVNS group (n=21) or the SSRIs group (n=22) and received 8 weeks of treatment. The taVNS group received 30 minutes of standardized parameter stimulation therapy daily, while the SSRIs group received medication treatment according to clinical guidelines. Sleep outcomes were assessed using the Hamilton Depression Rating Scale (HAM-D) sleep subscale at baseline and post-treatment. Baseline characteristics showed no significant differences between groups in HAM-D sleep scores ($F=2.302$, $p=0.494$; taVNS group: $M=3.71\pm0.332$; SSRIs group: $M=3.32\pm0.462$). Statistical analyses included paired t-tests for within-group comparisons and Mann-Whitney U tests for between-group differences, with effect sizes calculated using Cohen's d.

Results: Both treatment modalities demonstrated significant improvements in sleep symptoms after 8 weeks of intervention. In the taVNS group, HAM-D sleep scores decreased from 3.71 ± 1.52 at baseline to 2.33 ± 1.80 post-treatment ($t(20)=3.15$, $p=0.005$, $d=0.69$), representing a medium effect size

improvement. Similarly, the SSRI group showed reduction from 3.32 ± 2.17 to 1.64 ± 1.33 ($t(21)=3.00$, $p=0.007$, $d=0.64$), also demonstrating a medium effect size. Between-group comparisons using Mann-Whitney U tests revealed no statistically significant difference in treatment efficacy ($U=226.5$, $z=-0.112$, $p=0.911$), with comparable mean ranks between groups (taVNS=22.21; SSRIs=21.80). Both treatments were well-tolerated, with no serious adverse events reported in either group.

Conclusions: This study provides evidence that both taVNS and SSRIs are effective in improving sleep disturbances associated with depression, with comparable efficacy after 8 weeks of treatment. These findings position taVNS as a viable non-pharmacological alternative to SSRIs for managing sleep symptoms in depression, particularly for patients who prefer to avoid medication or experience side effects from pharmacotherapy. The comparable efficacy, combined with taVNS's favorable safety profile, supports its consideration in treatment algorithms for depressed patients with prominent sleep disturbances. Future research should investigate longer-term outcomes, optimal treatment parameters for taVNS, and potential differential effects on specific sleep architecture components.

Comparing sleep markers in a comparative micro-cohort study for mothers with depressive symptoms and a community cohort

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Introduction: Infant sleep is crucial for early development, with maternal mental health being linked to the infant's sleep patterns. While maternal depression can negatively affect various aspects of parenting, its direct impact on infant sleep remains underexplored.

This study aims to compare reported sleep markers of both infants and mothers from the Women's Emotional Health Service (WEHS) to those from the Sleep Easy Programme (SleEP). The WEHS supports mothers identified to have pre-and-postnatal depression or other types of emotional distress through the child's first year of life. The SleEP is the first community-based infant sleep screening and early intervention program in Singapore. We report findings from the first nine months of our collaboration (July 2024 to March 2025).

Hypothesis

It is hypothesized that infants of mothers with depressive symptoms will exhibit more frequent night wakings, shorter sleep durations, and disrupted sleep patterns compared to the community group. It is expected that in the former group, there will be a higher referral need to be referred for sleep interventions.

It is also hypothesized that mothers with depressive symptoms will report a shorter sleep duration compared to the community group.

Materials and methods: A 22-item questionnaire adapted from the Brief Infant Sleep Questionnaire, was administered on parents of infants for both groups during the enrollment. For the SleEP cohort, the parents completed the form during the infant's well-baby visits at the primary care.

A total of 30 mother-infant dyad from the WEHS group and a community sample comprising of 2185 mother-infant dyad are included in this study for the measured time range. Descriptive analysis is used to describe the study sample. Categorical data are presented as frequencies and percentage.

Results: The key findings support our hypotheses that (1) the percentage of infants referred for interventions is significantly higher at 70.0% for the WEHS cohort compared to the community SleEP cohort (26.5%). Of these, (2) they have more frequent night waking (3.5 times) than the SleEP cohort (2.3 times). Interestingly, the infants from the WEHS cohort sleep an average of nearly 30% more (12 hours) than their SleEP infants (8.4 hours).

The mothers from the WEHS cohort have reduced sleep quantity (5.4 hours) than the SleEP cohort (6.4 hours). There are double the number of mothers from the WEHS cohort (57.1%) who reported a significant lack of confidence than the SleEP cohort (29.7%). 66.7% of the WEHS mothers whose

infants needed interventions perceived their sleep to be a moderate or serious problem than 49.1% of the mothers from the SleEP cohort.

Conclusions: Potential mediating factors identified during our related to the WEHS cohort's elevated results are: (1) infants from the WEHS cohort sleep on the same bed and room as their parent(s), (2) there is lack of consistency in bedtime routines (42.9% in WEHS cohort versus 61.2% of the SleEP cohort) for the infants needing interventions.

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Comprehensive Sleep Phenotyping in the MoTrPAC Pediatric Study: the iSLEEP Health Profile

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Introduction: Integrating comprehensive sleep assessment into large-scale multidisciplinary studies remains a major challenge, particularly when it comes to generating high-quality, multilevel sleep data and communicating it effectively across disciplines. The Interacting Mechanisms of Sleep and Endurance Exercise in Pediatrics (iSLEEP) study, an ancillary project to the NIH-funded Molecular Transducers of Physical Activity Consortium (MoTrPAC), was designed to embed rigorous, multimodal sleep phenotyping into a systems biology framework. The iSLEEP protocol captures neurophysiological sleep architecture, habitual sleep patterns, and subjective sleep characteristics in youth aged 10–17 years who completed the MoTrPAC study. To support data integration, we developed the iSLEEP Health Profile; a standardized summary that visually synthesizes multimodal sleep data. The profile translates complex sleep data into an intuitive summary, supporting individual-level interpretation and fostering collaboration across research domains.

Materials and methods: A total of 158 MoTrPAC participants were consented to iSLEEP. Assessments included: (1) overnight polysomnography (PSG, Natus Systems) with high-density EEG (hdEEG, 128 channels cap by Waveguard), (2) 7–14 days of wrist-worn actigraphy, (3) daily sleep diaries, and (4) validated questionnaires including the School Sleep Habits Survey (SSHS). Sleep data were scored and reviewed by a boarded sleep physician using Natus SleepWorks software. EEG recordings underwent preprocessing, semi-automatic artifact rejection, and segmentation into concatenated NREM epochs. A Fast Fourier Transformation with a multitaper approach (11 tapers) was applied to estimate absolute and relative spectral power for slow-wave activity (SWA; 0.5–4.5Hz). Actigraphy data (Actiwatch) were scored with reference to sleep diaries and analyzed for sleep continuity metrics. Circadian activity rhythms were derived using parametric modeling (cosine and additive functions) and visualized using Shape Language Modeling (SLM) to capture habitual sleep patterns. A composite Ru-SATED score (composite score that includes regularity, satisfaction, alertness, timing, efficiency, and duration) was calculated by integrating subjective and objective measures. Social jet lag, defined as the difference in sleep timing and duration between school and non-school nights, was computed. Results were integrated into the iSLEEP Health Profile.

Results: 126 (50%, n=63 females) participants completed the full iSLEEP protocol with an additional 26 participants who provided partial data (actigraphy with sleep diary and questionnaires). Among those with full data, 54 (42.9%) were aged 10–13, 27 (21.4%) were classified by MoTrPAC as highly active. A standardized iSLEEP Health Profile page was designed to integrate PSG-derived sleep architecture and SWA topography, actigraphy-based sleep continuity and circadian activity rhythm metrics with SLM visualizations, subjective reports, Sleep Health score, and social jet-lag metrics.

Conclusions: The iSLEEP study was able to embed a detailed sleep phenotyping into large-scale pediatric study and can be used as a model for cross-discipline data integration and communication. The iSLEEP Health Profile offers a replicable framework for integrating behavioral and physiological data, advancing sleep phenotyping standards, supporting translational research, and enabling new cross-disciplinary collaborations. iSLEEP data will be made publicly available alongside MoTrPAC datasets to promote collaboration.

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Contemporaneous network analysis of mental health symptoms in middle-aged and elderly patients with OSA

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Introduction: To analyze the mental health status and severity of middle-aged and elderly patients with obstructive sleep apnea (OSA), and to construct a network of mental health symptoms in middle-aged and elderly patients with OSA through network analysis, and to identify the core symptoms. **Materials and methods:** A total of 741 patients with OSA who were admitted to the Sleep Medicine department of the People's Hospital of Guangxi Zhuang Autonomous Region from February 2022 to November 2023 were enrolled. The symptomcheck lis1-90 (SCI-90) was used to evaluate the psychological situation of the patients. According to whether the score of each factor of SCL-90 ≥ 2 , it was divided into positive symptom group and negative symptom group of each factor. The network analysis method was used to construct the psychological symptom network, and the core symptoms were identified through the central index, the bridge strength was analyzed, and the psychological and polysomnography characteristics of the positive and negative groups of bridge symptoms were compared.

Results: The most common psychological symptoms of middle-aged and elderly patients with OSA were other symptoms (60.46%), obsessive-compulsive compulsion (45.48%) and somatization (38.87%), and the results of centrality index analysis showed depression ($rs=1.433$, $rb=1.950$, $rc=2.024$), anxiety ($rs=1.109$, $rb=0.942$, $rc=0.727$) and interpersonal sensitivity ($rs=1.006$, $rb=1.278$, $rc=0.587$) as the core symptom. Depression is the primary bridging symptom, followed by interpersonal sensitivity and anxiety. Patients were grouped according to the presence of positive symptoms of anxiety or depression. It was found that patients with anxiety or depression symptoms had lower AHI (Apnea-Hypopnea Index) but were more prone to daytime somnolence.

Conclusions: Depression, anxiety and interpersonal sensitivity are the core symptoms of psychological symptoms in middle-aged and elderly patients with OSA, which provides new ideas for the clinical diagnosis of this population, determines the key intervention targets for clinical treatment, and provides a theoretical basis for reducing the symptom management burden of middle-aged and elderly OSA patients.

Cross-sectional and Longitudinal Relationships Between Multi-Dimensional Sleep Phenotypes and Cognition in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Introduction: Sleep is critical for maintaining overall brain health and may influence the onset and perpetuation of cognitive impairment. Since sleep is a complex and multi-dimensional construct, we hypothesized that methods employing multi-modal sleep measures across multiple domains (including multi-day sleep-wake rhythms, respiratory disturbances and brain activity during sleep) may help to identify phenotypic composites related to cognitive performance.

Materials and methods: Multimodal sleep measures (actigraphy, polysomnography, patient-reported outcomes) were completed at the 5th follow-up exam (2010 – 2013) of the Multi-Ethnic Study of Atherosclerosis (MESA), a large multiethnic community-based cohort in the United States. Cognitive testing was completed around the 5th follow-up exam, as well as at three other later timepoints during and between the 6th and 7th follow-up exams (2016 - 2024). We performed principal components

analysis (PCA) with varimax rotation on 39 sleep variables from multiple domains of sleep health among the 1,588 participants with complete sleep data at the 5th exam. Digit Symbol Coding Test (DSCT) scores from each of the cognitive timepoints were modeled as the primary outcome. In the cross-sectional analysis, DSCT was regressed onto scores derived from the principal components (PCs) while controlling for potential confounders. In the longitudinal analysis, DSCT was the outcome in linear mixed effects models, such that all participants were included who had a follow-up DSCT score.

Results: Thirteen sleep composites were derived from PCA that explained about 71% of the sample's variance. While adjusting for demographic and lifestyle factors, scores from five PCs representing: (1) EEG power spectral density, (2), rest-activity rhythms, (3), slow wave sleep, (4), spindle density, and (5) spindle and slow oscillation coupling were associated with DSCT, cross-sectionally. For the longitudinal analysis, only one PC, representing actigraphy-based sleep continuity, was associated with cognitive decline.

Conclusions: A data reduction approach to deriving sleep composites based on numerous polysomnography and actigraphy metrics yielded coherent and interpretable associations between multi-dimensional sleep and cognitive performance, identifying associations for both EEG-based and sleep-wake patterns. Future studies with comprehensive measurement of sleep may benefit from similar data-reduction methods to incorporate a high-dimensionality conceptualization of sleep.

Daily Associations of Sleep and Rest-activity Patterns with Pain Intensity in Adults with Chronic Pain

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Introduction:

Sleep and pain share a bidirectional relationship, with emerging evidence suggesting that poor self-reported sleep quality more strongly predicts subsequent pain intensity than vice versa, particularly in individuals with chronic pain (CP). However, sleep comprises only one component of the 24-hour rest-activity rhythm (RAR). Few studies have explored how sleep, daytime activity, and RAR patterns jointly influence next-day pain experiences in individuals with CP. Therefore, this study aimed to investigate whether temporal associations exist between self-reported and actigraphy-measured sleep, physical activity (PA), and 24-hour RAR patterns, and how these variables influence next-day pain in people living with CP in the UK.

Materials and methods: A total of 193 participants with CP wore a MotionWatch 8 (MW8) actigraphy device on their non-dominant wrist continuously for seven days in their natural sleep-wake environment. Participants also completed daily sleep diaries to report sleep efficiency (SR-SE; the proportion of time spent asleep in bed) and sleep quality (SR-SQ; subjective perception of sleep), as well as three daily surveys capturing pain intensity as the outcome variable. Objective actigraphic sleep metrics included actigraphy-derived sleep efficiency (A-SE) and fragmentation index (A-FI), while PA variables encompassed total activity counts (TAC) and total sedentary behaviour (TSB). RAR parameters included intradaily variability (IV; rhythm fragmentation) and relative amplitude (RA; rhythm robustness). Multilevel modeling (MLM) was used to examine the prospective associations between sleep, PA, RAR variables, and next-day pain, accounting for demographic covariates.

Results: In the multilevel modeling (MLM) analysis, higher self-reported sleep quality (SR-SQ; $\beta = -0.057$, $p < .001$, 95% CI [-0.085, -0.013]) and self-reported sleep efficiency (SR-SE; $\beta = -0.051$, $p < .01$, 95% CI [-0.089, -0.028]) significantly predicted lower next-day pain intensity. Conversely, actigraphic measures of sleep efficiency (A-SE) and fragmentation index (A-FI) were not significant predictors of next-day pain intensity. Regarding physical activity (PA) patterns, neither total activity counts (TAC) nor total sedentary behavior (TSB) from the previous day were significant predictors of next-day pain intensity. Similarly, rest-activity rhythm (RAR) parameters reflecting rhythm robustness or fragmentation, including intradaily variability (IV) and relative amplitude (RA), did not predict next-day pain intensity. The MLM results further indicated that pain intensity scores did not significantly vary across the daily surveys or days of measurement. Among demographic covariates, older age ($\beta = 0.152$, $p < .01$, 95% CI [0.053, 0.251]) and higher body mass index (BMI; $\beta = 0.110$, $p < .05$, 95% CI [0.019, 0.200]) were associated with greater reported pain intensity.

Conclusions: Self-reported sleep quality and efficiency emerged as robust and consistent predictors of lower next-day pain intensity, independent of objective activity levels or RAR characteristics. These findings underscore the critical role of high-quality sleep in managing daily pain in individuals with CP and suggest that improving sleep may help mitigate pain regardless of activity levels or circadian rhythm stability. Emphasizing subjective sleep quality could therefore serve as a practical target in chronic pain interventions to enhance daily functioning and quality of life.

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Das-Naglieri cognitive assessment system and serum A β levels contribute to the cognitive evaluation of OSAHS children

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Introduction: Obstructive sleep apnea hypopnea syndrome (OSAHS), a prevalent pediatric sleep disorder, is marked by recurrent episodes of apnea and hypoventilation throughout sleep. These events result in hypoxemia and disrupted sleep architecture, which are in turn linked to cognitive deficits. Presently, reliable tools for evaluating such cognitive impairment are scarce. This study aims to evaluate cognitive function in children diagnosed with OSAHS and primary snoring (PS) by employing the Das-Naglieri cognitive assessment system (DN: CAS), measure serum Amyloid- β (A β) protein and investigate the potential relationship between cognitive performance and A β levels in the pediatric OSAHS population.

Materials and methods: Based on the results of all-night polysomnographic monitoring, the 118 participants were categorized into OSAHS and PS groups. The cognitive function of all children from these two groups, along with an age-matched control cohort (n=82), was evaluated with the DN:CAS assessment and serum A β levels were quantified via Enzyme-Linked Immunosorbent Assay (ELISA).

Results: Children with PS showed poorer performance in Planning relative to their healthy counterparts. In the OSAHS group, significant reductions were observed in Full Scale, Planning, and Attention scores. These scores were also inversely associated with the lowest blood oxygen saturation (LSaO₂). Furthermore, serum A β levels were elevated in children with OSAHS and demonstrated a negative correlation with Full Scale and Attention scores, but a positive correlation with the obstructive apnea-hypopnea index (OAHl).

Conclusions: The DN:CAS assessment system is instrumental in evaluating cognitive function, and serum A β levels hold promise as a biomarker for the early diagnosis of cognitive impairment in children with OSAHS.

Daytime dysfunction, self-reported health, and hospitalizations predicting 3-year readmission in adults with systemic lupus erythematosus

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Introduction: Most systemic lupus erythematosus (SLE) patients have the risk of readmission after discharge, which seriously affects the quality of life of patients and increases the medical burden. However, there are few studies about the readmission of SLE patients. Therefore, this prospective cohort study aims to analyze the occurrence and the impact of mental health and sleep quality on rehospitalization within 3 years of discharge among adult SLE patients.

Materials and methods: Adult SLE patients hospitalized between April 2020 to April 2021 were followed for 3 years. Patients' rehospitalizations were collected through the electronic medical record system. Data was analyzed with descriptive statistics. Multivariate Cox regression analysis was applied to explore risk factors for their re-hospitalization during that period.

Results: A total of 135 SLE patients were included, 46 event cases and 89 censored cases were found in this analysis, with 3 years followed-up. Overall, 3.0% of SLE patients were re-hospitalized within 1 month; 7.4% within 3 months; 11.1% within 6 months; 22.2% within 1 year; 31.9% within 2 years; and 34.1% within 3 years. Multivariate Cox regression analysis showed that, among adult SLE patients, daytime dysfunction (HR=1.564, $P=0.016$) and the number of hospitalizations (HR=1.141, $P=0.011$) were the risk factors for 3-year re-hospitalization, while self-reported health being the protective factor (HR=0.812, $P=0.002$). More specifically, serum ferritin (hazard ratio (HR) =1.005, 1.003, respectively; all $P=0.047$) was the risk factor of 1-month re-hospitalization; serum ferritin and self-reported health were the predictors of 3-month re-hospitalization (HR=1.003, 0.670, respectively, all $P<0.05$); serum ferritin, number of hospitalizations, and number of other diagnoses were the risk factors of 6-month re-hospitalization (HR=1.003, 1.351, 2.200, respectively; all $P<0.05$). For 1-year rehospitalization after discharge in SLE patients, current smoking, number of hospitalizations, and daytime dysfunction were the risk factors (HR=3.631, 1.153, 1.528, respectively; all $P<0.05$). Current smoking (HR=4.919, $P=0.010$) and number of hospitalizations (HR=1.138, $P=0.011$) and were the risk factors of 2-year rehospitalization. Self-reported health was the protective factor for 1-year and 2-year re-hospitalization in patients with SLE (HR=0.821, 0.825, respectively; all $P<0.05$).

Conclusions: The 3-year re-hospitalization in SLE patients was 34.1%. Sleep quality, self-reported health, and number of hospitalizations were the main modifiable predictors for SLE patient's readmission within 3 years of discharge. It is recommended that clinical nurses pay attention to adult SLE with more hospitalizations, severe daytime dysfunction, and poor self-reported health to reduce the 3-year readmission rate.

Delaying Sleep Time: A Multidimensional Investigation of Personality Traits and Neural Correlates of Bedtime Procrastination

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Introduction: Bedtime procrastination is particularly prevalent among evening chronotypes and has been linked to lower self-control, present-oriented time perspective, and increased risk-taking behavior.

This study aims to investigate personality antecedents of bedtime procrastination and frontal alpha asymmetry (FAA) as a possible neural correlate of approach-avoidance motivation in the context of sleep-related decision-making. FAA, which reflects relative activation between the left and right frontal cortex, has been associated with motivational tendencies—greater left frontal activation indicating approach motivation, and greater right activation indicating avoidance.

We hypothesize that within-subject fluctuations in FAA, particularly a shift toward greater left frontal activation in the evening, may be more pronounced in evening chronotypes and individuals with higher levels of bedtime procrastination

Materials and methods: The study was conducted in two phases. Phase 1 (Study 1) involved an online assessment in which participants completed a series of standardized questionnaires to evaluate individual differences in traits such as bedtime procrastination, self-regulation, interoceptive awareness (via the MAIA), time orientation, daytime sleepiness, sleep quality, chronotype and handedness for EEG referencing.

The second phase, Study 2, was conducted in-person. An EEG measurement was conducted for each participant during two sessions on the same day: the first between 8–10 a.m., and the second between 6–8 p.m. During each session, participants also completed the Balloon Analogue Risk Task (BART) to evaluate risk-taking behaviour.

Results: Correlation analyses confirmed previous literature findings: greater morningness and higher self-control are linked to lower bedtime procrastination (BTP), while increased daytime sleepiness correlated with higher BTP. A future-oriented time perspective is negatively associated with BTP, whereas a hedonistic present orientation showed a positive correlation.

Notably, interoceptive awareness, particularly in the Self-Regulation and Not-Worrying domains, is negatively correlated with BTP. These two domains, along with Attention Regulation, also showed a significant negative correlation with sleep quality (PSQI).

AS for Study 2, FAA showed moderate intra-subject consistency between morning and evening session ($\rho = 0.700$, $p = 0.188$), suggesting it may reflect a stable trait-like pattern across the day. However, the difference between evening and morning FAA varied meaningfully among participants ($N=15$).

While no statistically significant correlations emerged, a positive trend was observed between FAA and rMEQ score, indicating that morning type individuals exhibited larger FAA fluctuations across the day, in contrast with evening types FAA. This interpretation contrasts with initial hypotheses and highlights the importance of correct trait-time alignment in neurophysiological measures.

FAA was not significantly associated with BPS or BART. A simple logistic model showed promising but not generalizable accuracy (80%), due to the limited sample.

Conclusions: These preliminary findings emphasize the multifaceted nature of bedtime procrastination, involving both psychological traits and neurophysiological patterns. Results offer a preliminary window into chronotype-sensitive FAA modulation and its potential role in behavioral regulation. Moreover, individual differences in chronotype, self-regulation, interoceptive awareness, and potentially chronotype modulated FAA variation may play a significant role in sleep-related decision-making. Future studies with larger samples and higher temporal granularity are needed to validate these exploratory trends.

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Development of a Trust-Building Research Framework to Address Sleep Health Disparities Among People Experiencing Homelessness (PEH)

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Introduction: Sleep health disparities disproportionately affect people experiencing homelessness (PEH), a population that faces significant barriers to accessing timely and effective healthcare. Environmental factors, mental health conditions, and systemic distrust further exacerbate sleep-related challenges. In addressing sleep health disparities among PEH, traditional methodologies often proved insufficient to foster trust and meaningfully engage participants as equal partners. Methods such as participatory action research and trauma-informed care provided valuable insights but lacked specific guidance on how to navigate cultural and systemic barriers in healthcare settings effectively. Recognizing these gaps, this study aimed to co-develop and apply a culturally responsive, trauma-informed research framework tailored to the lived realities of PEH.

Materials and methods: This study was conducted across seven shelters in Toronto, Canada, using a trauma-informed, patient-centered participatory action research (PAR) approach. Collaboration with a community advisory group, including individuals with lived experience, Indigenous knowledge holders, and shelter staff, informed the development of the framework. Research assistants were trained in trauma-informed and anti-oppressive care to ensure the prioritization of participants' dignity and autonomy. Quantitative tools (e.g., portable polysomnography, STOP-BANG) and qualitative methods (e.g., interviews, focus groups) were integrated to assess barriers and unmet needs.

Results: A Trust-Building Framework for Sleep Health Disparities was developed to address trust, systemic inequities, and cultural responsiveness in sleep health delivery. The framework was structured into six stages of the research cycle: readiness, engagement, data collection, analysis, implementation, and evaluation. Each stage incorporated strategies to enhance participant involvement. Specific elements include: training on trauma-informed care and cultural competency, identifying systemic

barriers to sleep health, and building trust-based relationships with stakeholders, including individuals with lived experience, shelter staff, and healthcare providers. Collaborative data interpretation informed tailored interventions such as CPAP devices, mental health supports, and culturally adapted educational materials. Outcomes were assessed through participant feedback, knowledge-sharing workshops, and monitoring the sustainable integration of practices within shelters.

Conclusions: The resulting Trust-Building Framework not only addresses the immediate health needs of PEH but also serves as a scalable model for integrating culturally responsive, community-driven solutions into shelter-based healthcare systems. Its foundation in trauma-informed, culturally responsive, and participatory methods ensures that interventions are grounded in the lived realities of participants. By centering participant voices and fostering interdisciplinary collaboration, this initiative lays the groundwork for sustainable change, promoting health equity and improved sleep outcomes for historically underserved populations.

Diagnostic accuracy of the Stopbang questionnaire against polysomnography for the screening of Obstructive Sleep Apnea in a tertiary hospital in Africa

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Introduction: Obstructive sleep apnea is a syndrome of upper airway and neuromuscular dysfunction that subsequently causes interruption of normal breathing during sleep. Polysomnography is the gold standard for the diagnosis of obstructive sleep apnea. Obstructive sleep apnea can be categorized as mild, moderate or severe based on an apnea-hypopnea index (AHI) on polysomnography. The recommended treatment using Continuous Positive Airway Pressure ventilation lowers morbidity and mortality rates. The STOPBANG questionnaire has been used as a screening tool for obstructive sleep apnea due to its easy and concise approach. However, even with the increasing prevalence of obstructive sleep apnea and its risk factors such as type 2 diabetes mellitus, obesity and hypertension in Africa, there is limited data on the validity and performance of the STOPBANG questionnaire in the clinical setting in the Sub-Saharan African population. The primary objective of the study was to determine the sensitivity, specificity and accuracy of the STOPBANG questionnaire in screening patients with obstructive sleep apnea as compared to polysomnography at our facility. The secondary objective was to determine the clinical characteristics of patients with obstructive sleep apnea.

Materials and methods: This was a retrospective cohort study of all patients who underwent polysomnography at the Aga Khan University Hospital, Nairobi, Kenya from 1st December 2020 to 30th June 2024. Data on variables was obtained from medical records and collected using the REDCap software based on the data abstraction tool. Data was analyzed using SPSS software.

Results: One hundred and twenty-nine patients underwent polysomnography. Out of the 129, 17 were excluded due to missing data and 112 patients were analyzed. The sensitivity of the STOPBANG questionnaire was 93.98% [CI 86.5%- 98.02%] with a specificity of 34.48% [CI 17.94% -54.33%]. The positive likelihood ratio was 1.43 [CI 1.10 -1.88] with a negative likelihood ratio of 0.17 [CI 0.07-0.47]. The positive predictive value was 80.41% [CI 75.82%-84.32%] while the negative predictive value was 66.67% [CI 42.71%-84.29%]. The accuracy of the STOPBANG questionnaire was 78.57% [CI 69.81%-85.76%]. Obstructive sleep apnea was associated with increasing age ($p=0.001$), male gender ($p=0.0272$), larger neck circumference ($p<0.001$), diabetes mellitus ($p=0.0193$), dyslipidemia ($p=0.001$) and hypertension ($p<0.001$). Presence of snoring, nocturnal hypoxemia and apneic episodes were significantly associated with obstructive sleep apnea ($p<0.001$, $p=0.003$, $p<0.001$ respectively). The above characteristics were also significantly associated with increasing severity of obstructive sleep apnea.

Conclusions: The STOPBANG questionnaire can be utilised for screening of obstructive sleep apnea in patients with sleep-disordered breathing in the clinical setting in Sub-Saharan Africa. As per our study, this should be done especially among patients who are 49 years and above, male patients, those who have diabetes mellitus, dyslipidemia, hypertension and those with an increased neck circumference >40 cm, and considered in those who are 47 years and above and a neck circumference of >37cm. Patients who are high risk for obstructive sleep apnea on the STOPBANG questionnaire should be offered polysomnography to diagnose or rule out obstructive sleep apnea.

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Differences in circadian sleep parameters depending on gender in patients on the waiting list for liver transplantation

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Introduction: Sleep is one of the fundamental pillars of health. However, it is not usually studied in patients prior to transplantation. The objective of this study was to determine whether circadian indicators of sleep quality differ between men and women on the liver transplant waiting list.

Materials and methods: Thirty men and 20 women on the waiting list at the Virgen de la Arrixaca University Hospital (Murcia) were included. Sleep-related parameters were monitored using a Kronowise K6 wrist device and the data were analysed using Kronowise 100 software (both from Kronohealth, Murcia, Spain). Patients wore the device on their non-dominant wrist for at least 7 days. Forty-two parameters related to sleep quality (Lights off and on (hh:mm), sleep onset and end time (hh:mm), sleep latency (min), total sleep time (min), WASO (min), number of awakenings/hour, sleep efficiency (%), actual sleep time (min), nap duration (min) and nap frequency, light received 2 hours before, during sleep and 2 hours after sleep; blue light received 2 hours before, during sleep and 2 hours after sleep, average activity 2 hours before, during and 2 hours after sleep and total time in bed) or circadian rhythm (distal temperature, movement in time and acceleration, light and sleep: Mean, IS, IV, RA, CFI, AN, SA and CHS; M5, time at M5, L5, time at L5; L10, time at L10, M10, time at M10) were analysed and a comparison was made using Student's t-test.

Results: As regards sleep parameters; differences were found in latency ($p=0.018$), average activity 2 hours before ($p=0.028$) and after sleep ($p=0.006$), total light ($p=0.027$) and blue light ($p=0.034$) received during sleep. Trends towards differences were also found for nap frequency ($H=1.11$ vs $M=0.78$; $p=0.073$). There were also differences in intradaily variability ($p=0.001$), the M5 value for movement time ($p=0.039$), the L10 value for total light received ($p=0.045$) and trends towards differences in the mean value for temperature ($p=0.054$) and the mean value for light received ($p=0.056$).

Conclusions: Although women sleep less in real terms, they enjoy better quality sleep. This could be related to lower exposure to blue light in the two hours prior to sleep, given that men receive up to 2.5 times more light than women, which could be related to the use of electronic devices or televisions before bedtime. Women have a sleep onset latency that is up to half an hour longer than men. of falling asleep than men. Sleep interventions should focus more on men, as they appear to have worse sleep habits than women.

Differential effects of sleep quality and sleep duration on stress reactivity: implications for mental health and wellbeing of young adults

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Introduction: Young adults frequently experience poor and insufficient sleep. Short sleep duration and poor-quality sleep are associated with dysregulation of the autonomic stress response and increased

risk of mental health problems. The mechanisms of this relationship are unclear. Heart rate variability (HRV) provides an indicator of autonomic stress response activity, with higher HRV reactivity often linked to better stress resiliency. We investigated the impact of objective sleep duration and subjective sleep quality on perceived stress and HRV reactivity to cognitive stress.

Materials and methods: 89 participants (mean age = 20.63 years, SD = 1.91 years, female = 63) participated in two laboratory sessions and two 2-week periods of naturalistic actigraphy monitoring to assess variability in habitual sleep duration. Heart rate variability (HRV), specifically root mean square of successive differences (RMSSD), was measured during rest and during the completion of computerised cognitive stress tasks. HRV (RMSSD) reactivity was calculated as the difference between RMSSD during stress and rest at each of two sessions (5 weeks apart), and the change in reactivity over time was assessed. The tasks included the *Flanker Task*, requiring participants to identify the direction of a central arrow while ignoring distracting surrounding arrows, and the *Dimensional Change Card Sort Test*, requiring participants to sort cards based on changing rules (e.g., colour, then shape). Participants also reported their subjective sleep quality and perceived stress levels using the PROMIS Sleep Disturbance and NIH Stress questionnaire.

Results: One-way ANOVAs revealed that improved subjective sleep quality was associated with reduced perceived stress and increased RMSSD reactivity to cognitive stress. This significant association between improved subjective sleep quality and RMSSD reactivity was evident only for a reduction in PROMIS Sleep Disturbances T-score of 6 points or more. Changes in objective habitual sleep duration were not significantly associated with either perceived stress levels or RMSSD reactivity to cognitive stress.

Conclusions: Our findings reinforce the association between sleep and stress, highlighting the role of subjective sleep quality in autonomic responses to stress. These findings identify specific consequences of poor sleep quality on stress physiology. Further research examining other dimensions of sleep (e.g. regularity, timing) and their role in autonomic functioning is needed. Exploration on how sleep duration may influence other important outcomes in young adulthood is also needed. Prioritising sleep as a preventive strategy remains important in both interventions and therapeutic treatments for mental health and wellbeing.

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Digital cognitive-behavioral therapy-based treatment for insomnia, nightmares and post-traumatic stress disorder symptoms in wildfire survivors: A randomized feasibility pilot trial

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Introduction: Background: Symptoms of insomnia, nightmares and trauma are highly prevalent in wildfire survivors. However, there are significant barriers to accessing evidence-based treatments for these conditions, leading to poor mental health outcomes for many wildfire survivors.

Objective: This pilot trial evaluated the feasibility of a four-week, digital, self-paced intervention combining cognitive behavioral therapy for insomnia (CBTi), and exposure, relaxation, and rescripting therapy for nightmares (ERRT) in wildfire survivors from Australia, Canada, and the United States of America.

Materials and methods: Methods: Study participants were recruited between May and December 2023 through social media platforms, workshops, conferences, and radio interviews. To be eligible, participants had to meet at least one of the following criteria: a score of ≥ 8 on the Insomnia Severity Index (ISI), and/or a score of ≥ 3 on the Nightmare Disorder Index (NDI), and/or a score of ≥ 31 on the PTSD Checklist – Civilian Version (PCL-5). Thirty wildfire survivors were allocated to either the treatment group (n=16) or the waitlist control group (n=14) in a sequential manner. Participants' ages ranged from 18 to 79 years, with a mean age of 52.50 years (SD = 16.26). The cohort consisted of 19 females (63.3%) and 11 males (36.7%). Participants also completed self-report secondary outcome measures, including the Generalized Anxiety Disorder Questionnaire (GAD-7), the Patient Health Questionnaire (PHQ-9), and the Pittsburgh Sleep Quality Index (PSQI), via the HealthZone digital platform. Participants were informed about the purpose, allocation, and the structure of the study. Assessments were conducted at baseline, post-treatment, and 3-months follow-up, with the waitlist group providing an additional assessment at pre-treatment, after 4 weeks of waiting, and prior to crossing over to treatment. The study employed two analyses including Intention-To-Treat analysis (ITT) as a principal analysis, and Per Protocol (PP) analysis as a secondary analysis.

Results: Results: Mixed-effects linear regression models and difference-in-difference analyses were utilized to assess the intervention's effects. The ITT revealed significant improvements over time (main effect of time) with a 1.64 point reduction ($P=.001$) on the NDI and 10.64 points reduction ($P=.009$) on the PCL-5 at post-intervention. No significant changes were observed in insomnia symptoms. On the secondary measures, there was an interaction effect of condition x time with a 2.22 point reduction ($P<.001$) on the PSQI and a main effect of time with a 6.48 point reduction ($P<.001$) on the PHQ-9. No significant changes were detected on the GAD-7. The PP analysis yielded comparable results for both the primary and the secondary measures.

Conclusions: Conclusion: The findings of this pilot trial demonstrated a reduction in nightmares and trauma symptoms. Future research studies should aim at evaluating the intervention in a more definitive trial with a larger sample size.

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Discrepancies Between Self-Set Sleep Plans and Sleep Regularity: Insights from Large-Scale Consumer Wearable Data

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Introduction: Consistent sleep-wake times are important components of good sleep health. This circadian stability impacts cardiovascular health and daytime cognition. While recent studies suggest that adhering to a sleep plan may support greater sleep regularity, empirical evidence regarding its role in promoting stable sleep-wake patterns remains limited. This study aimed to examine whether sleep/wake times differed based on the presence/absence of a sleep plan across age groups.

Materials and methods: Sleep data were collected from 770,835 Korean users who owned a Samsung Galaxy Watch and were using the Clock app (2,587,530 total records) between 2020 and 2023. The age distribution of the analytic sample included those in their 20s (27.6%), 30s (28.5%), 40s (25.6%), 50s (13.5%), and 60s (4.8%). The Clock app enabled users to set a target time for their bedtime and wake time. Users whose initial sleep plans matched the default system settings were excluded, which accounted for 19% of the sample. Sleep regularity was defined as the average standard deviation of bedtime and wake times. For related analyses, we examined two groups: (1) 595,954 users who had set sleep plans and logged actual sleep records, and (2) 308,437 users without sleep plans (not part of the full sample) who had ≥ 50 valid records during the same period.

Results: No significant difference in sleep regularity was observed between those with and without a sleep plan. Among users who had set sleep plans, those with low (≤ 5 th percentile) and high (≥ 95 th

percentile) sleep variability showed an average deviation of 43 and 182 minutes, respectively. In contrast, users without a sleep plan demonstrated deviations of 48 minutes for low variability and 139 minutes for high variability. Planned sleep schedules showed an age-related advance, with average bedtime of 00:00 (20s), 23:00 (30s–50s), and 22:00 (60s), and corresponding wake times of 07:00 (20s–30s) and 06:00 (40s–60s). The average sleep duration was 6.62 hours (20s), 6.45 hours (30s), 6.53 hours (40s), 6.39 hours (50s), and 6.39 hours (60s). Among participants with a sleep plan, we further examined the association between sleep regularity and discrepancies between planned and actual sleep and wake times. Those with high sleep regularity (≥ 90 th percentile) demonstrated mean discrepancies of 59 minutes for bedtime and 47 minutes for wake time. In contrast, those with low sleep regularity (≤ 10 th percentile) showed substantially larger discrepancies of 190 and 191 minutes, respectively.

Conclusions: In this large-scale study, sleep regularity did not differ by plan setting, suggesting that planning may not ensure more stable sleep–wake patterns. Notably, wake-time delays were also observed among participants with highly regular sleep patterns. These delays may be downstream consequences of late bedtimes or may reflect distinct processes such as sleep inertia, motivational avoidance of daytime activity, or impaired self-regulation upon waking. Future research is needed to clarify these possibilities and to further elucidate the nature of plan–behavior mismatches across sleep–wake patterns.

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DistillSleep: Real-Time, On-Device, Interpretable Sleep Staging from Single-Channel EEG

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Introduction: Sleep staging is a fundamental component of clinical decision-making in sleep medicine. Polysomnography (PSG), the current gold standard for sleep staging, requires controlled lab settings and manual scoring, making it inconvenient, time-consuming, and prone to inter-rater variability. These limitations restrict the widespread adoption of sleep medicine.

Although deep learning models have improved automatic sleep staging performance, existing methods depend on large-scale architectures with substantial computational demands, hindering their portability and real-time usability.

In this study, we present DistillSleep, a deep learning framework for on-device, real-time, interpretable sleep staging using single-channel electroencephalogram (EEG).

Materials and methods: DistillSleep consists of (1) a high-capacity teacher model and (2) a 109 k-parameter student model designed for edge-device deployment. Both incorporate a Multi-Wavelength Pyramid module and Transformer-based architecture to capture intra- and inter-epoch features. Feature- and prediction-level knowledge distillation transfers the teacher's expertise to the student, helping the student to not only improve its predictive performance, but also its interpretability. Training and evaluation used >10,000 overnight recordings from six cohorts (SHHS1, PhysioNet 2018, DCSM, KISS, Sleep-EDF, ISRUC), following AASM guidelines. Performance was assessed with Macro-F1. Our tailored architecture enables the clinicians to review intra- and inter-epoch mechanisms internally processed by the model, making DistillSleep interpretable to mitigate 'black-box' concerns.

Results: The teacher achieved state-of-the-art Macro-F1 scores (SHHS1 81.1%, PhysioNet 78.9%, DCSM 81.2%, KISS 80.0%) and provided frequency-resolved saliency maps, inter-epoch context and well-calibrated confidence (ECE 0.07). The student maintained competitive accuracy (up to 79.7% Macro-F1 on four large datasets and two external datasets) while executing <10 ms per 30-second epoch on three embedded platforms (Raspberry Pi 4, Jetson orin nano, Coral dev board), reducing computational load 115-fold versus the best prior method (SleepPyCo). Interpretability was transferred intact to the student, offering clinicians frequency-band importance and inter-epoch context visualizations, and model calibration was further improved by 2.7x.

Conclusions: DistillSleep combines expert-level accuracy, millisecond-scale latency, and transparent decision logic in a single-channel EEG form factor. Our extensive experiments prove its practicality and deployability in real world applications. These capabilities pave the way for point-of-care diagnostics, same-night therapy titration, and large-scale home monitoring, expanding the reach of sleep medicine while retaining clinical trust.

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Does gaming disorder symptom status predict poorer sleep quality?

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Introduction: This study investigates the association between Internet Gaming Disorder (IGD) symptoms and self-reported sleep quality in a large international survey. We assessed whether IGD symptom status (five or more) is associated with poorer sleep outcomes.

Materials and methods: We analysed 2023 survey data from 35 countries (n ≈ 35,000; ~1000 participants per country) to examine how Internet Gaming Disorder (IGD) status relates to self-reported sleep quality across countries (see <https://sync.ithra.com/research>). The survey utilises the Internet Gaming Disorder Scale–Short Form (IGDS9-SF), which is a widely used instrument for assessing Internet Gaming Disorder (IGD) based on the nine Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria. IGD status was derived from a gaming disorder symptom score based on DSM-5 proposed criteria: participants scoring 5 or more were categorized as “Screening positive for IGD,” all others were classified as “Not Screening positive for IGD”. Sleep quality was assessed using a scale from 0 (Terrible) to 10 (Excellent). Multivariable linear regression analyses were estimated with sleep quality as the outcome and IGD status as the primary predictor variable with additional adjustment for sociodemographic variables (country, age, sex, highest level of education and employment status).

Results:

In the survey, 11.0% met the criteria of screening positive for IGD.

Unadjusted analyses revealed that average sleep quality scores varied across IGD groups. Participants not screening positive for IGD reported the higher mean sleep score (M = 6.38, S = 2.23), while those screening positive for IGD had lower sleep quality (M = 6.19, S = 2.41).

At the country level, the prevalence of IGD ranged from as low as 2.5% in Germany and 2.6% in the UK, to as high as 24.6% in India, 22.1% in Egypt, and 21.3% in Kuwait. In several countries, the gap in sleep scores between IGD positive and not IGD positive groups exceeded one full point, for example, Chile (5.19 vs. 6.49), Brazil (5.59 vs. 6.67) and Italy (4.79 vs. 5.84).

Regression analysis further confirmed these trends. Compared to participants who are not IGD positive, those with IGD reported significantly lower sleep scores ($\beta = -0.418$, $p < .001$), even after adjusting for country, gender, age, education, and employment status.

Conclusions: These global findings indicate that individuals screening positive for Internet Gaming Disorder (IGD), report consistently lower sleep quality compared to those without IGD. Although IGD prevalence and associated sleep outcomes vary significantly across countries, the overall pattern suggests a negative relationship between problematic gaming behaviors and sleep health. The magnitude of these differences, along with substantial country-level variation, highlights the potential influence of sociocultural, behavioral, or structural factors in shaping how IGD affects sleep.

Does the Child-Pugh classification influence circadian sleep parameters?

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Introduction: The approach to patients on transplant waiting lists should be holistic, including nutrition, physical exercise and sleep quality, beyond the care of the pathology that afflicts them. However, sleep is not usually evaluated in these patients. In this study, we aimed to evaluate the parameters related to sleep quality and circadian rhythm in patients on the waiting list for liver transplantation depending on the severity classification of the disease using the Child-Pugh scale.

Materials and methods: Fifty patients on the waiting list for liver transplantation at the Virgen de la Arrixaca University Hospital were included. Sleep-related parameters were monitored using a Kronowise K6 wrist device and the data were analysed using Kronowise 100 software (both from Kronohealth, Murcia, Spain). Patients wore the device on their non-dominant wrist for at least 7 days prior to transplantation. At the time of recruitment, they were classified using the Child-Pugh scale, with 13 patients classified as A, 25 as B and 12 as C.

Results: Of all the sleep parameters analysed, differences were found when comparing Child-Pugh B patients with those classified as C in Total Time in Bed (min) (B=509,7±26,1 vs C=573,3±22,4 p=0.048), WASO (min) (B= 50,8±8,1 vs C=92,9±20,1; p=0.04), Number of Awakenings/Hour (B= 2,5±0,5 vs C= 5,1±0,4; p=0.017). Trends towards differences were also found for Lights On (hh:mm) (p=0.077), Total Movement Time (min) (p=0.065) when comparing B and C, in the number of naps per day (p=0.059) comparing A and B, and in WASO (p=0.089), number of awakenings/hour (p=0.089) and average activity 2 hours before bedtime (s) (p=0.085) comparing Child A patients with Child B patients.

Conclusions: A worsening of parameters is observed when comparing patients classified as B versus C, although there are no such differences between A and B. There appears to be a threshold for sleep parameter disturbance, which is more pronounced among patients with intermediate and severe severity. In general, as severity increases, patients spend more time in bed, wake up more times per night, and these awakenings last longer. They also experience more restless sleep with more time spent awake during sleep and less activity in the two hours before going to bed. This sets the guidelines for a possible sleep intervention depending on the severity of the liver disease.

Do perceived sleep sufficiency and measured duration relate to health and well-being in the same way?

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Introduction: Sleep is crucial for health and well-being, but different dimensions of sleep may affect health differently. This cross-sectional study explores the associations of sleep sufficiency and sleep duration with mental health, physical health, and life satisfaction.

Materials and methods: Data from 1,022 individuals (age ≥16 years) from the Danish Health and Morbidity Survey 2023 were used. Sleep sufficiency was self-reported, while sleep duration was measured by accelerometer. Mental and physical health were assessed using the SF-12 questionnaire, and life satisfaction with the Cantril Ladder scale. Multiple adjusted linear regression models were used to examine associations separately and in four combined categories: (1) low sufficiency, <7/>9 hours (n=106), (2) low sufficiency, 7-9 hours (n=89), (3) high sufficiency, <7/>9 hours (n=271), and (4) high sufficiency, 7-9 hours (n=556).

Results: Low sleep sufficiency was strongly associated with poorer mental health and lower life satisfaction. Specifically, individuals sleeping <7/>9 hours and reporting low sleep sufficiency had

mental health scores 8.6 points (95% CI: -10.8; -6.25) lower than those sleeping 7-9 hours and reporting high sleep sufficiency. In addition, deviations from recommended sleep duration combined with low sleep sufficiency was associated with poorer physical health.

Conclusions: Sleep sufficiency showed a more strongly associated with mental health and life satisfaction than sleep duration alone, indicating that these dimensions are not interchangeable. This highlights the need to consider both aspects in population-based sleep monitoring and public health initiatives.

Dreaming of death: an exploration of the relationship between death anxiety and nightmare severity

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Introduction: Throughout history and across cultures, humans have been interested in the relationship between dreams, nightmares and death. There is a scarcity of research examining this relationship, and findings have been mixed. This study aimed to (i) quantify the potential prevalence of nightmare severity and death anxiety, explore associations and differences between sexes and age groups, and (ii) examine typical dreams and their relationship to death-related themes.

Materials and methods: A total of n=432 participants (n=128 males and n=304 females) completed a cross-sectional study using the Death Anxiety Beliefs and Behaviour Scale (DABBS), Disturbing Dream and Nightmare Severity (DDNSI) and the Typical Dreams Questionnaire (TDQ).

Results: This study found that 10% had a self-reported sleep disorder, and 47% reported a mental health diagnosis. We found that 15% had clinical scores for DABBS, which was significantly higher in females, and in those with a mental health diagnosis ($p < 0.001$ for all), DDNSI was at 26% for the group. Linear regression identified a significant relationship between DDNSI and DABBS score. Greater levels of death anxiety were significantly associated with ($p = .003$) increased DDNSI scores ($\beta = 0.08$, Adj. $R^2 = 0.019$). When analysing the TDQ, those who had death-related dreams had significantly higher death anxiety and disturbing dreams and nightmares.

Conclusions: This study shows the need for more clinical attention and research on sleep health and its impact on health and well-being.

Effectiveness Of Sleep Intervention on Self-Reported Sleep Indices in Elite Male Cricketers: A Pilot Study from India

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Introduction: While sleep is increasingly recognized as a critical component in aiding the recovery process and enhancing performance in elite athletes, however, research in this area remains quite limited in the Indian context. This study aimed to evaluate the impact of a 4-week sleep intervention on sleep quality, duration, daytime sleepiness, sleep behaviours, issues, and disruptions in elite athletes.

Materials and methods: 20 elite male cricketers (mean age=23.5) underwent 2 weeks of baseline sleep monitoring and assessments (PRE), followed by a 4-week sleep intervention, and a further 2 weeks of monitoring and assessments (POST). Standard questionnaires (PSQI, ESS, ISI, ASSQ, ASBQ) were used to evaluate key sleep indices along with daily self-monitoring with a sleep diary. The sleep intervention focused on sleep education, improving sleep hygiene, enhancing total sleep time, and providing strategies for better recovery. Paired-sample t-tests were used to assess pre- and post-intervention differences.

Results: At baseline, the mean scores on all standardised measures indicated suboptimal sleep patterns among the participants. However, from baseline to post-intervention, analysis showed significant reductions (at $p < 0.05$) in ESS, ASBQ, and (at $p < 0.01$) in ISI, PSQI. Additionally, total sleep time

increased from 7.82 hours at baseline to 8.16 hours post-intervention ($p=0.001$), suggesting positive intervention effects.

Conclusions: Results provide evidence of the effectiveness of sleep intervention in elite male cricketers.

The study highlights a critical concern regarding the prevalence of significant sleep disturbances and daytime dysfunction among the participants. It indicates that there is ample room for sleep improvement. It is strongly recommended that structured sleep interventions (including education on the importance of sleep, optimizing sleep hygiene, and specifically targeting maladaptive sleep behaviours) be integrated into the training programs of elite athletes to enhance both recovery and performance. This may facilitate the sleep upgrading process for recovery and performance by effectively improving sleep indices in elite athletes.

keywords: Sleep quality; Sleep hygiene; elite athlete; sleep behaviour; cricket, recovery.

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Effect of a Combined Lifestyle-Based Intervention on Sleep among Postgraduate Nursing Students: A Pilot Study of the SEED Program

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Introduction: Sleep plays a crucial role in the well-being and functional performance of healthcare professionals. Postgraduate nursing students are particularly vulnerable to poor sleep due to the competing demands of their curricula and shift-based clinical rotations. Moreover, sleep disturbances in this population can significantly impair both learning and clinical performance. While lifestyle factors have been linked to improve sleep outcomes, limited studies have explored the combined synergistic effects of these factors. This pilot study evaluated the impact of the SEED programme—consisting of Sun exposure, Exercise, Education on sleep hygiene, and Diet —on sleep hygiene behaviours and subjective sleep quality among postgraduate nursing students.

Materials and methods: A six-week quasi-experimental study was conducted among 28 postgraduate nursing students, who were non-randomly assigned to intervention ($n = 17$) or control ($n = 11$) groups. Sleep hygiene was assessed using the Sleep Hygiene Index(SHI), and subjective sleep quality was measured using the Pittsburgh Sleep Quality Index(PSQI) at baseline and post-intervention. Due to the small sample size and group baseline differences, non-parametric tests were utilised for PSQI analyses, and ANCOVA was performed to SHI outcomes to adjust for baseline SHI scores.

Results: The intervention group exhibited a modest improvement in mean sleep hygiene scores (Mean $\pm$ SD) (-0.47 ± 3.69), while the control group showed a deterioration in these scores ($+ 2.73 \pm 4.13$). The Mann-Whitney U Test suggests a potential protective effect of the SEED programme on sleep hygiene ($p = 0.055$). However, the group assignment was not a statistically significant predictor of post-intervention SHI scores($p = 0.118$). Notably, baseline SHI emerged as a significant covariate($p=0.011$), indicating that participants with poorer sleep hygiene at baseline were more likely to demonstrate improvement following the intervention. PSQI analyses showed that the intervention group's median PSQI scores decreased from 6.0 to 4.0, while the control group's scores increased from 5.0 to 6.0. Wilcoxon signed-rank test was also done to evaluate within-group changes, revealing that none reached statistical significance for the intervention group ($Z = -1.34, p = 0.179$) nor the control group ($Z = -1.60, p = 0.109$).

Conclusions: The SEED intervention was feasible to implement and demonstrated promising trends towards improving sleep hygiene and maintaining subjective sleep quality among postgraduate nursing students. While statistical significance was not achieved, descriptive trends suggested a protective effect of the SEED programme against worsening sleep among this population. These findings suggest that targeted, multi-component lifestyle interventions may be beneficial in supporting the sleep health of this population. Future studies with larger sample sizes and longer duration are needed to validate such preliminary findings. Incorporating subjective and objective sleep measures may also capture meaningful changes in sleep quality and consolidate behaviour change.

Effect of differences in human ipRGCs stimulation under lighting during sleep

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Introduction: In hospital intensive care units (ICUs), nurses want to keep patient rooms as bright as possible at night to facilitate observation. However, the bright lighting conditions at night are not necessarily healthy for the quality of patients' sleep. The intrinsically photosensitive retinal ganglion cells (ipRGCs) are the cells in the retina, which contribute to photic entrainment of human circadian rhythm. Recently, it has become possible to change the ipRGCs stimulus level while maintaining the same light intensity and color rendering using LED light sources. This light source may provide a light environment that ensures clear visibility for nurses without disturbing patients' sleep. In fact, there is no clear evidence as to how differences in ipRGCs stimulation levels at night affect sleep quality. The purpose of this study is to clarify whether the differences of ipRGCs stimulus dose affect human sleep efficiency under lighting during sleep.

Materials and methods: Twenty-two healthy adult males (mean $\pm$ SD: 21.4 $\pm$ 1.9 yr. old) participated in this laboratory experiment. All participants had normal color vision variation (Ishihara test), had no sleep disorder (the score of Pittsburgh Sleep Quality Index), had no medication, and were not smokers. None of the participants were extreme morning or evening types (Morningness-Eveningness Questionnaire) and were shift workers. Experiments were conducted between January and May 2025. For three days prior to experiment onset, participants were asked to maintain a regular sleep-wake schedule (sleep onset at 0000 and waking at 0730). The participants arrived at the experimental chamber at 1300 and stayed for five days. The light condition was kept in 500 lx and 5000 K using special LED light source (ELM Inc. Japan). The participants retired to bed at 0000 and awakened at 0730. The participants slept under dark (0lx, baseline) on the first and the third night, and under lighting (500 lx, 5000 K) on the second and fourth night. Sleep parameters were compared under two lighting conditions: standard LED lighting typically used in hospitals (Control, Melanopic Efficacy of Luminous Radiation, ELR: 1.14 mW/lm), and special lighting to reduce ipRGCs stimulation (Intervention, Melanopic ELR: 0.96 mW/lm) at night. The difference caused by these lighting conditions were not distinguished to the participants. The order of these light conditions was counterbalanced among the participants. Wrist activity was continuously measured with the actigraph (Motion Watch 8, CamNtech Ltd) throughout the experiment. The sleep parameters were used to analyze. This study was approved by the Kyoto University Graduate School and Faculty of Medicine, Ethics Committee. Informed consent was obtained from the participants after an explanation of the purpose of the study.

Results: The sleep efficiency was compared between Control and Intervention at night using a one-way ANOVA. There was no significant difference between Control (84.5 $\pm$ 4.7%) and Intervention (84.7 $\pm$ 5.5%).

Conclusions: The differences in ipRGCs stimulus dose did not affect young healthy people's sleep efficiency under lighting during sleep. Other parameters including rectal temperature and saliva melatonin are ready to be analyzed.

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Effect of elinzanetant on wakefulness after sleep onset across subjective and objective measures: post hoc analysis of the NIRVANA phase 2 pilot study in postmenopausal women with sleep disturbances

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Introduction: Nighttime wakefulness is a common and disruptive symptom in postmenopausal women with vasomotor symptoms (VMS). Elinzanetant, a dual neurokinin (NK)-targeted therapy (NK-1 and NK-3 receptor antagonist), has previously shown improvements in patient-reported sleep outcomes. The Phase II NIRVANA pilot trial was the first to evaluate the elinzanetant effect on wakefulness after sleep onset (WASO) using both objective (polysomnography [PSG], Sleepiz One+) and subjective measures (Sleep Diary) in postmenopausal women with moderate-to-severe VMS. This abstract reports the findings from a post hoc analysis to determine whether changes in WASO with elinzanetant were observed across all three modalities.

Materials and methods: In this randomized, double-blind trial, 110 postmenopausal women (mean [standard deviation; SD] age: 54.8 [4.6] years) with PSG-confirmed sleep disturbances (WASO ≥ 30 minutes) and ≥ 20 moderate-to-severe VMS per week were randomized to elinzanetant 120 mg (n=55) or placebo (n=55) once daily for 12 weeks. Sleep disturbances were assessed using in-lab PSG and a patient-reported Sleep Diary for all participants, and with the Sleepiz One+ (Sleepiz AG, Zurich, Switzerland) contactless home-monitoring device in a sub-sample (n=66; elinzanetant: n=33, placebo: n=33). PSG was conducted at baseline, week 4, and week 12 (two consecutive nights per time point). Sleepiz One+ and Sleep Diary data were collected nightly throughout the 12-week treatment period. Data were analyzed on the original scale to provide consistency in data presentation across measures. A post hoc random coefficient model estimated the treatment effects on WASO over the 12-week treatment period across all available nights for each method.

Results: Elinzanetant demonstrated numerical reductions in WASO relative to placebo across all assessment modalities.

PSG: Mean (SD) WASO at baseline was 74.7 (34.8) minutes in the elinzanetant group and 82.8 (34.4) minutes in the placebo group. Random coefficient modeling suggested an overall treatment effect over the 12-week treatment period favoring elinzanetant over placebo (least squares [LS] mean difference: -10.1 minutes; unadjusted 95% confidence interval [CI]: -18.5, -1.6).

Sleepiz One+: Mean (SD) WASO at baseline was 77.7 (52.6) minutes in the elinzanetant group and 61.7 (27.6) minutes in the placebo group. Random coefficient modeling indicated a treatment effect over the 12-week time period favoring elinzanetant over placebo (LS mean difference: -17.7 minutes; unadjusted 95% CI: -27.1, -8.2).

Sleep Diary: Mean (SD) WASO at baseline was 42.4 (25.7) minutes in the elinzanetant group and 45.5 (25.6) minutes in the placebo group. Random coefficient modeling indicated a treatment effect over the 12-week time period favoring elinzanetant over placebo (LS mean difference: -8.1 minutes; unadjusted 95% CI: -14.2, -1.9).

Conclusions: NIRVANA is the first study to integrate gold-standard PSG, continuous home sleep monitoring, and patient-reported outcomes to assess treatment effects on WASO in postmenopausal women with VMS and sleep disturbances. In this post hoc analysis, greater numerical reductions in WASO were seen in the elinzanetant arm compared with placebo across all measurements. These results align with improvements in sleep disturbances observed in previous OASIS trials using patient-reported outcomes, though the exploratory nature and sample size of this analysis highlight the need for larger confirmatory studies.

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Effect of Sleep Quality on Heart Rate Variability in Medical Students: A Cross-sectional Study

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Introduction: In addition to being a biological necessity, sleep is a key regulator of cardiovascular health, emotional stability, and cognitive functioning. Medical students have particularly poor sleep quality due to their busy schedules, lifestyles choices, and high levels of academic stress. This vulnerable group frequently exhibits early symptoms of autonomic imbalance, a marker of long-term health risks. Heart rate variability (HRV) is a sensitive biomarker of autonomic nervous system (ANS) activity that offers non-invasive window to this physiological interaction. Studies demonstrating the connection between autonomic dysregulation and insufficient sleep continue to underrepresent

medical students. This study aimed to examine the connection between HRV and sleep quality in order to offer a distinct physiological understanding of how sleep disruptions may subtly harm cardiovascular health.

Materials and methods: After receiving the Institutional Review Board Ethical approval, 84 MBBS students, aged 18 to 25, with normal BMIs (18.5-24.9 kg/m²), participated in a descriptive, cross-sectional correlational study. The validated Pittsburgh Sleep Quality Index (PSQI), which measures subjective sleep quality over the previous month, was filled out by the participants. With an ECG recorded in lead II configuration, HRV recordings were made using the Power Lab AD instruments (Australia) under controlled conditions. To determine HRV parameters, a stable 5-minute ECG segment was examined offline using Lab Chart Pro 8. Frequency-domain measurements (Low Frequency [LF], High Frequency [HF], LF/HF) and time-domain indices (SDNN, RMSSD, pRR50) were calculated. Pearson or Spearman tests with a significance threshold of $p < 0.05$ were used to analyze statistical correlations between PSQI components and HRV indices using SPSS v26.0.

Results: Around 71% of students slept fewer than the recommended 7 hours, and a startling 76.2% of students had poor sleep quality (PSQI ≥ 5). 6.44 ± 2.62 was the average global PSQI score. Parasympathetic HRV indices, including HF ($r = -0.358$, $p < 0.01$), pRR50 ($r = -0.288$, $p < 0.01$), and RMSSD ($r = -0.227$, $p < 0.05$), were strongly inversely correlated with poor sleep quality. On the other hand, positive correlations with LF ($r = 0.375$, $p < 0.01$) and LF/HF ratio ($r = 0.390$, $p < 0.01$) indicated sympathetic dominance. Autonomic imbalance was substantially associated with subjective sleep quality, sleep efficiency, and dysfunction during the day.

Conclusions: The study provides a compelling physiological narrative: autonomic dysregulation, which is characterized by decreased parasympathetic and increased sympathetic activity, is significantly linked to poor sleep quality in the medical students. These changes could predict cardiovascular risks in the future. In order to protect the health of tomorrow's healers, there is an increasing need for focused interventions that give sleep hygiene top priority in medical curricula.

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Effects of a 12-Week Machine-assisted Strengthening Program on sleep health in Frail Older Adults

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Introduction: Insomnia is a common sleep-related complaint in the elderly. Rehabilitation has been shown to have multiple benefits for the elderly, and a new trend of machine-assisted strengthening programs has been developed. Therefore, we compared the effects of a 3-month machine-assisted strengthening program to traditional physical therapy according to composite insomnia symptoms related to falling and the SATED questionnaire among community-dwelling frail older adults.

Materials and methods: A randomized controlled trial included 59 frail older adults (mean age: 78.0 ± 8.2 years) in north-eastern Taiwan. The intervention group (N=31) underwent a 12-week machine-assisted strengthening program using SMARC system, performing twice-weekly sessions that targeting 8 muscle groups, while the control group (N=28) received traditional physical therapy. We reviewed the sleep health of the participants with a self-reporting questionnaire, including composite insomnia symptoms related to falling and the SATED scale.

Results: The control group showed no statistical significant change in SATED questionnaire and composite insomnia symptoms related to falling before and after traditional rehabilitation. The intervention group showed improvement in composite insomnia symptoms related to falling (-0.65 ± 0.91 , $p < 0.01$). When focusing on individual insomnia symptoms, the intervention group showed statistical improvement on 'trouble falling asleep' (-0.13 ± 0.34 , $p = 0.04$), 'trouble with waking up during the night' (-0.29 ± 0.46 , $p < 0.01$), and 'trouble with waking up too early and not being able to fall asleep again' (0.20 ± 0.40 , $p = 0.01$).

Conclusions: Machine-assisted strengthening can improve the participants' composite insomnia symptoms related to falling and individual aspects of insomnia. Larger-scale research is still needed for further understanding.

Effects of a behavioral sleep extension intervention on actigraphically measured sleep and patient reported outcomes

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Introduction: Up to 1/3 of adults in the world sleep less than the recommended 7 hours, which increases risk for chronic disease, depression and poorer quality of life. The goal of this study was to test the effects of an 8 week behavioral sleep extension intervention among adults with elevated blood pressure and objective sleep duration < 7 hours per night.

Materials and methods: Adults ages 18 and above with self-reported sleep duration <7 hours were screened in person for blood pressure criteria and then underwent 7 nights of at home actigraphy, 24 hours of ambulatory blood pressure recording and one night of home sleep apnea screening. Inclusion criteria were sleep duration <7 hours and time in bed <7 hours, insomnia severity index <15 and apnea hypopnea index ≤15 events/hour and resting office blood pressure >120 systolic blood pressure and/or 80 diastolic blood pressure. Eligible participants were randomized to an 8 week intervention that consisted of brief telephone coaching, a fitbit and weekly educational content versus health education and a brief phone call. Participants received monthly follow-ups from 8 weeks to 6 months and no intervention from 6-12 months. Data were analyzed using longitudinal models.

Results: The study screened 360 participants for objective study criteria and 120 participants were eligible and randomized into the study, N=60 were assigned to the sleep extension intervention (age m=42.2, sd=11.3, n=25 females) and N=60 were assigned to the health education control group (age m=41.0, sd=10.2, n=23 females). Retention was high in both groups (intervention =97% at 8 wks and 96% at 12 mos, control 98% at 8 wks and 97% at 12 mos). Most participants (79%) were working full time. Adherence to the intervention and control sessions was 100% because any missed sessions could be completed the following week. The intervention group demonstrated a greater change in sleep duration (m= +25.0 sd=4.8 min compared to the control group (m=+10.8 sd=4.8 min, p=.032) at the primary endpoint of 8 weeks. We detected no significance differences between the groups in sleep duration changes from baseline at 6 or 12 months or in other actigraphy measures including sleep efficiency, wake after sleep onset or sleep midpoint at any of the timepoints. The intervention group demonstrated greater improvement in depression scores (intervention m=-1.8 sd=.33 versus control m=-0.1, sd= 0.33, p<.001) but there were not other significant changes in self-reported sleep quality, sleep related impairment or perceived stress.

Conclusions: Results demonstrate a behavioral sleep extension led to increased sleep duration and improved mood with short term coaching but effects were not maintained following the intervention. Future research is needed to understand variability in sleep outcomes and techniques to maintain sleep changes over time.

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Effects of B vitamin intake on sleep duration and pulse wave velocity: a cross-sectional study based on NHANES

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Introduction: Sleep duration exhibits a U-shaped relationship with cardiovascular disease (CVD) risk and arterial stiffness, where both short (<7 h) and long (>9 h) sleep are independent risk factors. Although B vitamins, particularly riboflavin (B2), improve vascular endothelial function, their association with sleep duration remains mechanistically unclear. Our prior genetic study identified a missense variant in the riboflavin transporter *SLC52A3* (OR=0.83; 95%CI: 0.79-0.88; P<0.01) associated with obstructive sleep apnea severity, suggesting a nutrient-sleep-vascular link. Leveraging NHANES 2021-

2023 data, this cross-sectional study aimed to examine associations between dietary B vitamin intake and sleep duration categories and to assess their joint effects on arterial stiffness.

Materials and methods: We analyzed adults from NHANES 2021-2023 with complete data on dietary B vitamins (B1/B2/B3/B6/B9/B12, choline), sleep duration, and pulse wave velocity. Sleep duration was categorized as short (<7 h), optimal (7-9 h), or long (>9 h) according to National Sleep Foundation guidelines. Total vitamin B intake was calculated from both dietary sources and supplements. ePWV was calculated using a validated equation from the Reference Values for Arterial Stiffness Collaboration. Survey-weighted multinomial logistic regression assessed associations between B vitamin intake and sleep duration categories, with restricted cubic splines (RCS) used to model non-linear relationships. Models were adjusted for age, sex, BMI, race and blood pressure as key covariates. **Results:** Among 4,599 adults (median age 46.8 years; 48.5% male), participants meeting recommended B vitamin intake had higher odds of optimal sleep (OR=1.62, 95%CI: 1.38-1.91). This association followed U-shaped curves, strongest for vitamin B2. ePWV was higher in short sleepers (843 cm/s) than in optimal sleepers (827 cm/s; $P<0.001$). Moreover, vitamin B intake significantly modified the sleep-ePWV association: among short sleepers, each 1-SD increase in B2 intake reduced ePWV by 3.36 cm/s (95%CI: 2.36-4.36; $P<0.05$). Significant interactions were also observed for vitamins B1, B3, B6, and choline ($P<0.05$).

Conclusions: Adequate B vitamin intake, especially riboflavin, is associated with optimal sleep duration and reduced arterial stiffness in short sleepers. While the cross-sectional design limits causal inference, nutritional interventions targeting B vitamins may nonetheless benefit cardiovascular health in individuals with sleep disturbances.

Effects of Physical Activity on Sleep and Cardiovascular Health Across the Adult Lifespan in Singapore

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Introduction: Regular physical activity is widely recognised to improve sleep and is associated with reduced cardiovascular disease risk and mortality. However, prior literature has typically focused on a single age group, often relying on subjective measures of physical activity. The present study examined the relationship between objectively measured daily physical activity (PA; defined as the combined duration of light and moderate-to-vigorous physical activity) and both sleep and cardiovascular health across three cohorts spanning the adult lifespan in Singapore.

Materials and methods: A four-week subset of activity and sleep data, collected using the Oura Ring, was drawn from three cohorts: university students ($n = 500$, mean age = 19.9 ± 1.34), working adults ($n = 329$, mean age = 41.4 ± 10.2), and older adults ($n = 1,030$, mean age = 74.0 ± 2.63). Cardiovascular risk factors – body mass index (BMI) and pulse wave velocity (PWV) – were collected and analysed only for the working and older adult cohorts, given the lower expected risk among student age range. Sleep outcomes (duration, timing, efficiency) were analysed across all cohorts. Multilevel models were conducted on 38,586 nights of data to uncover the within-subject impact of PA duration on sleep outcomes.

Results: Descriptive analyses showed that older adults engaged in the longest PA durations ($M = 416.91$ min, $SE = 2.9$), predominantly in the morning. In contrast, working adults ($M = 345.23$ min, $SE = 3.7$) and university students ($M = 313.83$ min, $SE = 3.05$) had shorter PA durations, predominantly occurring in the evenings. Among working adults, PA was clustered around commute and meal times, while university students' PA typically flanked their academic lessons. After adjusting for age and gender, PA duration was negatively correlated with BMI ($r = -0.12$, $p < .001$) and PWV ($r = -0.10$, $p < .001$). A linear mixed-effects model, controlling for age, gender, weekdays and PA timing preferences, across all subjects revealed that longer PA duration predicted shorter total sleep time ($p < .001$), later bedtimes ($p < .001$), and earlier wake times ($p < .001$) within subjects. However, longer PA duration was also associated with higher sleep efficiency ($p < .001$) and shorter wake-after-sleep-onset (WASO; $p < .001$).

Conclusions: These results highlight increasing objectively measured PA duration with increasing age, which differs from subjective findings in other cohorts. However, the association between greater PA

duration and reduced cardiovascular risk align with existing literature, as indicated by lower BMI and PWV. Moreover, despite longer PA duration predicting shorter sleep duration, its associations with higher sleep efficiency and lower WASO suggest that it does not negatively impact sleep.

Effects of thermal and olfactory control of bedroom air on sleep restfulness during summer: A randomized crossover trial

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Introduction: An optimized and relaxing bedroom environment is essential for maintaining sleep health. Experimental evidence suggests that dynamically controlling the ambient temperature during the night promotes homeostatic and circadian regulation of sleep more effectively than static control. Olfactory stimulation with fragrances (e.g., lavender oil) has been reported to affect sleep through parasympathetic modulation. Sleep restfulness, the feeling of being rested after sleep, is considered a marker of sleep health because it is related to health outcomes, including mortality. However, it is unclear whether the dynamic thermal and olfactory control of bedroom air alters sleep restfulness.

Materials and methods: In this randomized crossover trial, 23 healthy adults were recruited and instructed to sleep at home under 3 different thermal and olfactory conditions using an air conditioner and a diffuser for 3 consecutive weeks during the summer months. The conditions were Constant Temperature (CT), in which the bedroom temperature was maintained at 26°C; Dynamic Temperature (DT), in which the bedroom temperature was gradually increased from 26°C to 28°C; and DT with Olfactory Stimulation (DT/OS), in which DT was combined with olfactory stimulation using lavender oil during the sleep onset period. Each condition consisted of three consecutive nights and was separated by a four-day washout period. Sleep restfulness, a subjective measure of sleep quality, was assessed using a visual analog scale and compared across conditions. Participants' night sleep was quantified using in-home sleep electroencephalography. Linear mixed models were used to determine whether thermal and olfactory interventions in bedroom air promoted sleep restfulness.

Results: Seven participants were omitted, primarily due to technical issues, resulting in a final sample of 16 participants (14 male/2 female; mean $\pm$ SD age: 53.8 $\pm$ 7.2 years). Participants reported feeling more rested after sleep in the DT/OS condition (mean $\pm$ SD: 67.1 $\pm$ 21.3) than in the CT (59.7 $\pm$ 19.1, P = .010) and DT (59.3 $\pm$ 23.3, P = .007) conditions. Sleep duration, sleep continuity, and sleep structure did not differ across conditions.

Conclusions: The data suggest that olfactory stimulation during sleep onset promotes restorative sleep. The development of novel dynamic thermal control of bedroom air warrants further investigation. Optimizing bedroom air may be important for promoting sleep health.

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Emotional labor moderating the impact of work rumination on sleep quality among newly graduated nurses in China

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Introduction: The year 2024 marks the first year that Jiangsu Province deeply implemented the national policy of two-year standardized training for newly graduated nurses. The work intensity and learning content faced by newly graduated nurses in 2024 have increased significantly. Under such heavy pressure, coupled with the pressure of role transformation, their psychological state trend requires the urgent attention of nursing managers. For this group, maintaining a healthy mindset, getting sufficient sleep, working when it's time to work and resting when it's time to rest are the keys for them to smoothly get through this period. However, the sleep and working conditions of newly graduated nurses in the first year of policy implementation remain unclear at present. Therefore, this study aims to explore the sleep and working status of this group, investigate the moderating role of

emotional labor on the associations of rumination with sleep quality, so as to identify a reference for the subsequent arrangement of standardized training work.

Materials and methods: In the descriptive, cross-sectional study, one hundred and ninety-three newly graduated nurses (nurses with <1 year of work experience) were included in the study. Data were collected using the Chinese version of the Pittsburgh Sleep Quality Index (PSQI), Work-Related Rumination Questionnaire (WRRQ), Emotional Labor Scale (ELS) to measure sleep quality, rumination, and emotional labor, respectively. SPSS and Mplus were applied to perform descriptive and moderated mediation analysis, respectively.

Results: In the first year of work, the prevalence of poor sleep quality among newly graduated nurses was as high as 72.2%, and 62.2% of them slept for less than 7 hours per day. The total score of newly recruited nurses' surface acting strategy was 25.83 ± 4.35 , 14.58 ± 2.51 for deep acting strategy, and 10.50 ± 1.87 for expression of genuine emotion. Newly recruited nurses-emotional labor strategies were used from highest to lowest frequency as the expression of surface acting, deep acting, and genuine emotion, with the mean entry score of 3.69, 3.62, and 3.50, respectively. The mean values of affective rumination and problem-solving pondering were 15.23 ± 0.36 and 15.32 ± 0.26 respectively, indicating the medium level of work rumination. Work rumination and emotional labor strategies were associated with sleep quality (Standardized $\beta = 0.676$, $P < 0.001$; $\beta = -0.191$, $P = 0.043$, respectively). In addition, work rumination had an indirect impact on sleep quality by influencing emotional labor strategies (Standardized $\beta = 0.318$, $P = 0.001$). Thus, a moderated model involving emotional labor for explaining the impact of work rumination on poor sleep quality was supported among newly graduated nurses within <1 year of work experience.

Conclusions: In the first year of the two-year standardized training, the sleep quality of newly graduated nurses during the standardized training period is very poor, and the sleep duration was seriously insufficient. Emotional labor strategies moderated the relationship between work rumination and sleep quality. Nursing managers need to pay attention to the sleep of nurses during this period, adjust the training content in a timely manner to relieve their stress, help regulate their psychological state, distinguish work from life, and ultimately improve their sleep quality.

Enhancing Pediatric Sleep Health: Development of an Interdisciplinary Educational Course for Primary Care and Sleep Medicine Providers

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Introduction: Pediatric sleep disorders are common, underrecognized contributors to behavioral, cognitive, and physical health problems in children. While pediatric sleep medicine is a growing field, most primary care and general sleep medicine providers receive minimal training in pediatric-specific sleep assessment and management. To address these gaps, the American Academy of Sleep Medicine (AASM), in collaboration with eight pediatric sleep medicine experts and AASM education staff, developed a targeted educational course to build knowledge and clinical confidence in this area. The course was designed using evidence-based instructional practices grounded in adult learning theory, which emphasizes learner self-direction, practical application, and integration with prior experience (Knowles, 1980; Merriam & Bierema, 2014). Development followed best practices in curriculum design, including needs assessment, goal alignment, and iterative content review (Harden, 2000). AASM staff with formal training in instructional design and adult education played an integral role in shaping the structure, delivery, and accessibility of the course.

Materials and methods: Eight pediatric sleep practitioners from diverse clinical and academic settings collaborated with AASM instructional design staff to plan and create the course. A comprehensive needs assessment was conducted using member surveys, literature review, and feedback from AASM-accredited centers. The course was designed to be asynchronous, modular, and adaptable to various

practice environments. It features didactic content, case-based learning, clinical algorithms, and downloadable decision-support tools. Key topics include behavioral insomnia, circadian rhythm disorders, sleep-disordered breathing, parasomnias, and appropriate referral strategies.

Results: The final course includes eight modules totaling approximately six hours of CME-accredited content. Each module is designed for flexible, self-paced engagement and includes evidence-based materials, real-world case vignettes, and practical tools for clinical use. Content is tiered to accommodate varying levels of experience among learners and emphasizes actionable strategies for screening, diagnosis, management, and interdisciplinary collaboration.

Conclusions: This collaborative initiative highlights the effectiveness of combining clinical expertise with professional instructional design to create relevant, high-impact education for healthcare providers. By addressing critical knowledge gaps in pediatric sleep medicine, the course serves as a scalable model for cross-disciplinary learning. Future efforts will focus on evaluating learner outcomes, updating content based on emerging evidence, and expanding access to a broader provider audience. This effort supports the AASM's mission to promote high-quality sleep care and improve outcomes for children and families

Acknowledgments: · Knowles, M. S. (1980). *The Modern Practice of Adult Education: From Pedagogy to Andragogy*. Cambridge Books.

· Merriam, S. B., & Bierema, L. L. (2014). *Adult Learning: Linking Theory and Practice*. Jossey-Bass.

· Harden, R. M. (2000). The integration ladder: a tool for curriculum planning and evaluation. *Medical Education*, 34(7), 551–557.

Environmental Sleep Disruptors: The Role of Thermal Comfort and CO₂ Levels

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Introduction: Sleep is a vital physiological process essential for physical recovery, cognitive function, and emotional balance. Its quality is influenced not only by individual and behavioral factors but also by environmental conditions in the sleep setting. Among these, thermal comfort and indoor air quality, particularly ambient temperature and carbon dioxide (CO₂) concentration, are increasingly recognized as important modulators of sleep architecture and continuity. Suboptimal thermal conditions and elevated CO₂ levels may impair sleep efficiency, reduce total sleep time, and increase the frequency of nocturnal awakenings. This study presents preliminary data from the HypnosAir Project (www.hypnosair.com), which investigates the impact of indoor environmental conditions on sleep quality.

Materials and methods: Participants were recruited through convenience sampling and met strict inclusion criteria: age between 25 and 45 years, healthy, non-smokers, and free of diagnosed sleep, cardiovascular, respiratory, neurological, or psychiatric disorders. Female participants were included only if they were not pregnant, breastfeeding, menstruating, or in peri- or post-menopausal stages. Each participant underwent continuous monitoring over seven consecutive days and nights between February and April 2025. Sleep was assessed using actigraphy, while environmental conditions—temperature, relative humidity, and CO₂ concentration, were measured continuously in the bedroom environment. A total of 295 nights were analyzed. Sleep parameters included total sleep time (TST), sleep onset latency (SO), wake after sleep onset (WASO), number of awakenings, and sleep efficiency (SE). Data analysis was performed using SPSS, applying descriptive statistics and multiple linear regression, with confirmation of Gauss-Markov assumptions.

Results: The average values observed were as follows: TST 447.85 ± 83.19 minutes, SO 41.84 ± 31.16 minutes, WASO 10.67 ± 14.81 minutes, number of awakenings 16.46 ± 9.90, and SE 89.39 ± 5.74%. Environmental measurements showed an average temperature of 19.72 ± 1.92 °C, relative humidity of 77.34 ± 7.00%, and CO₂ concentration of 1684.32 ± 925.61 ppm. Regression results indicated that a

1 °C increase in ambient temperature was associated with a 5.8-minute reduction in TST and 1.1 fewer awakenings per night. No statistically significant associations were observed between temperature and SO, WASO, or SE. Likewise, CO₂ concentration was not significantly associated with any sleep parameter in this preliminary analysis

Conclusions: These initial results suggest that thermal comfort, especially ambient temperature, has a measurable impact on sleep, particularly in reducing total sleep time and the number of awakenings. Although no significant effects of CO₂ were identified at this stage, ongoing data collection and analysis are expected to elucidate further the interplay between indoor environmental conditions and sleep physiology. These findings highlight the importance of considering environmental optimization as a component of sleep health promotion strategies.

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ESTeeM: Burden of Menopause-Related Sleep Disturbances, Quality of Life, and Work Productivity in a Real-World Setting

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Introduction: Sleep disturbances affect up to two-thirds of menopausal women, elevating the risk of cardiometabolic, cognitive, and mental health issues and affecting quality of life (QoL). Menopausal hormone therapies, antidepressants, and hypnotics only provide transient or incomplete relief and/or can raise safety/tolerability concerns. The Evaluation of Sleep disturbances in Menopause (ESTeeM) is an observational cohort study quantifying the burden, unmet need, and treatment patterns of women with menopause-related sleep disturbances.

Materials and methods: ESTeeM is recruiting up to 1,000 U.S. women aged 40–65 years in natural or surgical menopause who self-report sleep disturbances. For 28 days, women complete a Daily Morning Diary (DMD; sleep- and vasomotor symptoms [VMS]-related questions). At baseline (study entry), Day 14, and Day 28, women complete surveys including the Insomnia Severity Index (ISI), the Menopause-specific Quality Of Life (MENQOL) questionnaire, and the menopause-specific Work Productivity and Activity Impairment (mWPAI) questionnaire. Here, we conducted an interim analysis to characterize sleep disturbances assessed with the DMD across the first week, along with MENQOL and mWPAI at baseline. Unless otherwise stated, results are reported as mean (standard deviation).

Results: This analysis included 404 women (age: 55.0 [5.3] years; age at menopause: 48.2 [7.3] years); 88.1% had natural menopause and 11.9% surgical. Overall, 71.8% were white, 13.4% Black/African American, 10.6% Asian, 3.2% other races, and 1.0% multiracial. Over half (61.4%) of the sample did not use any intervention (pharmacological or non-pharmacological) for sleep, while 34.4% used supplements (e.g., melatonin [45.3%], *Valeriana officinalis* [1.4%]), 5.9% menopausal hormonal therapies, 3.2% sedating antidepressants or other psychiatric agents, 2.7% Z-drugs, and 2.0% benzodiazepines (data points not mutually exclusive).

Week 1 DMD VMS data (n=348) revealed that 76.7% reported nocturnal VMS on an average of 4.0 (2.1) nights/week with 3.9 (13.4) episodes/night; 63.8% reported daytime VMS on an average of 3.8 (2.2) days/week with 4.3 (13.9) episodes/day.

Week 1 DMD sleep data (n=347) revealed that 85.9% of women reported ≥1 sleep disturbance(s), with an average of 2.3 (1.2) awakenings per night. Sleep onset latency was 51.0 (44.2) minutes, wakefulness after sleep onset was 41.7 (30.9) minutes, total sleep time was 6.3 (1.4) hours across 8.4 (1.3) hours in bed, and sleep efficiency was 75% (14%).

Of 313 women who completed the ISI, 44.4% reported sub-threshold insomnia, 39.3% had clinical insomnia (33.2 % moderate, 6.1 % severe), and 16.3 % had no clinically significant insomnia. MENQOL total score (n=319) was 3.7 (1.43). Among women completing the mWPAI questionnaire (n=313), general activity impairment was 30.8% (25.2%). Of the 73.2% who reported current employment,

absenteeism was low (2.9% [9.1%]), but productivity losses were evident with work impairment at 28.7% (25.7%) and presenteeism at 27.3% (24.3%).

Conclusions: In a cohort of menopausal women with sleep disturbances, nighttime awakenings were common; sleep efficiency was low, and ~40% had clinical insomnia. Menopause symptoms moderately impacted health-related QoL, and impaired activity and work productivity. Further analyses will investigate smartwatch-derived sleep metrics, treatment patterns (e.g., usage, adherence, and satisfaction), and subgroup comparisons by VMS status and medication use.

Estimating Apnea-Hypopnea Index from Short-Duration Electrocardiograms

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Introduction: Sleep apnea, a disorder characterized by recurrent upper airway collapse during sleep. This leads to intermittent hypoxia, sleep fragmentation, and notable cardiovascular issues. The Apnea-Hypopnea Index (AHI), typically assessed via overnight polysomnography, is crucial for diagnosis. This study explores the feasibility of estimating AHI using just one hour of single-channel electrocardiogram (ECG) data.

Materials and methods: The Physionet SA-ECG database was utilized for this study. This open-access dataset comprises 70 ECG recordings, typically 8 hours long, with expert-labeled apnea annotations based on simultaneously recorded respiration signals. These recordings are categorized into groups reflecting varying apnea severity (Class A: AHI ≥ 10 and at least 100 minutes of apnea; Class B: AHI ≥ 5 and 5-99 minutes of apnea; Class C: AHI < 5 and less than 5 minutes of apnea). The ECG signals in the database are sampled at 100 Hz. For this study, a one-hour segment from these overnight recordings was used to demonstrate the efficacy of short-duration analysis.

Our methodology involves extracting heart rate variability (HRV) from short-duration ECG recordings and utilized Heart Rate Fragmentation (HRF), a novel measure of signal nonlinearity, alongside conventional frequency-domain features to characterize apnea. An XGBoost classifier was then trained on these features to estimate AHI. We employed a leave-one-out cross-validation approach to evaluate performance. Additionally, a correlation analysis was conducted to assess the relationship between our short-duration HRV features and the overnight clinical apnea scores.

Results: The results indicate that HRV dynamics effectively characterizes apnea severity even with limited signal duration ($p < 0.05$). Both short-duration HRF ($p > 0.4$) and frequency-domain features ($p < 0.6$) showed significant correlation with long-term AHI scores ($p < 0.05$). In the classification task, these features, combined with the XGBoost classifier, resulted in a F1-score of 93.55%.

Conclusions: In conclusion, we demonstrate that HRV analysis with HRF metrics, provides a reliable and efficient method for early detection and severity assessment of sleep apnea. This proposed framework, leveraging short-duration ECG data and machine learning, has strong potential for scalable and accessible sleep apnea screening in both clinical and home-based settings.

Evaluating Obstructive Sleep Apnea as a Predictor of Postoperative Bleeding in Chronic Rhinitis Surgery

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Introduction: According to published literature, patients diagnosed with obstructive sleep apnea (OSA) are at a higher risk of postoperative complications, such as adverse cardiac events, respiratory complications, reduced oxygen saturation, and an increased likelihood of admission to the intensive care unit (ICU). Additionally, patients with sleep-disordered breathing often experience nasal obstruction and seek surgical solutions. However, the relationship between obstructive sleep apnea and the risk of complications following nasal obstruction surgery has not been previously explored.

Materials and methods: From March 2023 to July 2024, records were reviewed for patients diagnosed with chronic rhinitis lasting over six months who underwent nasal obstruction surgery after showing poor response to one month of treatment with corticosteroid nasal sprays or oral medications. These patients experienced significant impacts on their quality of life or sleep quality. The study evaluated the treatment outcomes, complications, and risk factors one month after undergoing surgery for chronic rhinitis. The surgical procedure primarily involved inferior turbinate radiofrequency surgery. Variables analyzed included age, sex, body mass index (BMI), allergic rhinitis scores (24-hour reflective total nasal symptom score, rTNSS), nasal obstruction scores (nasal obstruction symptom evaluation scores, NOSE), hypertension, OSA, medication-induced rhinitis, history of nasal surgery, and concurrent procedures such as septoplasty, posterior nasal nerve ablation, adenoidectomy, tonsillectomy, and soft palate surgery.

Results: A total of 325 patients undergoing nasal surgery for CR were included, with 48 patients (14.8%) classified as having OSA and 277 patients (85.2%) as non-OSA. The mean age was similar between groups (41.1 ± 7.7 vs. 38.9 ± 10.0 years, $p = 0.147$). Males constituted a significantly higher proportion in the OSA group compared to the non-OSA group (91.7% vs. 62.5%, $p < 0.001$). BMI was also higher in the OSA group (28.9 ± 4.9 vs. 25.1 ± 4.3 kg/m², $p < 0.001$). Preoperative rTNSS scores averaged 6.3 ± 2.8 , improving to 2.5 ± 2.0 postoperatively (60.3%, $p < 0.001$). NOSE scores improved from 11.5 ± 4.1 to 2.7 ± 3.7 (76.5%, $p < 0.001$), with nasal obstruction-related sleep disturbance scores improving by 79.43% ($p < 0.001$). Diagnosed as OSA (OR, 5.105; 95% CI, 1.222–21.328; $p = 0.025$) and hypertension (OR, 5.809, 95% CI, 1.134–29.744; $p = 0.035$) were identified as independent risk factors for major epistaxis-related complications in our study cohort. OSA patients also exhibited significantly higher overall complication rates (22.9% vs. 4.3%, $p = 0.005$), epistaxis events (18.8% vs. 3.6%, $p = 0.012$), and major epistaxis (14.6% vs. 1.8%, $p < 0.018$). Both OSA and non-OSA groups showed significant postoperative symptom improvement in rTNSS and NOSE scores ($p < 0.001$).

Conclusions: Obstructive sleep apnea and hypertension were identified as significant risk factors for postoperative complications and bleeding following chronic rhinitis surgery, with no significant association observed between these factors and the preoperative severity of rhinitis or the inclusion of additional surgical procedures during the operation. Chronic rhinitis surgery effectively improves poor nighttime sleep quality in patients with nasal obstruction, with significant differences observed as early as one month postoperatively.

Evaluating the Effectiveness of Awareness of Environmental Stressors on Improving Sleep Quality in a Hot Climate Region: A Longitudinal Randomised Controlled Trial

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Introduction: Environmental stressors, such as temperature and light, can negatively affect occupants' health and wellbeing. Likewise, sleep can be affected by various environmental stressors; particularly hot temperatures often disturb sleep. However, evidence-based interventions on behavioural and psychological adaptation (BPA) in the context of sleep and the built-environment remain scarce.

Therefore, this study aimed to test the effectiveness of an educational intervention that increases awareness of managing environmental stressors at bedtime to improve sleep quality through BPA.

Materials and methods: A randomised-controlled field study including a BPA intervention took place from August to November 2024 in Cyprus, where daily maxima were predicted to exceed 35°C (World Meteorological Organization). The intervention comprised a 3-hour awareness session, aimed at educating participants about the significance of sleep and strategies for improving sleep quality in the presence of environmental challenges. Key topics included the impact of elevated temperatures, indoor and outdoor noise, the role of the circadian rhythm in regulating sleep, and the effects of indoor air quality.

The intervention group (IG) received the awareness session before data collection and monitoring of their sleep environment, while the control group (CG) received the session after data collection. Both groups received wearable sensors (ActiGraph wGT3X-BT® for sleep quality and iButton® for

peripheral skin temperature) and stationary sensors (MSR145® and VOLTcraft DL-161S for environmental conditions) to wear/install in their bedrooms, for five consecutive days. The primary outcomes were objective sleep quality measures: sleep onset latency, sleep efficiency, total sleep time, wake after sleep onset, and the sleep fragmentation index. Concurrently, as secondary subjective measures around sleep and awakening time, participants completed behavioural and psychological questionnaires (such as restoration, alertness, bedtime activities and routine), as well as perception and comfort questionnaires for each environmental aspect (thermal, visual, acoustic, and olfactory).

Results: Thirty-two adults (14 females, 2 non-binary) were randomly assigned to the CG (n=16; mean±SD; age: 32.3±9.7 years, body mass index [BMI]: 26.1±4.9 kg/m², Chronotype: 04:20±78.2) or the IG (n=16; age: 36.3±13.2 years, BMI: 23.9±3.9, Chronotype: 03:48±102.5). At baseline, sleep quality was measured employing the Pittsburgh Sleep Quality Index (CG: 7±3, IG: 5.6±2, p=0.152) and Snyder et al.'s (2018) single-item subjective sleep quality questionnaire (CG: 5.8±2, IG: 7.1±1.7, p=0.026). The highest recorded outdoor temperature over the study period was 35.6°C (23.2±4.3) on 14. and 28.09.2024 at 13:20 and 12:30, respectively. While the lowest recorded temperature was 12.9°C on 06.11.2024 at 02:15. Relative humidity ranged from 19% to 97% (59±18).

During the congress, we will present our findings on the objective sleep data, the behavioural and psychological variables, and the differences between the two groups, alongside a QR code for accessing the awareness material.

Conclusions: By evaluating the effectiveness of raising awareness about the link between environmental stressors and sleep quality in hot climates, the present study could guide practical strategies for addressing sleep disturbances in hot climates.

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Evaluating the Sleep Cancer Rest (SleepCaRe) Trial for Improving Health-Related Quality of Life (HRQoL) in Women Undergoing Chemotherapy for Breast Cancer - A Randomised Controlled Trial

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Introduction: Sleep disturbances are prevalent among women undergoing chemotherapy for breast cancer and impact health-related quality of life (HRQoL). Few trials have evaluated sleep-targeted interventions in this population using preference-based HRQoL outcomes. We present a pre-registered, secondary outcome of HRQoL for sleep intervention trial among women with early or advanced breast cancer receiving chemotherapy.

Materials and methods: This six-week, remotely delivered, randomised controlled trial compared Cognitive Behavioural Therapy for Insomnia (CBT-I), Bright Light Therapy (BLT), their combination (CBT-I+BLT), and an active control (Sleep Hygiene Education, SHE) on self-reported HRQoL as measured by the PROMIS Preference (PROPr) score (-0.022 "All Worst", 1.0 "Full health"). All interventions involved emails, a therapist-assisted consultation, and midpoint check-in tailored to cancer patients, providing varying therapeutic and psychoeducational content (e.g., CBT-I's behavioural/cognitive strategies, BLT's structured morning light exposure). Assessments occurred at baseline, midpoint (3-weeks), post-intervention (6-weeks), and follow-ups (3-months; 6-months).

Results: 219 women receiving chemotherapy (Mean 50.7y) were recruited. At baseline, average HRQoL was low (PROPr score = 0.27). Main effect analyses showed that CBT-I led to a significant improvement from baseline to post-intervention (0.06 point-change, p = .012; SMD = 0.34), though

these gains were not sustained at six-months follow-up ($p = .096$). BLT showed no significant effects at either timepoint ($p \geq .519$), and no CBT-I*BLT interaction was observed (all $p \geq .759$). From baseline to post-intervention, within-group analyses showed the largest HRQoL improvements in the CBT-I (0.14 point-change, $p < .001$; SMD = 0.83) and CBT-I+BLT groups (0.14 point-change, $p < .001$; SMD = 0.79), while smaller gains were seen in SHE (0.09 point-change, $p = .003$; SMD = 0.53) and BLT groups (0.07 point-change, $p = .024$; SMD = 0.42).

Exploratory analyses suggested treatment effects may differ by cancer stage and insomnia severity. In metastatic cancer patients, neither CBT-I nor BLT showed significant main effects (all $p \geq .210$), though both yielded small-to-moderate effect sizes with BLT yielding a slightly larger improvement in HRQoL than CBT-I at both timepoints. Significant within-group improvements were observed across all groups at post-intervention only (all $p \leq .013$). In individuals with clinically significant insomnia (ISI ≥ 15), CBT-I significantly improved HRQoL at post-intervention ($p = .014$, SMD = 0.51), and BLT had no meaningful change (SMD = 0.01). Significant within-group improvements were observed across CBT-I and CBT-I+BLT groups at post-intervention only (both $p \leq .034$). In individuals with subthreshold insomnia (ISI ≤ 14) showed no significant main effects (all $p \geq .212$), though significant within-group improvements were observed across all groups at post-intervention (all $p \leq .038$).

Conclusions: CBT-I improves HRQoL in women undergoing chemotherapy for breast cancer, with effects strongest post-treatment. These findings highlight the importance of addressing sleep disturbances in cancer care. Benefits were particularly notable in patients with clinically significant insomnia symptoms, suggesting CBT-I may be especially effective for this subgroup. These findings point to the value of brief, targeted interventions during active treatment. Future research should explore strategies for specific groups, including patients with metastatic disease or varying insomnia severity.

Exacerbated sleep disorders, delayed sleep pattern, and effectiveness of online interventions during COVID-19 pandemic

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Introduction: COVID-19 pandemic and its following social response have been posing extra stress on sleep health and new challenges to sleep health management. This study aims to evaluate the direct and indirect association between COVID-19 and sleep health, including obstructive sleep apnea (OSA), insomnia, and sleep patterns.

Materials and methods: First, standard procedures for meta-analysis were performed. Weighted Mean Difference (WMD) and Odds Ratio (OR) were respectively applied to assess the severity and risk differences of sleep disturbances between the compared groups. OR was also applied to assess COVID prognosis risk differences between those with sleep disturbances and controls. p value of <0.05 is defined as significant. Then, questionnaires were collected from mainland China about COVID-19 infection and sleep quality from January 2023 to March 2023. Also, impairment and related factors for sleep quality before, during, and after COVID-19 infection were identified.

Results: COVID-19 infection is associated with a higher risk for OSA (OR=1.22, $p=0.0002$) and insomnia (OR=1.82, $p=0.01$). Among COVID-19 patients, those comorbid with OSA were at higher risk for worse clinical outcomes (OR=2.18, $p<0.00001$). Additionally, , COVID-19 lockdown is associated with delayed sleep pattern, exacerbated insomnia (Insomnia Severity Index (ISI), WMD=1.44, $p<0.0001$). Despite the pandemic, online Cognitive Behavioral Therapy for Insomnia (CBTI) improves overall insomnia severity by ISI (WMD=-4.34, $p <0.00001$), insomnia symptoms, and psychiatric health. COVID-19 infection significantly reduced sleep quality ($p<0.001$), and it did not recover to pre-infectious level even after recovery from COVID-19 infection ($p<0.001$). Among the participants, risk factors for decreased sleep quality included age, gender (female), poor lifestyle habits such as smoking and drinking, risk associated with comorbid severe COVID-19.

Conclusions: There is a bidirectional association between the COVID-19 pandemic and sleep disturbances. Online CBTI is effective in improving insomnia during the pandemic.

Examining the Associations of Sleep Duration and Disturbances With Hypertension in Metropolitan Cities in India

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Introduction: In South Asia, rapid and unplanned urbanization coupled with globalization has led to lifestyle changes characterized by high intake of calorie-rich foods, reduced physical activity, and elevated psychological stress, thereby increasing the risk of overweight, hypertension, diabetes, and cardiovascular diseases. Sleep duration and disturbances are potential risk factors for hypertension. Although hypertension is highly prevalent in South Asia, there is limited knowledge about how these sleep-related factors are associated with it in this region.

Materials and methods: This study utilized cross-sectional data from the baseline survey of the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS), which recruited representative samples of adults aged over 20 years from Delhi and Chennai (India) between 2018 and 2021. Hypertension was identified based on either self-reported treatment or measured blood pressure (BP) readings of $\geq 140/90$ mm Hg. Information on usual sleep duration, insomnia, and snoring was gathered through the 'Sleep Habits Questionnaire,' while excessive daytime sleepiness (EDS) was assessed using the Epworth Sleepiness Score. Logistic regression and linear regression analyses were conducted with hypertension and BP as the outcome variables, respectively. Covariates included age, gender, education level, wealth index, family history of hypertension, and body mass index (BMI). Multiple imputation methods were employed to address missing data.

Results: The prevalence of hypertension in the study population was 34.7%, with an average sleep duration of 8.2 hours. Insomnia, snoring, and excessive daytime sleepiness (EDS) were reported by 13.6%, 28.7%, and 4.6% of participants, respectively. After adjusting for covariates, both moderate and habitual snoring were found to be significantly associated with higher odds of hypertension (odds ratios [OR] of 1.18 and 1.47, respectively). Additionally, rare, occasional, and frequent insomnia were linked to elevated odds of hypertension (ORs of 1.41, 1.39, and 1.34, respectively). No significant associations were observed between sleep duration or EDS and hypertension.

Conclusions: Moderate and habitual snoring were highly prevalent and showed a positive association with hypertension, particularly among young adults and women living in metropolitan areas of South Asia. Insomnia at any severity level was also linked to increased odds of hypertension. Further research, particularly robust longitudinal studies, is needed to better understand the relationship between sleep-related factors and hypertension in this population.

Experts' Perceptions of the Potential of Exergames to Improve Sleep Quality: An Exploratory Analysis

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Introduction: Promoting regular physical activity is recognized as an effective approach to improving sleep health and overall well-being. Exergames, which combine physical activity with digital interactivity, have been proposed as an innovative strategy to encourage consistent exercise engagement. While these technologies are gaining traction as tools to support both physical and mental health, their effectiveness in enhancing sleep quality, particularly in comparison to traditional exercise modalities, remains insufficiently explored. This study aimed to investigate expert perceptions of the potential of exergames to improve sleep quality, with particular attention to differences across professional backgrounds and years of experience in the field.

Materials and methods: A cross-sectional exploratory study was conducted using an online questionnaire (Google Forms®) administered to experts identified through a bibliometric analysis of

databases (PubMed, Scopus, and Web of Science) focused on the intersection of physical activity and sleep research. Quantitative data were analyzed using descriptive statistics, chi-square tests, the Mann-Whitney U and Kruskal-Wallis tests, along with effect size estimates (Cohen's d). For qualitative data, thematic clustering of open-ended responses was performed to identify recurring physiological mechanisms attributed to exergames with the potential to enhance sleep health. The study was approved by the Research Ethics Committee of São Paulo State University (UNESP) under protocol number CAAE: 87225025.8.0000.5465.

Results:

A total of 15 experts from diverse fields—primarily Exercise Science (40%), Sleep Medicine (33%), and Neuroscience (27%)—participated in the study. Most held a PhD (73.3%) and had over 10 years of experience (73.3%) in the sleep-exercise interface. The majority had published on the topic (86.7%), were familiar with exergame literature (66.7%), and 46.7% had practical or academic experience with exergames. Overall, 76.9% considered exergames potentially effective for improving sleep. Experts with >10 years of experience were significantly more likely to endorse efficacy ($p = .032$, $d = 0.59$). Frequently cited mechanisms included reduced arousal, shorter sleep onset latency, stress modulation, and mood improvement. Thematic clustering of open responses identified three profiles: (0) psychobiological modulation, (1) neuroendocrine/circadian regulation, and (2) general physical benefits. A heatmap showed Exercise Science experts aligned with clusters 0 and 1, while Sleep Medicine experts were more associated with cluster 2, suggesting disciplinary differences in perceived mechanisms.

Conclusions: Most experts perceive exergames as a potentially effective tool to improve sleep quality, especially through mechanisms related to arousal reduction, mood, and circadian modulation. These perceptions vary by academic background and years of experience. Findings support further investigation into exergames as a non-pharmacological intervention for sleep, and highlight the need to tailor approaches based on user profiles and professional guidance in shaping evidence-based strategies for integrating exergames into sleep health promotion.

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Exploring Barriers to Sleep Hygiene Among Chronic Short Sleepers Using Reflexive Thematic Analysis: A Pilot Study

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Introduction: Sleep hygiene (SH), a set of behavioural and environmental practices conducive to good sleep is essential for achieving sufficient and restorative sleep (Irish et al., 2015). For individuals experiencing chronic short sleep, maintaining good SH is particularly important because limited sleep duration already hinders restorative processes. Drawing on the Health Belief Model (HBM; Becker et al., 1974) and Social Cognitive Theory (SCT; Bandura, 1977), various barriers may hamper the implementation and execution of SH practices effectively. Therefore, the current pilot study aimed to uncover a) the most common barriers to SH in chronic sleepers, and b) whether some barriers are more easily addressed than others.

Materials and methods: 11 chronically short sleepers ($M_{age} = 25$, $SD = 1.5$) completed sleep hygiene (SH) and extension (SE) interventions carried out in two sessions conducted by one of two trained researchers in motivational interviewing. In the first (T1) session, a) the SH intervention aimed to identify and address any potential barriers (e.g., late-night media use) to good sleep and to provide SH psychoeducation. Conducted four (± 1) days after the SH intervention (T2), b) the sleep extension (SE) intervention aimed to review the contents and goals of the SH intervention, to provide further guidance on SH issues, and to set a 90-minute sleep extension schedule for the following week. To evaluate the most common barriers, SH goals, and whether one is able to address poor SH, we adopted

the six-phase qualitative reflexive thematic analysis (Braun & Clarke, 2020) due to the narrative nature (i.e., notes made by experimenters) of the interview data with our small sample size. The intervention notes were first translated into English and formatted. The cleaned data was then assigned labels based on the identified theme of the content, with this step repeated two more times to reduce redundancies (i.e., conceptual overlap) by combination or removal of theme categories.

Results: The most commonly reported barrier to SH and sufficient sleep was media use (i.e., late-night use; in-bed use right before sleep). While most behavioural barriers were addressed at T2 (e.g., caffeine intake; late-night media use), factors associated with one's sleep setting (e.g., noisy surroundings; small and messy bedroom; late-night interaction with roommates) appear more persistent and difficult to modify (see [Table 1](#)).

Conclusions: Using thematic analysis, we identified late-night media use as the most common and modifiable barrier, while environmental factors related to sleep setting might be more resistant to change. Our findings, aligned with the HBM and SCT models, underscore the importance of setting personalised and specific goals to effectively address barriers, as evidenced by the reported reduction or elimination of behavioral barriers following the SH intervention. These results highlight the need for future SH interventions to personalize goal-setting strategies and to target key barriers to action.

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Exploring Social Determinants and Gender Variations in Sleep Health Disparities: Initial Findings from a Descriptive Study in Hong Kong 2024

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Introduction: Sleep health is influenced by social and structural factors such as income, housing, commuting, and noise. This study examines sleep duration, sleep latency, and sleep adequacy and associated factors in Hong Kong, the city with high income inequality and the lowest per capita living space in the world.

Materials and methods: An anonymous, cross-sectional telephone survey was conducted on adults in Hong Kong, 2024 (n=500). Descriptive statistics (mean, standard deviation, and frequencies) summarized sleep data: (1) sleep duration, (2) time to fall asleep (sleep latency), and (3) sleep adequacy. Associated sociodemographic (e.g. sex, income), behavioural (e.g. exercise habits, commuting time) and environmental factors (e.g. housing type, ambient noise, residential area) were also examined to identify patterns in sleep disparities using multivariable regression analyses.

Results: Preliminary findings show that sociodemographic factors are significantly associated with sleep. In particular, females and people with lower income reported shorter sleep duration (mean < 6.1 hrs), longer time to fall asleep (mean > 36 minutes), and lower sleep adequacy (mean < 7.6 hrs) than higher income groups and males (p<0.05). Noise disturbances were more also common in lower-income groups, worsening sleep outcomes. Behavioural and environmental factors also contribute significantly to poor sleep quality (p<0.05).

Conclusions: Targeted interventions are required to address sleep inequalities in those sociodemographic groups with poor sleep such as women and lower income individuals. Since personal and environmental factors contribute to sleep health disparities in Hong Kong, there is a need for sleep interventions that go beyond the personal level. As sleep is a vital component of good health, sleep health should be included in public policy discussions in high population density, urban environments.

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Exploring the Bidirectional Causal Associations between Sleep Traits and Metabolomic Profile in Humans

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Introduction: Unhealthy sleep patterns are common phenomena which may lead to a spectrum of adverse cardiometabolic outcomes. Metabolites play pivotal roles in the relevant underlying mechanisms, yet the causal associations between sleep and metabolome in humans remain unclear.

Materials and methods: This study applied one-sample Mendelian randomization (MR) to explore the relationship between sleep traits (sleep duration per day, short sleep duration (≤ 6 h), long sleep duration (≥ 9 h), and insomnia) and 249 metabolites among 166,436 participants from UK Biobank. Initially, the two-stage least squares approach was performed to explore causality. Subsequently, inverse-variance weighted and complemented methods were used as sensitivity analysis to further test the robustness of the results. Reverse MRs from each metabolites to sleep variables were also conducted.

Results: Genetically predicted insomnia was causally associated with level of most lipids and led to increased levels of acetoacetate, glycoprotein acetyls, and decreased levels of citrate. Genetically predicted sleep duration was causally associated with increased average diameter for low density lipoprotein particles. Short sleep duration caused an increased the level of triglycerides in very low density lipoprotein subclass, apolipoprotein B to apolipoprotein A1 ratio and a decreased level of high density lipoprotein. We found no causal evidence for the effects of metabolites on any sleep variable.

Conclusions: Our study found that insomnia may lead to a wide range of metabolic disturbances, particularly in lipid metabolism, with short sleep similarly impacting lipid metabolic processes. This suggests that sleep traits may cause adverse outcomes through certain metabolic pathways.

Exploring the Impact of Sleep Hygiene Knowledge and Practices on Sleep Health: A Cross-Sectional Survey of Hong Kong Adults, 2024

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Introduction: Sleep health, a critical component of overall well-being, has previously been closely linked to sleep hygiene (SH). The study aims to investigate how SH knowledge and actual SH behaviors, along with self-reported health status, influence sleep quality outcomes across different age groups and demographics among Chinese adults residing in a high living density region.

Materials and methods: An anonymous, cross-sectional, telephone survey was conducted on adults from Hong Kong (n=500) in 2024. The study obtained information about the participant's sociodemographic information, living situation, self-rated health, SH knowledge, SH behaviors (using Sleep Hygiene Index instrument). Multiple linear regression analysis, controlling for sociodemographic factors, was used to explore how these factors predicted self-reported sleep quality, as assessed with the Pittsburgh Sleep Quality Index.

Results: Over the past month, the mean overall sleep quality score (scored 0 to 3, 3 indicating poor sleep quality) was 1.2 with a standard deviation (SD) of 0.77. Their average sleep duration was 6.36 hours (SD = 1.28). The mean SH knowledge score was 11.1 out of maximum 14 points (SD = 1.74), and the mean SH behaviors score was 9.98 points out of 26 (SD = 5.13). Multivariable analysis showed that individuals with higher SH knowledge scores reported better sleep quality, while those with poorer SH behaviors scores had worse sleep outcomes. Self-rated mental health, including stress, anxiety, and depression, significantly predicted sleep quality, with poorer mental health linked to worse sleep outcomes ($p < 0.05$). Additionally, older age, female gender, and diagnosed sleep apnea were significantly associated with worse sleep health ($p < 0.05$). Furthermore, the SH knowledge score ($B = 0.65$, $p < 0.05$) was a significant predictor of SH behaviors score, indicating that higher SH knowledge scores were associated with better SH behaviors scores.

Conclusions: Both personal factors, such as SH knowledge, and health factors, contribute to sleep health disparities. As SH knowledge predicts actual SH behaviors scores, enhancing this knowledge should be a priority in health promotion. Future interventions should aim to improve sleep hygiene through education while also addressing broader issues like mental health and sleep disorders.

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Exploring the Influence of Emotion Regulation on Emotional Naps: A Preliminary Study

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Introduction:

Previous studies identified five types of naps: dysregulative, replacement, emotional, appetitive, and mindful naps. Among these, emotional naps are taken explicitly to enhance mood, alleviate stress, or avoid particular behaviors. While the mutual relationship between sleep and emotions is well-established, existing research predominantly emphasizes naps' capacity to enhance mood rather than explicitly examining their emotion-regulation properties. Addressing this gap, the current research aimed to investigate the phenomenon and emotional regulatory effects of emotional naps within a Taiwanese context.

Materials and methods:

Participants were initially recruited through an online survey. This initial screening phase collected comprehensive data including demographic information, sleep and nap habits, napping motivations, chronotype, depression (CES-D), perceived stress (PSS), coping strategies (Brief COPE), and emotional states (assessed via the Self-Assessment Manikin, SAM scale). From this initial pool, 22 individuals were selected to participate in a subsequent, more intensive one-week experimental phase designed to examine the direct effects of emotional regulation. Inclusion criteria for this experimental phase were stringent, ensuring a focused and relevant sample. Participants were required to: (1) self-report taking emotional naps, (2) be non-shift workers who did not nap after dinner, (3) have no history of major physiological diseases or significant surgical history, (4) be free from severe psychiatric conditions (e.g., schizophrenia, bipolar disorder) or psychotic symptoms (e.g., hallucinations, delusions), (5) report no sleep disorders, and (6) not be continuously using illicit substances or non-prescription medication. During the one-week experimental period, participants maintained daily sleep diaries and wore actigraphy devices continuously. Emotional states were recorded twice daily using the SAM scale at 1 PM and 5 PM, with participants additionally noting any occurrences of emotional naps. SAM scale indicators included pleasure, arousal, dominance, stress, and fatigue, each ranging from 1 to 5.

Results:

Nonparametric analyses (Wilcoxon signed-rank test) indicated that emotional naps significantly reduced fatigue ($Z = -2.174$, $p = .03$; pre-nap: $M = 3.14$, $SD = 0.52$; post-nap: $M = 2.70$, $SD = 0.57$), but showed no significant differences in pleasure, arousal, dominance, or stress. In contrast, in non-emotional nap conditions, a significant increase in dominance was observed post-nap ($Z = -2.04$, $p = .04$; pre-nap: $M = 2.48$, $SD = 1.02$; post-nap: $M = 2.93$, $SD = 0.86$), while no significant changes were found in pleasure (pre: $M = 2.29$, $SD = 0.64$; post: $M = 2.43$, $SD = 0.77$), arousal (pre: $M = 3.19$, $SD = 0.87$; post: $M = 2.92$, $SD = 1.16$), stress (pre: $M = 2.04$, $SD = 0.82$; post: $M = 2.28$, $SD = 0.76$), or fatigue (pre: $M = 2.49$, $SD = 0.71$; post: $M = 2.32$, $SD = 0.45$).

Conclusions: Emotional naps effectively alleviated fatigue but did not significantly influence emotional or stress regulation. Due to the reliance on self-reported home-based experiments in this study, confounding factors cannot be entirely excluded. Future research is encouraged to further elucidate the nuanced impacts and underlying mechanisms of emotional naps.

Exploring the Sleep of Young Children in Aotearoa New Zealand: Associations with Ethnicity and Maternal Depression in and Beyond the Perinatal Period

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Introduction: Sleep plays a vital role in children's health. Sleep development is influenced by a complex interplay of biopsychosocial factors. There is emerging evidence to suggest perinatal depression (PND) is one such factor, but further investigation is needed. In Aotearoa/New Zealand, ethnic inequities in the social determinants of health produce sleep health disparities that are evident from preschool age through adulthood; it is currently unclear whether they exist in infants. To address these research gaps, secondary data from the *Moe Kura: Mother and Child, Sleep and Wellbeing in Aotearoa/New Zealand* study (Moe Kura) were analysed in two studies. Kaupapa Māori research principles informed the study designs.

Materials and methods: First, sleep health equity, socio-ecological factors associated with infant sleep, and the characteristics of mother-perceived infant sleep problems were investigated using data from 383 Māori and 702 non-Māori mother-infant dyads at 12 weeks postpartum. Next, longitudinal relationships between maternal depression and infant and pre-schooler sleep health in 262 Māori and 594 non-Māori dyads were examined using data collected during pregnancy, 12 weeks postpartum, and 3 years post-birth. Multivariable and ordinal logistic models assessed the impact of different socio-ecological factors on infant sleep. Binary logistic models examined longitudinal associations between PND and infant and preschooler sleep, adjusting for key socio-demographic variables.

Results: Key developmental markers of infant sleep did not differ by maternal ethnicity. There were some ethnicity-based differences in sleep location. Bed-sharing and several socio-demographic factors were related to different dimensions of infant sleep and mother-perceived sleep problems. Bivariate associations were found between prior and concurrent depressive symptomology and many of the infant and pre-schooler sleep outcomes. Prenatal depressive symptoms remained independently associated with shorter-than-recommended sleep durations in preschoolers after controlling for key covariates.

Conclusions: Results show sleep at 12 weeks is highly variable and is associated with numerous socio-ecological factors. Sleep appears to be one pathway by which PND confers risk for poor child health outcomes. Findings support the need for more and better perinatal psychological services.

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Eyes Wide Open: Understanding the Barriers, Facilitators, and Motivators to Adolescent Sleep through Photovoice

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Introduction: Poor sleep among adolescents is a growing public health concern. At present, efforts to improve adolescent sleep have largely focused on individual-level behaviour change, with limited population level impact. Public health efforts to improve sleep, such as school-based sleep education, have demonstrated mixed-effectiveness and implementation challenges in real-world settings. Existing interventions have also failed to engage stakeholders in their development, potentially limiting their effectiveness and acceptability. The aim of this study was to engage adolescents, parents, and teachers through Photovoice, to understand the barriers and facilitators to adolescent sleep, as well as motivating factors to promote healthy sleep among adolescents. Photovoice is Community-Based Participatory Research method that gives voice to and empowers participants, providing unique insights into health issues, and promotes critical dialogue for change.

Materials and methods: This study was conducted in three schools across Scotland between January – December 2024. Forty-two adolescents aged 11 – 15 years (M = 13.1, 56% female) were conveniently sampled to participate in a photography exercise, participatory analysis workshop, photo-elicitation interview (n = 36) and share their photos at a school exhibition. Focus groups were also conducted with teaching staff (n = 14) and parents (n = 10). Thematic analysis of interview/focus group data was conducted, guided by themes from the participatory analysis, along with narrative analysis of texts, workshop discussions and exhibition feedback. Themes were inductively analyzed across the

socioecological model to identify leverage points and potential intervention targets to improve adolescent sleep.

Results: Factors influencing sleep identified among adolescents, parents, and teachers included societal factors (social norms, curriculum, school start times, and public health policy), physical and social environmental factors (school, home, digital, physical and social spaces), and individual factors (lifestyle choices and behaviours, mental wellbeing). Factors motivating young people included knowledge and beliefs about sleep, perceived and experienced benefits of good sleep, and social support.

Conclusions: Using Photovoice gave voice to young people and facilitated engagement and discussion with stakeholders. Potential areas identified for development include earlier school intervention, sleep education, parental support, peer influence, public health messaging, gamification, online spaces, and whole-school approaches to sleep health. Findings highlight the complexity of individual, environmental and societal factors influencing sleep, which will inform the development of a multi-level intervention to promote healthy adolescent sleep.

Factors and associations related to sleep quality in patients with tinnitus

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Introduction: Tinnitus is a phantom symptom of hearing sounds with an unexplained source. The sound could become more perturbing when sleeping in quiet surroundings at night. Many people with tinnitus suffer from sleep difficulties, and some have psychological distress, such as depression and anxiety. Here, we aim to explore the relationship among the severity of tinnitus, sleep quality, and anxiety/depression.

Materials and methods: This prospective cross-sectional study was conducted at Chakri Naruebodindra Medical Institute (CNMI), a medical school hospital, from May 2023 to March 2025. Patients diagnosed with tinnitus aged over 18 years and lasting more than 3 months were enrolled. Data were collected using three standardized questionnaires: Tinnitus Handicap Inventory (THI) for tinnitus severity, Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and Hospital Anxiety and Depression Scale (HADS) for symptoms of anxiety and depression. PSQI is divided further into 3 subscores of sleep efficiency, perceived sleep quality, and daily disturbance. Pure tone audiometry was also administered to objectively evaluate hearing in participants. Correlation analyses among the three questionnaire scores were performed by IBM SPSS statistical software.

Results: A total of 115 participants met the inclusion criteria after careful evaluation and completed the questionnaires. Sixty-one (61) of 115 participants were female (53%) with an average age of 59.44 ± 12.60 years. The tinnitus severity across all participants was predominantly classified as mild handicap severity (18-36 points), with a mean total THI score 31.51 ± 21.64 points. The sleep quality assessment using the PSQI in tinnitus patients shows a mean total PSQI score of 7.84 ± 3.77 , indicating poor sleepers. Additionally, total THI scores showed a positive correlation with the total score of PSQI ($r = 0.19$ p value 0.042). The daily disturbance subscale of PSQI exhibited a strong correlation with total THI scores, with correlation coefficients of $r = 0.280$ (p value 0.002).

In the corner of psychological distress, assessment using the HADS revealed that most participants were within the normal range (76.5% for the anxiety subscale and 82.6% for the depression subscale). However, both the anxiety and depression subscales of HADS showed a positive correlation with tinnitus severity ($r = 0.284$, p value 0.002).

Conclusions: Patients with tinnitus may have an associated impact on sleep quality. This might lead to daily disturbance, which may worsen tinnitus perception and contribute to emotional distress.

Acknowledgments: We would like to thank the patients for their participation in this study. We also extend our gratitude to Miss Oranitcha Chanthawon and Miss Boontharik Boonrod for their dedicated efforts in coordinating the project management.

Factors influencing sleep quality among persons with systemic lupus erythematosus through the lens of Spielman's three-factor insomnia model

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Introduction: Individuals with systemic lupus erythematosus (SLE) have reported poor sleep quality both globally and in China. Previous studies have identified several factors associated with sleep quality in this population. However, the influencing factors remain unclear and inconsistent. According to Spielman's Model (3P Model), existing evidence has primarily focused on predisposing and precipitating factors, while perpetuating factors have been under-explored. Therefore, this study aimed to investigate the predisposing (age, BMI, disease activity), precipitating (fatigue, pain, depression, anxiety), and perpetuating (sleep hygiene practices) factors associated with sleep quality among Chinese individuals with SLE.

Materials and methods: This cross-sectional study was conducted among individuals with SLE recruited from a tertiary hospital in China between December 2024 and April 2025. Data were collected online using a demographic questionnaire, the Chinese version of the Pittsburgh Sleep Quality Index (PSQI), the Fatigue Severity Scale (FSS), the Hospital Anxiety and Depression Scale (HADS), the Sleep Hygiene Practices Scale (SHPS), the Pain Visual Analogue Scale (VAS), and the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). Descriptive statistics and regression analysis were used to analyze the data.

Results: A total of 329 individuals with SLE were included in the analysis. The mean age was 37.15 ± 11.51 . Females accounted for 93.0%. Of these, 210 (63.8%) reported poor sleep quality. Regression analysis revealed that age ($\beta=0.197, p < 0.001$), disease activity ($\beta=0.100, p = 0.022$), fatigue ($\beta=0.113, p = 0.021$), pain ($\beta=0.190, p < 0.001$), anxiety ($\beta=0.221, p < 0.001$), and sleep hygiene practices ($\beta=0.298, p < 0.001$) were significant predictors of sleep quality, explaining 43.2% of the variance in PSQI scores ($F(6, 322) = 40.742, p < 0.001$). Among these, sleep hygiene practices, which are a perpetuating factor, were the most influential predictor, followed by anxiety, age, pain, fatigue, and disease activity.

Conclusions: In line with the 3P Model, this study identified predisposing, precipitating, and perpetuating factors that influence sleep quality among Chinese individuals with SLE. These findings provide valuable insight for designing targeted and effective interventions aimed at improving sleep quality and overall well-being in this population.

Factors influencing the implementation of a general practice nurse-delivered model of care for the assessment and management of chronic insomnia and obstructive sleep apnea: a qualitative study of patient and practice staff perspectives

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Introduction: Long wait times for obstructive sleep apnea (OSA) and limited access to cognitive behavioural therapy for insomnia (CBTi) have led to a re-evaluation of traditional approaches to assessment and management. General practice nurse-delivered models of care have been explored to improve access to best practice care. Randomised controlled trials have demonstrated efficacy of models of care within the context of a controlled setting however they are not yet integrated into routine care. Understanding factors that influence implementation will inform translation into clinical practice. This study explored the barriers and facilitators to the implementation of a nurse-delivered model of care for the assessment and management of chronic insomnia and OSA in an Australian general practice from the perspective of clinicians and patients.

Materials and methods: A qualitative study informed by implementation science theory and phenomenology. Semi-structured interviews were conducted with patients after they were offered or received the model of care and with clinicians as they implemented the model of care. Patients with chronic insomnia were offered nurse-delivered CBTi or digital CBTi. Patients at high risk of OSA were offered a limited channel sleep study for assessment of OSA, followed by APAP titration and CPAP setup if needed. Interviews were audio recorded and transcribed verbatim. Patient data were analysed using a deductive Framework Analysis followed by an inductive thematic analysis to ascertain the barriers and facilitators to implementation from the perspective of patients. Clinician data were analysed using Interpretive Phenomenological Analysis to explore the perspective of clinicians throughout the implementation process and the factors influencing implementation of the model of care.

Results: Interviews were conducted with 31 patients, 13 with a diagnosis of chronic insomnia and 18 at high risk of OSA, and five general practitioners, two practice managers, and one general practice nurse. General practice nurse-delivered models of care for non-complex chronic insomnia and OSA were acceptable to patients and clinicians on the proviso that there is adequate funding for staff to deliver the interventions and that models of care are within the financial reach of patients. General practice staff were motivated to deliver the model of care by improved access to sleep health care and expected benefits for patients. Patient motivation to engage with the model of care was influenced by their perceived severity of their condition and by their trust in the staff delivering the intervention. Fear of the negative implications of not treating OSA motivated patients who were diagnosed with OSA to engage with treatment. A lack of access to government-subsidised CPAP machines in general practice was identified by clinicians as a significant barrier to future translation of the OSA pathway.

Conclusions: This study demonstrates that patients and clinicians are supportive of general practice nurse-delivered models of care and highlights the importance of co-design with patients and clinicians when designing models of care for chronic sleep disorders. Exploring the perspectives of patients and clinicians has identified factors that should be considered in future implementation trials of general practice nurse-delivered models of care for chronic sleep disorders.

Fewer pre-night shift awakenings is associated with positive mood during the night shift among female rotating shift nurses

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Introduction: Sleep plays a vital role in emotional regulation. The circadian misalignment that occurs with night shift work can negatively impact mood and well-being. Nursing can be highly emotionally and demanding work. Failure to control or manage one's mood can affect patient outcomes and the long-term mental health of the nurse. The purpose of this secondary analysis was to explore associations between pre-shift sleep measures and mood reported during the night shift among female rotating shift nurses.

Materials and methods: This study used data from a pilot/feasibility ecological momentary assessment (EMA) study that collected, in real-time, objective sleep and mood from rotating shift nurses for up to 24 days. Objective sleep data, including total sleep time (TST), sleep onset latency (SOL), sleep efficiency (SE), wake after sleep onset (WASO), and number of awakenings, were collected using a Spectrum Plus actigraph worn on the non-dominant wrist. EMA monitoring included up to three random prompts during waking hours that assessed location and mood. Mood responses were classified as positive (e.g., happy, energetic) or negative (e.g., tense, annoyed, frustrated). The associations between pre-night shift sleep measures and the presence of positive (no/yes) and negative mood (no/yes) during the night shift were explored using logistic mixed-effects modeling. Only EMA data collected while participants worked the night shift were used in the analysis.

Results: The female participants who completed the random EMA prompts when working night shift (N = 18) had a mean ($\pm$ SD) age of 27.7 ± 5.0 years and a mean 4.6 ± 4.5 years of night shift experience. Participants completed the random prompts on a mean of 3.7 ± 2.0 night shifts. Mean pre-night shift sleep measures were TST of 434.3 ± 142.5 minutes, SOL of 15.0 ± 19.3 minutes, SE of $83.8 \pm 7.9\%$, WASO of 42.0 ± 31.5 minutes, and 35.1 ± 13.6 awakenings. Negative and positive mood were reported on 50.0% and 23.5% of shifts, respectively. Pre-shift sleep measures were not associated with

reports of negative mood during the subsequent night shift. However, fewer pre-night shift awakenings ($\text{Exp}(B) = -0.841$, 95% CI = $-0.707, -0.961$; $p = 0.009$) were associated with higher odds of reporting a positive mood during the following night shift.

Conclusions: While negative mood was highly prevalent on night shift in this sample, pre-shift sleep measures were not associated with reports of negative mood. This suggests that other, unmeasured, factors such as patient acuity, staffing ratios, or personal issues may be contributing to the presence of negative mood. Reports of positive mood during the night shift were less common but associated with fewer pre-shift awakenings. Healthier sleep may allow night shift nurses to better manage the challenges and issues faced during the night shift, resulting in a more positive mood. Additional studies are needed to further examine the factors contributing to the mood of nurses working the night shift and its impact on patient and nurse outcomes.

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Floor routine to sleep routine: A qualitative inquiry into the retirement of female ex-gymnasts

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Introduction: Currently, little is known about how retirement from youth sport affects wellbeing. Gymnastics is a unique sport, requiring intense devotion from a young age and often results in early retirement, presenting equally unique challenges during the transition out of sport. Previous research has explored female gymnasts' athletic identity, body image, and eating behaviours following retirement, but aspects such as sleep, education, and support post-retirement have been overlooked. This study aimed to identify former elite female gymnasts' challenges regarding sleep post-retirement and how they can be better supported during this transition.

Materials and methods: Critical realism and the biopsychosocial model underpinned this research. Thirteen female ex-gymnasts (mean age = 21.1 ± 3.1 years) from New Zealand participated in one-on-one semi-structured interviews to better understand the challenges they face in relation to their sleep and mental health. Interviews were conducted online via Microsoft Teams or Zoom, with an average duration of 31.5 ± 8.1 minutes. Transcribed interviews were analysed using reflexive thematic analysis techniques.

Results: Four key themes were identified: (i) abuse of the coach-athlete relationship (coach-originated pressures culminate into poor wellbeing); (ii) drastic lifestyle and social change (transition out of sport impacting identity, sleep, and mental health); (iii) inadequate education and support (insufficient resources and support, and misinformation/lack of education surrounding mental health and sleep); and (iv) potential for change (improvement is viable with indication of imminent change).

Conclusions: Findings indicate why mental health and sleep issues occur for gymnasts during and after their sporting careers and highlight why they remain untreated. This research informs how gymnasts can be better supported while competing and transitioning out of the sport. Findings provide preliminary insight into how sleep and mental health are influenced by youth gymnastics participation and potentially other high-performance sports that may result in retirement at an early age.

Acknowledgments: The authors would like to thank the participants who shared their vulnerable stories to improve knowledge and attitudes towards sleep in sport.

Global Sleep Patterns: A Large-Scale Multivariate Analysis of Sleep Determinants and Health Interactions

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Introduction: Sleep is a fundamental biological process essential for cognitive function, emotional regulation, and overall physiological well-being. Despite its importance, modern lifestyles have significantly altered sleep behaviors, leading to widespread concerns about sleep deprivation and

quality deterioration. The proliferation of digital technology, increasing work-related stress, and environmental disruptions have emerged as key contributors to sleep disturbances. While numerous studies have examined sleep patterns, most research has been limited in scope, focusing on specific populations, geographic regions, or singular determinants. A large-scale, comprehensive investigation that incorporates multiple interrelated factors affecting sleep across diverse global populations remains a crucial gap in sleep science. Addressing this gap is imperative for developing targeted interventions aimed at improving sleep health worldwide.

Materials and methods: This study aims to provide an extensive, data-driven examination of global sleep patterns by analyzing 722,538 individual responses. Through a multivariate analytical approach, we seek to elucidate the intricate interactions between demographic, technological, psychological, and environmental determinants influencing sleep architecture. By leveraging advanced statistical methodologies and machine learning techniques, this study presents a novel perspective on sleep epidemiology, highlighting key predictive factors that contribute to sleep quality and duration.

A cross-sectional, observational study was conducted utilizing a validated 30-item sleep assessment instrument distributed across diverse global populations. A combination of hierarchical regression, structural equation modeling, and machine learning algorithms was applied to analyze sleep determinants. The study examined variables including sleep duration, bedtime routines, technology usage, psychological stress, environmental factors, and demographic influences. Data-driven insights were extracted to model the multifaceted nature of sleep interactions.

Results: Our findings reveal key determinants of sleep patterns across a large, diverse sample:

- **Sleep Duration:** The mean sleep duration was 6.4 ± 1.2 hours, with 52% of individuals experiencing chronic sleep insufficiency (<7 hours/night). Significant age-related variations in sleep duration were observed ($F = 42.3$, $p < 0.0001$).
- **Technological Influence:** 67% of participants engaged in pre-sleep electronic device use, which correlated with increased sleep latency ($r = 0.476$, $p < 0.0001$) and an average sleep onset delay of 38.2 ± 12.5 minutes.
- **Psychological Stress:** Work-related stress was the leading self-reported sleep disruptor (62%), with high-stress individuals exhibiting a 3.7-fold increased risk of insomnia (OR 3.7, 95% CI: 3.2-4.3). Anxiety was identified as a barrier to sleep in 55% of respondents.

Our findings challenge traditional, unidimensional sleep models by unveiling a dynamically interconnected sleep experience shaped by modern societal influences. The research underscores the necessity of holistic, personalized sleep interventions that address digital exposure, stress management, and environmental modifications. These insights provide an empirical foundation for public health initiatives aimed at mitigating sleep-related disorders and enhancing overall well-being.

Conclusions: This large-scale analysis illustrates the profound complexity of contemporary sleep experiences, emphasizing the need for integrative strategies that account for technological, psychological, and environmental interactions. By leveraging data-driven methodologies, our study contributes to a deeper understanding of sleep health, paving the way for more effective, personalized interventions.

Green space exposure and sleep among pregnant women in the GEMS study

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Introduction: Greenspace has been linked to numerous health benefits among pregnant women, such as improving birth outcomes, reducing the risk of developing obesity, and decreasing symptoms associated with adverse mental and physical health outcomes. Consequently, the UN has adopted universal access to greenspace among women and

children as a Sustainable

Development Goal to reach by 2030. Although exposure to greenspace has been shown to have numerous health benefits in relation to pregnancy, few prospective studies using non-static measures of green space with low-income pregnant women currently exist in the United States. This pilot study sought to address these gaps by following pregnant women through their pregnancy (beginning in the first 24 weeks), using objective measures of greenspace exposure and sleep (e.g., GPS- and accelerometer- derived).

Materials and methods: Low-income pregnant women (n=32) in the ongoing Project GEMS study in Rhode Island were recruited to concurrently wear a GPS and an actigraph for seven days at a minimum of two time points during pregnancy. Specific inclusion criteria include a) aged 18 years of age or older, b) within the first 24 weeks of pregnancy, c) expecting a singleton birth. The actigraph was used to derive Total Sleep Time (TST, hours), Sleep Efficiency (SEF), and Wake After Sleep Onset (WASO, minutes). The GPS was used to identify stay points (defined as spending five minutes or more in one particular place) and trajectory paths across the day. Measures of green space exposure included the Normalized Difference Vegetation Index (NDVI) values which were extracted and averaged and tree canopy coverage within 100m, 200m, and 500m circular buffers surrounding each participant's stay points and trajectory paths. T-test results compared sleep measures between high and low greenspace exposure groups, based on a median green-space cut-off among pregnant women.

Results: Seventy-five percent of the women in our project identified as Hispanic or Latino, 37% had a yearly income of less than \$5000, and a mean age of 30.5 ($\pm$ 4.3) years during the first 24 weeks of pregnancy. On average, TST was 6.83 hours, SEF 78%, and WASO 52 minutes. Women residing in areas with higher levels of green space exposure based on NDVI values had higher TST (7.9hrs vs. 6.9hrs, $p=0.02$) at the 500m circular buffer. Moreover, women living in areas with higher percentages of tree canopy had higher TST (7.98hrs vs. 7.0hrs, $p=0.04$) at the 200m and 500m circular buffers, and lower WASO (58minutes vs. 45 minutes, $p=0.05$) at the 100m circular buffer. There were no statistically significant differences observed for SEF between the groups for any green space measures.

Conclusions: Green space exposure is positively associated with total sleep time and WASO among this sample of low-income pregnant women. A larger sample size of women, including measures over the course of the entire pregnancy, and the exploration of additional socio-environmental factors are needed to confirm the robustness of the findings.

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Head Rocking Enhances Deep Sleep During Daytime Naps: Evidence from a Motorized Pillow Study

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Introduction: Recent attention to sleep quality has highlighted its impact on physical and mental health. Short naps, in particular, have been shown to improve attention and memory (Dutheil et al., 2021). As interest in daytime productivity and health maintenance grows, so does the demand for better nap quality. Vestibular stimulation has been reported to enhance sleep, with whole-body rocking shown to promote sleep onset and increase NREM sleep (Perrault et al., 2019). However, most studies focus on whole-body movement, and the effects of head-only rocking remain unclear. This study investigates how head rocking during napping, using a specially designed motion pillow, affects sleep architecture as measured by polysomnography (PSG).

Materials and methods: The pillow used in this study was designed with a structure that allows control of its height using a stepping motor and a ball screw mechanism. By utilizing this mechanism, the pillow can periodically change its vertical position, providing sinusoidal rocking stimulation to the head at a frequency of 0.125 Hz (one cycle every 8 seconds). Eleven participants completed two nap sessions on separate days: one with head rocking, the other without. Polysomnography (PSG) was used to record electroencephalography (EEG), electrooculography (EOG), and electromyography (EMG). Sleep stages were scored, and the time course of the proportion of delta waves in the EEG was analyzed.

Results: After excluding two participants due to incomplete recording data, the analysis was conducted on the remaining nine participants. In the rocking condition (S), the number of wake epochs was higher, and the number of N2 stage epochs was lower compared to the no-rocking condition (NS). Additionally,

the number of N3 stage epochs was higher in the S condition. Furthermore, the proportion of delta waves during non-wake EEG periods was significantly higher in the S condition. A Mann-Whitney U test revealed a statistically significant difference ($p < 0.05$).

Conclusions: In this study, we investigated the effects of head-only rocking during napping using a motorized pillow on sleep architecture. The observed increase in N3 sleep and the elevated proportion of delta waves suggest that head-only rocking can induce effects similar to those reported with whole-body rocking. This may be attributed to the activation of the vestibular system in the head, which is thought to mediate these effects (K. Kompotis et al., 2019). The increase in wake epochs can be explained by the inclusion of two participants who were unable to fall asleep under the rocking condition, likely due to a mismatch between the stimulation frequency and their physiological preferences. It is assumed that the 0.125 Hz stimulation may have overly activated their vestibular system, causing symptoms akin to motion sickness (O'Hanlon & McCauley, 1974). Future studies should focus on designing individually optimized stimulation parameters to prevent such adverse responses.

Head-to-head comparison of a contactless home sleep monitor with polysomnography in women with sleep disturbances associated with menopause

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Introduction: Sleep disturbances are common in menopausal women, yet repeated in-lab polysomnography (PSG) assessments are often limited by cost and inconvenience. Sleep monitoring in a natural environment may provide valuable insights in clinical trials. This study evaluated the agreement and accuracy between the reference standard PSG and the Sleepiz One+, a contactless home sleep monitor using radar technology to measure vital parameters and bodily movements during sleep, in assessing sleep/wake status in this population.

Materials and methods: In the NIRVANA study, menopausal women with sleep disturbances underwent simultaneous Sleepiz One+ and PSG recordings for six nights, across three assessments (two consecutive nights each at baseline, week 4, and week 12). PSG was conducted in qualified sleep laboratories by trained staff and scored manually by two independent scorers blinded to treatment, following American Academy of Sleep Medicine (AASM) guidelines. Sleepiz data were analyzed automatically using proprietary algorithms. Time synchronization between modalities was achieved using PSG's "lights-off"/"lights-on" markers and respiratory signal alignment. Only high-quality, synchronized datasets were included, resulting in 237,258 epochs (standard 30-second intervals used in sleep scoring) from 66 subjects for analyses, which were compared one by one to assess sleep/wake classification. Agreement between modalities was assessed using sensitivity, specificity, overall accuracy, and prevalence-adjusted bias-adjusted kappa (PABAK), presented as the mean across subjects with 95% confidence intervals (CIs). Parameter-level comparisons (e.g., wakefulness after sleep onset [WASO], total sleep time, sleep efficiency) are ongoing. Data from both methods contribute to the assessment of fitness-for-purpose of the home sleep monitor to assess sleep-related endpoints in the study population in future clinical studies.

Results: Epoch-level comparison showed that Sleepiz achieved a mean sensitivity of 0.91 (95% CI: 0.89, 0.94) for detecting sleep, a specificity of 0.64 (95% CI: 0.60, 0.68) for detecting wake, and had an overall accuracy of 0.86 (95% CI: 0.84, 0.88) compared with PSG. PABAK was 0.72 (95% CI: 0.68–0.76), indicating substantial agreement. Analysis at the parameter-level is ongoing; however, preliminary parameter-level comparisons showed that Sleepiz underestimated WASO by 4.8 minutes, latency to persistent sleep by 9.6 minutes, total sleep time by 7.1 minutes, number of awakenings by 0.4, and duration of awakenings by 1.0 minutes. Sleep efficiency was overestimated by 2.1%.

Conclusions: Epoch-level comparison and preliminary parameter-level results show good agreement between Sleepiz and PSG in menopausal women with sleep disturbances. These results support the use of Sleepiz as a contactless tool for sleep assessment at home in clinical trials. Without the burden of traditional PSG, the Sleepiz device enables continuous home recordings over longer periods and broader data collection in a natural setting. This study extends previous validations of Sleepiz in healthy

and sleep-disordered populations, confirming the device's fitness for purpose in menopause-related sleep research. Ongoing analyses will further validate the technology for clinical applications.

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Healthcare measures adopted by medical students to mitigate brain function impairment caused by sleep deprivation: a qualitative interview study using health belief model

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Introduction: Research indicates that sleep deprivation impairs brain function in healthy adults. As future healthcare providers, medical students' strategies to address these effects may offer insights into managing sleep-related health issues. This study explored sleep-deprived medical students' willingness to adopt compensatory measures and decision-making processes when experiencing symptoms of impaired brain function.

Materials and methods: Approved by the Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine (No. YE2022-266), semi-structured qualitative interviews were conducted with participants who reported notable symptoms of brain function impairment following sleep deprivation, focusing specifically on whether they had adopted any measures to alleviate symptoms, the reasons for their choice, and their subjective evaluations of these measures. The participants were all full-time Chinese medicine students interning in Guangzhou, reporting an average sleep duration <7 hours in the past week. Thematic analysis and the health belief model (HBM), including perceived susceptibility (PSU), perceived seriousness (PSE), perceived benefits (PBE), perceived barriers (PBA), self-efficacy (SE), and cues to action (CA), guided data analysis. Each participant signed a written informed consent form before enrolment.

Results: Informed by HBM, qualitative data shows that all respondents reported using one or more measures to mitigate symptoms of sleep-deprivation-related brain impairment, demonstrating high PSU. These strategies were categorized as: lifestyle adjustments (sleep extension, dietary modifications including caffeine and sugar intake, and physical exercise) which were most preferred for accessibility and minimal side effects, indicating high PBE, and medical treatments including Chinese herbal medicine (CHM) like proprietary Chinese medicines and CHM decoctions, external traditional Chinese medicine (TCM) therapies including acupuncture, tuina massage, and foot bathing, and over-the-counter (OTC) non-TCM supplements such as melatonin. CHM and external TCM therapies were preferred over non-TCM supplements because of fewer side effects. PBA included significant side effects, high cost, and poor accessibility. Participants with higher PSE chose more strategies, while those with lower PSE believed adjusting lifestyle habits was sufficient to alleviate their current symptoms, without considering medical treatments. These choices are mainly driven by life experience, medical knowledge reserves, and independent research (SE). In addition, peer recommendations (CA) also influenced choices. Notably, the academic background did not uniformly predict preferences as some participants avoided or even resisted medical treatments, even the TCM treatments they were familiar with.

Conclusions: HBM analysis reveals that medical students' compensatory measure selection is primarily driven by subjective factors (high PSU/PSE/PBE/SE promoting engagement) and hindered by objective barriers (PBA). Interventions for sleep deprivation-related impairment should employ dual strategies: cognitive restructuring to enhance risk awareness and improved resource allocation to increase accessibility. The personalised preferences of different participants highlight the necessity of customised health promotion methods. However, these findings should be interpreted with caution. All participants received TCM training as part of their education, and the city of Guangzhou, where they lived and studied, has a well-established TCM culture.

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Healthcare-seeking and paediatric sleep disordered breathing in substandard housing: preliminary findings from an urban cohort

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Introduction: Physical housing environment has a crucial role in sleep health in early life and childhood. However, little is known about the prevalence of parent-reported sleep disordered breathing and its socioeconomic determinants in housing vulnerable populations.

Materials and methods: A territory-wide survey was conducted from April to June 2025 with a convenient sample of Chinese subdivided unit residents and their children aged 2 – 17 years. Household socioeconomic information (income, education, social status), years of residence in substandard houses, children's sex, age and body mass index (BMI) z-score, healthcare utilisation, and Paediatric Sleep Questionnaire (PSQ)-measured sleep-related breathing disorder (SRBD) symptoms were collected. Logistic regressions were used to examine associations between positive PSQ scores (defined as ≥ 0.33) and household socioeconomic information, after adjusted for the child's BMI.

Results: Among 164 dyads interviewed (mean age of child [SD]= 8.46 [3.43] years; 57.1% male), 17.1% (n=28) had PSQ score ≥ 0.33 , indicating a high risk for SRBD, but only 2 dyads (3.57%) have sought medical attentions. A positive PSQ score (≥ 0.33) had a marginally significant association with female children (adjusted odds ratio (aORs) [95% confidence intervals (CIs)] = 2.87 [0.99 - 10.22], $p=0.078$). Household income, parental education, self-perceived social status and years of residence had no significant associations with positive PSQ scores after adjusting for children's BMI z-score.

Conclusions: SRBD symptoms are common among children in subdivided housing, but few seek medical care. Socioeconomic factors showed no significant association with the presence of significant SRBD symptoms, though a marginal gender difference warrants further study.

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Healthy shiftwork: Co-designed, clickable, credible

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Introduction: Young adults (18–25 years) working shifts face increased risks of sleep and circadian disruption, contributing to long-term health consequences. Despite this, age-appropriate and accessible sleep health resources are lacking. This project aimed to develop and translate tailored, evidence-based content into engaging formats for young shiftworkers.

Materials and methods: A participatory co-design approach was used, involving 48 co-designers including young, current, and former shiftworkers, workplace health and safety professionals, science communicators, and academic researchers. Co-designers participated in online workshops to identify relevant content areas and shape the tone and delivery of the resources. Reflexive thematic analysis of workshop transcripts identified core themes, which were aligned with scientific evidence to guide resource development.

Results: Five key themes were identified: (1) sleep science, (2) impacts of poor sleep, (3) habits influencing sleep, (4) strategies to improve sleep, and (5) workplace recommendations. These themes were translated into three primary delivery modes:

a) An interactive website featuring in-depth, accessible content; b) A pictorial infographic summarising key takeaways; c) an animated video for digital and social media use.

A consistent visual identity and tone were applied to ensure appeal and usability for young audiences.

Conclusions: This project demonstrates how participatory methods can inform not only what content is developed, but how it is delivered. Translating sleep health science into youth-friendly formats may enhance engagement and impact. Evaluation of reach, usability, and behaviour change outcomes is now warranted.

High Resolution Measurement of Sleep Position During Pregnancy and the Impact on Infant Birthweight

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Introduction: Pregnant women are advised to sleep laterally from 28 weeks of gestation, due to increased risk of stillbirth in those who report “going-to-sleep” in the supine position. Whilst sleep onset position is modifiable, body position throughout the night occurs in a state of altered consciousness and may be challenging to control, and to self-report accurately. Objective measurement is needed to confirm sleep position as a risk factor for stillbirth. Sleep position in polysomnography is traditionally classified as supine or lateral, but during pregnancy this dichotomy fails to consider important subtleties regarding the haemodynamic mechanisms of tilted sleeping positions and fetal wellbeing. Firstly, this study aimed to characterise sleep position during pregnancy with precise measurement techniques and assess the impact of discretisation of supine sleep on infant birthweight. Secondly, this study aimed to evaluate the accuracy of self-reported sleep position during pregnancy.

Materials and methods: A tri-axial accelerometer was worn around the abdomen for 7 nights, between 32-36 weeks of pregnancy. Body position was measured continuously in degrees of roll. Supine was defined crudely as 0°= fully supine to 45° left or right tilt versus more precisely as 0-15°, 15-30° and 30-45°. Participants completed a sleep diary each morning reporting if they slept on their back the previous night (“no”, “yes - <1hr”, “yes - >1hr”). Infant birthweights were converted into customised centiles based on gestation at delivery, gender, parity and maternal height and weight.

Results: A total of 565 nights were recorded across 85 women. The median (IQR) proportion of supine positioning (0-45°) across the week was 13.1% (5.0, 25.0) equivalent to 65.9 (25.4, 124.6) minutes per night, however this was reduced to 2.1% (0.1, 4.7) or 9.6 (0.8, 24.3) minutes when considering only strict supine positioning (0-15°). Of time spent supine, 45.4% was within 30-45°, compared to 26.1% and 28.5% in less tilted positions of 15-30° and 0-15° respectively. Birthweight centile was not related to overall time spent supine (0-45°) overnight ($r_s = -.07$, $p = .54$) or when constrained to 0-30° supine ($r_s = .03$, $p = .78$) or 0-15° supine ($r_s = .06$, $p = .59$). Women reported “no” back sleeping on 57% of nights, however only 38% of these nights were considered accurate (<10 minutes objectively recorded). Conversely, the 14% of nights reported as >1 hr back sleeping were accurate 97% of the time. Overall, self-reported time-on-back category was accurate only 43% of nights (Kappa = 0.21 (0.16, 0.25), $p < .001$ indicating poor agreement).

Conclusions: Over half of the pregnant women studied spent at least an hour in the supine position overnight, although a favoured 30-45° lateral tilt meant that little time was spent sleeping flat on the back. Supine sleep was not associated with birthweight, suggesting that, at the measured supine exposures, the fetus was minimally impacted from aortocaval compression potentially impacting uteroplacental supply. The inaccuracies surrounding self-reported sleep position highlights the need for objective evaluation of educational campaigns around sleep position during pregnancy.

Home-Based Oropharyngeal Myofunctional Therapy for Habitual Snoring: A Randomized Controlled Trial of Snoring Severity and Sleep Quality

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Introduction: Habitual snoring affects up to 45 % of adults, leading to sleep fragmentation, daytime fatigue, and partner disturbance. Upper-airway collapse during sleep often stems from weakened oropharyngeal muscles. Myofunctional exercises targeting the tongue, soft palate, and related structures have shown promise in small case series, but most studies focus solely on acoustic snore metrics, overlooking overall sleep quality. We therefore designed a randomized, assessor-blinded trial

to determine whether a 6-week home-based oropharyngeal exercise program could concurrently reduce snoring severity—measured by our novel Snoring Severity Scale (SSS; frequency, loudness, duration, partner disturbance, daytime symptoms; range 0–20 and improve subjective sleep quality (PSQI; range 0–21)

Materials and methods: In this Parallel-group RCT forty adults aged between 18–60 with habitual snoring (≥ 3 nights/wk; SSS ≥ 8 ; PSQI > 5) were randomized (1:1) to Exercise (daily 20 min oropharyngeal routine 6 days/week for 6 weeks, $n=20$) or Control (single sleep-hygiene session, $n=20$) for 6 weeks, with a 2-week follow-up. Co-primary outcomes were Snoring Severity Scale (SSS) and Pittsburgh Sleep Quality Index (PSQI) at Week 6; secondary outcome was daytime sleepiness (Epworth Sleepiness Scale, ESS; 0–24). Outcome assessors and analysts were blinded. Data was analyzed by ANCOVA for SSS and PSQI and ESS and maintenance tested via paired t-test

Results: Thirty-eight participants completed Week 6 (Exercise $n=19$; Control $n=19$). Adherence in Exercise arm was 92% (SD 5%); no serious adverse events. At Week 6, the Exercise group showed a mean SSS reduction of 5.6 ± 1.8 points versus 0.7 ± 1.0 in Control (between-group Change -4.7 ; 95% CI -5.8 to -3.6 ; $p < 0.001$; $d=2.2$). PSQI improved by 4.3 ± 1.2 points in Exercise versus 1.1 ± 1.0 in Control (Change -3.0 ; 95% CI -3.8 to -2.2 ; $p < 0.001$; $d=2.5$). ESS decreased by 3.2 ± 1.0 versus 1.0 ± 0.9 (Change -2.1 ; 95% CI -3.1 to -1.1 ; $p = 0.002$; $d=1.7$). Gains persisted at Week 8.

Conclusions: A structured, home-based oropharyngeal myofunctional therapy program significantly reduces snoring severity and improves sleep quality with sustained effects. The Snoring Severity Scale proves a responsive, practical tool for clinical and research monitoring. This low-cost, scalable intervention merits broader implementation and further investigation in diverse populations

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How the Visual Urban Landscape Influences Sleep Health via Subjective Neighborhood Evaluation

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Introduction: Sleep is closely linked to neighborhood qualities, and since vision plays a central role in how we experience urban environments, exploring the influence of landscape features offers promising insights into sleep research. Environmental effects on sleep partly operate through psychological mechanisms. However, most previous urban sleep studies have focused either on objective landscape characteristics or individuals' subjective evaluations of their neighborhoods, rarely both in conjunction. Additionally, few studies have considered how landscapes influence sleep through environmental evaluations. For measuring landscapes, previous studies used street audits, which are inefficient and limited in capturing quantitative features such as sky and greenery. Subjective evaluations have often been assessed through questionnaire surveys. Although effective in capturing neighborhood evaluations, this method is subject to individual bias and limited in reproducibility.

This study aims to address the above research gaps by examining the complex relationship between objective visual landscapes, subjective neighborhood evaluations, and sleep health outcomes.

Materials and methods: Sleep health data were collected from 1,089 adults. Insomnia and sleepiness were assessed using the Athens Insomnia Scale and the Epworth Sleepiness Scale, where higher scores indicate poorer sleep health.

Using Computer Vision techniques, pixel-level landscape elements (e.g., greenery, sky) were identified in neighborhood street view images (SVIs), localized to participants' postal codes. Based on existing theories, we derived objective measures of visual landscape quality, as reflected in greenness, walkability, enclosure, and complexity.

We fine-tuned models linking landscapes to subjective evaluations using the Place Pulse 2.0 dataset, which provides global imagery and crowdsourced evaluations reflecting collective judgment. Using those models, we batch-generated model-predicted subjective evaluations of the neighborhood SVIs: safety, non-boredom, non-depressiveness, wealth, liveliness, and beauty.

Structural equation modeling was used to evaluate indirect pathways from objective landscape quality to sleep outcomes via subjective evaluations, while controlling demographic factors.

Results: Regarding insomnia, positive significant indirect effects were observed from visual greenness via non-depressiveness ($\beta = -0.030$, $p = 0.05$); walkability via non-boredom (-0.009 , 0.05); complexity

via both non-depressiveness ($-0.018, < 0.001$) and non-boredom ($0.014, 0.025$).

Regarding sleepiness, greenness showed positive marginally significant indirect effects via safety ($-0.017, 0.056$), non-depressiveness ($-0.034, 0.037$), and wealth ($-0.018, 0.050$). Walkability had a significant indirect effect via non-boredom ($-0.012, 0.019$). Complexity showed marginally significant indirect effects via non-depressiveness ($-0.018, 0.077$), and negative significant indirect effects via non-boredom ($0.015, 0.020$) and liveliness ($0.014, 0.020$).

Conclusions: This study suggested the mediating role of subjective evaluations in linking visual landscape to sleep outcomes. Greenness was associated with lower levels of insomnia and sleepiness, primarily via reduced depression, enhanced safety and perceived wealth. Walkability also contributed to reduced sleep problems through decreased boredom. Complexity had mixed effects, reducing sleep problems via non-depressiveness but increasing them via liveliness, suggesting visually stimulating environments may raise arousal.

One limitation is the lack of analysis on which specific visual elements in street qualities were most influential. Future studies should isolate these components to better guide urban design for sleep health.

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Hyperbaric Oxygen Therapy And Its Physiological Mechanisms Affecting Sleep Disturbances: A Narrative Review

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Introduction: Hyperbaric oxygen therapy (HBOT), traditionally utilized to improve oxygen for conditions such as decompression sickness and non-healing wounds, has recently garnered attention for its potential therapeutic effects on various sleep disturbances. Sleep is a complex physiological process that is sensitive to oxygen homeostasis, and disruptions in oxygenation can significantly alter sleep architecture and sleep efficiency.

Materials and methods: This narrative review explores the evolving evidence on HBOT's role in modulating sleep physiology and alleviating common sleep disorders, including obstructive sleep apnea (OSA), central sleep apnea (CSA), insomnia, and altitude-related sleep disturbances.

Results: We figure out the basic principles of HBOT, including pressure settings, treatment therapy, and the physiological responses associated with hyperoxia. The effects of HBOT on sleep disturbances through multiple physiological mechanisms, including the reduction of inflammation and oxidative stress, reversal of tissue hypoxia, modulation of cytokines and immune response, improvement in sleep architecture, reduction of sleep-related pain and fatigue, effects on brain regions involved in sleep regulation, improvement in pulmonary function and oxygenation, reduction of arousal threshold and loop gain, and effects on psychological symptoms, all of which are critical in the pathophysiology of sleep disorders.

For OSA, HBOT has shown promise in modulating upper airway muscle tone and reducing intermittent hypoxia-induced oxidative damage, potentially improving apnea-hypopnea index (AHI) and oxygen saturation in select patient populations. In the context of CSA, especially in patients with heart failure or opioid-induced apnea, HBOT may influence central respiratory drive through effects on brainstem chemoreceptor sensitivity and autonomic balance. However, clinical data remain limited, and the risk of suppressing hypoxic ventilatory drive must be considered.

Insomnia, particularly in cases associated with neuroinflammation or traumatic brain injury, may respond to HBOT through its neurorestorative and anti-inflammatory effects. Preliminary clinical studies suggest improvements in sleep efficiency, latency, and subjective sleep quality following multiple sessions of HBOT, though standardized protocols and randomized trials are lacking.

At high altitudes, hypobaric hypoxia commonly induces periodic breathing and sleep fragmentation. HBOT has been investigated as a countermeasure to altitude-induced sleep disruption, with studies indicating improved nocturnal oxygenation, reduced arousals, and stabilization of breathing patterns in both acclimatized and unacclimatized individuals. Overall, the current literature provides compelling

physiological rationale and preliminary clinical evidence supporting the application of HBOT in select sleep disorders. However, significant gaps remain, including heterogeneity in treatment protocols, small sample sizes, and limited long-term follow-up. Further studies are needed to elucidate optimal patient selection, treatment duration, and safety considerations, especially in vulnerable populations.

Conclusions: This review highlights the potential of HBOT as an adjunctive or alternative approach in sleep medicine and encourages future interdisciplinary research to validate its efficacy and safety. Understanding the mechanistic links between hyperoxia, neurophysiology, and sleep regulation may open new therapeutic pathways for refractory or comorbid sleep disturbances.

Identifying and managing sleep disorders in patients with fibromyalgia

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Introduction: Fibromyalgia is a chronic condition marked by widespread pain, fatigue, and sleep problems. However, little is known about the presentation and management of sleep problems in these patients. This study aimed to 1) characterise sleep/wake patterns and sleep disorder presentations in participants with fibromyalgia, and 2) assess changes in sleep and fibromyalgia symptoms with individualised sleep disorder treatment.

Materials and methods: Women with fibromyalgia were recruited from the Rheumatology Unit at The Queen Elizabeth Hospital, South Australia. Participant sleep and activity for two-weeks was established using an under-mattress sleep sensor (Withings Sleep Analyser, WSA), sleep diaries and a wrist accelerometer (GENEActiv). Screening questionnaires included Berlin Sleep Questionnaire (OSA), Epworth Sleepiness Scale (ESS), Flinders Fatigue Scale (FFS), the Sleep Condition Indicator (SCI), and Fibromyalgia Impact Questionnaire Revised (FIQ-R). Self-reported anxiety, depression, other co-morbidities, as well as medication use, were collected. Results were reviewed by sleep psychologists and a sleep physician. Those determined to be at risk for a sleep disorder were offered individualised sleep disorder treatment, which involved cognitive behaviour therapy for insomnia (CBTi) and personalised chronotherapeutic approaches (bright light therapy, melatonin) delivered by sleep psychologists, and/or continuous positive airway pressure (CPAP) therapy with or without positional (POS) therapy, as appropriate and prescribed by the sleep physician.

Results: Data from 23 women (aged 50.5±15.6years, BMI 32.8±9.3kg/m²) with pain duration ranging from 18 months to over 40 years were investigated. Sixteen women completed a sleep diary, indicating low sleep efficiency (73%±11.5). All were assessed as 'high-risk' for a sleep disorder, with eight at 'high-risk' for two or more sleep disorders (7 obstructive sleep apnoea; OSA), 12 insomnia, 6 circadian rhythm sleep wake disorders; CRSWD). Five women had delayed, and one had advanced, circadian rhythms. Fatigue scores exceeded those commonly observed for participants living with medical conditions more broadly in the community (21.7±5.8 vs. 20.4±6.2). Co-morbid anxiety and depression were reported by 65% and 35% of the women, respectively. Thirty-nine percent of participants reported being woken by pain nightly, and 43.5% reported their pain prevented sleep on 1-3 nights per week. Over half of the participants (56.5%) reported taking medication at night for pain. Ten women were referred for individualised sleep disorders treatment. Seven provided responses to post-treatment questionnaires and reported clinically meaningful improvements in their fatigue (mean change=6.7; Minimal Clinically Important Difference [MCID]=3.4), and FIQ score (mean change=10.6; MCID=8.1).

Conclusions: Fibromyalgia is associated with complex and co-morbid sleep disorders. Screening, identifying and managing sleep disorders using personalised treatment approaches may be an important therapeutic target for patients with fibromyalgia to improve sleep quality, daytime functioning, and fibromyalgia symptoms.

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Identifying and Predicting Emotionally Relevant Sleep Disturbance Patterns in Dementia Family Caregivers: A Machine Learning Approach to Objective-Subjective Discrepancy

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Introduction: One of the major challenges in home-based care for older adults with dementia is sleep disruption experienced by family caregivers, often caused by dementia-related symptoms such as day–night reversal and nighttime urinary frequency. These disruptions significantly impact caregiver burden and mental health; however, the actual conditions and patterns of such disturbances remain poorly understood. In particular, repeated awakenings after bedtime are difficult to detect through self-reported sleep measures alone. This study aimed to comprehensively assess caregiver sleep disturbances by combining objectively measured sleep data (via accelerometer-based activity trackers), subjectively reported sleep disruption, and daily self-reported psychological health indicators. These integrated data were used to classify patterns of sleep disruption and to evaluate the predictive accuracy of next-day psychological outcomes—such as emotional exhaustion—as well as depressive symptoms assessed after 60 days, using machine learning techniques.

Materials and methods: Family caregivers who provided care at least once a week to community-dwelling older adults aged 65 and over—certified as requiring long-term care in Japan—were recruited nationwide through an online survey company. Participants were instructed to wear an activity tracker to monitor sleep and to record daily caregiving status along with self-reported emotional indicators over a 60-day period. A baseline questionnaire was administered to collect demographic and caregiving-related information. Sleep and wake data were recorded at 2-minute intervals (yielding 720 data points per day), and were combined with both subjective reports of sleep disturbances and daily emotional indicator data. Non-wear periods during nighttime were excluded from analysis. For classification of sleep disturbance patterns, dimensionality reduction was performed using t-SNE, followed by k-means clustering. To predict multiple psychological health indicators, including emotional exhaustion, deep learning was applied using a neural network model with 5-fold cross-validation. The study was approved by the Ethics Committee of the Tokyo Metropolitan Institute for Geriatrics and Gerontology.

Results: A total of 199 participants (57.3% male; mean age 55.5 years) completed the activity tracker measurements and recordings, excluding 9 who withdrew before the study and 2 who dropped out due to the death of the care recipient or the caregiver's health issues. A total of 11,815 sleep disturbance datasets (excluding non-wear nights) were analyzed. Clustering via t-SNE revealed five distinct groups of caregiver sleep/wake patterns. This classification enabled the prediction of subjective emotional exhaustion with 73.1% accuracy, exceeding the accuracy of random prediction.

Conclusions: These findings suggest that machine learning can be used to quantify and predict emotional burden using only objectively measured data from activity trackers. This indicates that such objective data contain embedded information related to caregivers' emotional exhaustion. The predictive model demonstrates the potential for integrating technology into caregiver support systems.

Identifying sleep associations in women across five countries: a global smartwatch-based study

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Introduction: Sleep disturbances—including difficulties falling asleep, staying asleep, or waking early—are common among midlife women and may be influenced by age, physical activity, weekend/weekday patterns, and cultural context. However, large-scale, cross-cultural comparisons using objective sleep measures remain limited. Wearable devices offer a novel, scalable approach to study sleep health globally. Using Samsung Galaxy Watch data, this study examined associations of age, BMI, physical activity, and country with sleep parameters in a large, international cohort of women.

Materials and methods: We analyzed sleep data from 192,500 women aged 20–65 years, each with ≥7 nights of sleep recordings, from the US, South Korea, Germany, France, and the UK (n=38,500 per

country). Sleep parameters included total sleep period duration (TSPD; time from sleep onset to final awakening), total sleep time (TST; time asleep within TSPD), and wake after sleep onset (WASO; log-transformed). Linear mixed models assessed associations with age (5-year intervals), weekday/weekend patterns, physical activity (step counts and active time tertiles), and country (US as reference). An exploratory model included age-by-country interactions.

Results: Overall, across the whole data set, mean (SD) values were: TSPD 439.4 (92.0) minutes, TST 391.2 (81.9) minutes, and WASO 48.3 (33.5) minutes. Age distributions were comparable across countries, with approximately 1/3 of women aged ≥ 50 years.

TSPD: Weekend nights were associated with ~24 minutes longer TSPD (+5.4%). Age and physical activity effects were small (± 5 minutes). Women in South Korea had the shortest TSPD, averaging 27 minutes less (-6.2%) than US women.

TST: TST declined with age, with women aged 60–65 sleeping 17 minutes less (-4.4%) than those aged 20–24. Women in age groups ≥ 50 had 13–17 minutes less TST (-3.3 to -4.4%) than those aged 20–24. Weekend nights were associated with ~21 minutes longer TST (+5.3%) compared to weeknights, while activity-related differences in TST were small (< 3 minutes; $< 1\%$). Similar to TSPD, women in South Korea showed, on average, a 25-minute shorter TST (-6.3%) vs. US women.

WASO: WASO increased with age; women in age groups ≥ 50 had 5–11 minutes more wakefulness (+15–32%) than those aged 20–24. A small weekend effect was observed (+2 minutes; +5.4%). Activity effects were minimal (< 1 minutes; -1.1% to -2.5%). Country differences were small: UK (+1.5 minutes) and South Korea (-1 minute) vs. US.

Interaction Effects: Age-related WASO increases were consistent across countries, except in South Korea, where effects were more pronounced. Other significant interactions are thought to be due to the large sample size and have limited clinical relevance.

Conclusions: In this large, international cohort of women, who provided multiple nights of wearable data, country-specific differences in TST and TSPD were evident, particularly in South Korea. The effects of age on TST and WASO were generally similar across countries, except for South Korea, where age effects on WASO were more pronounced. These findings underscore the potential of smartwatch data for large-scale sleep research.

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Individual Variations in Stress-Related Sleep Patterns

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Introduction: Stress is a pervasive factor that can disrupt sleep, which plays a crucial role in recovery and overall health. While the harmful effects of stress on sleep are widely recognized, the degree of this impact may vary across individuals. This study aims to investigate the relationship between daily stress and subsequent sleep duration in order to identify distinct patterns of stress-related sleep behavior.

Materials and methods: Self-reported daily stress and sleep duration from 800 participants across three weeks ($M = 15.5$ days, $SD = 4.36$ days), were analyzed to explore the relationship between daytime stress and sleep duration the following night. A linear mixed model was used to assess within-person associations between stress and subsequent sleep duration, including random intercepts and slopes. To further examine heterogeneity in stress-sleep dynamics, k-means clustering analysis was conducted based on the individual slopes derived from the mixed model.

Results: Higher daily stress was significantly associated with shorter sleep duration the following night, with a decrease of approximately 7.5 minutes per unit increase in stress ($b = -7.47$, $SE = 0.67$, $p < .001$). The model also indicated substantial variability in both baseline sleep duration and individual stress-sleep slopes, and a likelihood ratio test confirmed significant individual variability in the stress-sleep association ($\chi^2(2) = 41.59$, $p < .001$), justifying the inclusion of random slopes.

To explore this variability, the clustering analysis revealed three distinct groups, each with unique stress-sleep dynamics. One group ($n = 417$) exhibited a moderate negative relationship between stress and sleep, with an average slope of $b = -7.40$. As stress increased, sleep duration decreased moderately. Another ($n = 196$) showed a steeper decline in sleep duration with a slope of $b = -13.07$, indicating a higher sensitivity to stress, where even moderate increases in stress predicted a significant reduction in sleep. The third group ($n = 187$) displayed a minimal negative relationship between stress and sleep, with a slope of $b = -1.77$, suggesting that stress had little predictive effect on sleep duration for these individuals.

Conclusions: While the group-level trend suggests that daily stress generally predicts shorter sleep, large individual differences exist. For some sleep may function as a deliberate recovery response protecting from the negative impact of stress, while for others, stress may moderately or heavily impair sleep. These findings underscore the heterogeneity in the stress-sleep relationship, reinforcing the importance of tailoring interventions to individual stress-sleep profiles, as uniform strategies may overlook key subgroups.

Influence of Climate Changes on Sleep. Systematic Review

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Introduction: Climate changes could lead in changes of sleep and sleep pattern as well as in sleep disorders and chronobiological changes, beginning with a poor quality of sleep, reinforced by a shift of the sleep-wake rhythm and lead in severe sleep disorders. Their prevalence and incidence are unknown until now. Both sleep disorders and chronobiological changes have a wide variety of causes and usually appear as a comorbid disorder in various somatic and psychiatric diagnoses, mental disorders and treatments. There can be many different predictors of sleep disorders and chronobiological changes, such as predisposition or pre-existing diseases, caused and / or reinforced by climate changes.

Materials and methods: A systematic literature review related to Climate changes and Sleep was carried out and 1,649 studies were evaluated. The articles were identified through PubMed, PsycInfo, and Web of Knowledge; a total of 30 publications were included in the analysis.

Results: A total number of ninety-five studies of the topic climate changes and sleep were identified; thirty of them were analysed, based on different criteria (climatic and civilization-related changes, natural disasters and special weather phenomena).

Conclusions: The review found that changes of sleep, of sleep pattern and of sleep quality as well as different sleep disorders (such as insomnias, hypersomnias, parasomnias) and chronobiological changes can be predicted for very different reasons. Personalized treatment of climatic-related changes would be needed to improve the mental and / or physical condition of these patients.

Influence of Sociodemographic, Personal and Lifestyle Factors on Sleep Quality and Stress-Coping Strategies Among Trainees in a Tertiary Hospital

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Introduction: Healthcare workers, especially physician trainees, are often required to work demanding shifts exceeding 24 hours, which expose them to various stressors and impact sleep quality and patterns.

Materials and methods: This study investigated the impact of sociodemographic, personal, and lifestyle factors on sleep quality among hospital trainees in a tertiary hospital in the Philippines and explored their coping mechanisms for managing stress. This analytic, cross-sectional study was conducted among hospital trainees (fellows, non-surgical, and surgical residents) in a tertiary hospital. Data were gathered through an online survey using three validated questionnaires: the Pittsburgh Sleep Quality Index, Brief COPE, and FANTASTIC Lifestyle Questionnaire.

Results: Out of 107 respondents, 92 were included in the study, with the majority of respondents single, female, and working shifts over 24 hours. The study revealed an 85% prevalence of poor sleep

quality, with an average sleep duration of 5.7 hours. Sleep duration was significantly associated with working hours and marital status in the non-surgical resident group. Poor sleep quality in general negatively impacted lifestyle factors, especially in surgical residents. Problem-focused coping was the most commonly used strategy, especially among fellows, while surgical residents scored lower in emotion-focused strategies like humor and religion. Avoidant coping, though generally low, was more evident through self-distraction.

Conclusions: This study highlights a high prevalence of sleep deprivation among physician trainees, linked to poor sleep quality and influenced by lifestyle factors. It recommends implementing consistent work shifts, reducing long consecutive hours, and introducing educational programs on sleep hygiene and institutional support to improve trainees' well-being and coping strategies.

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Integrative analysis of association and causal inference identify interactions between asthma and multiple sleep traits

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Introduction: The overlap of asthma and sleep traits is common, and possibly vary depending on patient age. This study aimed to estimate the associations and causal links of asthma with sleep traits including obstructive sleep apnea (OSA), insomnia, excessive daytime sleepiness (EDS) and sleep duration in adults and non-adults.

Materials and methods: Quantitative analysis was performed to find impaired sleep domains in asthma and assess their risk associations by odds ratio (OR). Then, a two-sample Mendelian randomization (MR) was conducted to evaluate their causality by using published Genome-wide association study summary statistics. The primary method was inverse-variance weighting, and several complementary methods were applied as sensitivity analyses.

Results: A total of 90 studies with 2556734 participants were included in quantitative analysis. Our results showed that parameters representing the severity of OSA, sleep quality and sleepiness were higher in asthma than non-asthma controls. Besides, asthma was related to high risk of these sleep traits (ORs of 1.44~2.08). Conversely, these sleep traits were associated with increased asthma risk with ORs ranging from 1.24 to 1.82. However, these findings were not consistent in some subgroup analyses. In MR analysis, primary results demonstrated that genetically predicted asthma was associated with a higher risk of OSA (OR[95% CI]=1.075[1.032,1.121]), which was consistent in three sensitivity analyses with ORs ranged from 1.075 to 1.089.

Conclusions: There are mutually reinforcing risk associations between asthma and four sleep traits. Further, asthma has robust causal effect on increasing OSA risk. These findings may provide direction and evidence for studying related mechanisms and intervention strategies.

Intervening in sleep early to support maternal mental health: short sleep and symptoms of sleep disordered breathing prior to pregnancy are associated with depressive symptoms in late pregnancy

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Introduction: The identification and treatment of sleep problems in pregnancy has shown promise for supporting maternal mental health. The current study aimed to add to our understanding of when to intervene and what aspects of sleep to intervene in, by investigating a range of sleep metrics prior to

and in late pregnancy and their association with depressive symptoms in late pregnancy for Indigenous and non-Indigenous women.

Materials and methods: Data were drawn from the first data collection wave (late pregnancy) of a prospective longitudinal study of perinatal sleep health in Indigenous and non-Indigenous women. Clinically significant symptoms of depression, measured with the Edinburgh Postnatal Depression Scale (<13 vs. ≥13), was the outcome variable in logistic regression models. Predictors in a pre-pregnancy model were usual sleep duration in 24 hours (≤6 hrs, >6hrs - ≤9hrs, >9 hrs); frequency of a good night's sleep (<3 days/week vs. ≥3 days/week); and presence of loud snoring, long pauses between breaths while asleep, and legs twitching or jerking while asleep (all present/absent). Ethnicity (Māori/non-Māori), socio-economic deprivation (NZ Deprivation Index quintiles), parity (nulliparous/multiparous), history of diagnosed depression (yes/no), relationship status (happy/unhappy and not applicable), life stress (<2 vs. ≥2 stressful events) and BMI (obese/not obese) were covariates. The late pregnancy model included the above with the addition of daytime sleepiness (Epworth Sleepiness Scale, <10 vs. ≥10), presence of restless legs (yes/no), and poor sleep quality and symptoms of insomnia (General Sleep Disturbance sub-scales, <3 nights/week vs. ≥3 nights/week).

Results: Data were provided by 406 Māori and 738 non-Māori women between 35-37 weeks gestation. Twenty-two percent of Māori women and 15% of non-Māori women had clinically significant depressive symptoms. In pre-pregnancy models, after adjusting for all covariates and sleep variables simultaneously, short sleep (≤6 hours) and reports of any loud snoring prior to pregnancy independently increased the odds of depressive symptoms in late pregnancy 2.7 and 1.5 times respectively. In late pregnancy models, short sleep and any loud snoring increased the odds of depressive symptoms 1.6 and 2.0 fold. Difficulty falling asleep and excessive daytime sleepiness were also significant in this adjusted model, with an increase in the odds of depressive symptoms by 1.8 and 1.6 times.

Conclusions: The finding that sleep pre-pregnancy was associated with depressive symptoms in late pregnancy points to an opportunity to identify and intervene in sleep issues very early in pregnancy as one possible way of supporting perinatal mental health. Any interventions must be designed to meet the needs of Indigenous women who are at greatest risk of experiencing poor mental health in the perinatal period.

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Interwoven threads: hormonal regulation, stress and the sleep-pain dyad in women

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Introduction: Sleep and pain, chronic pain in particular, share a deeply intertwined and bidirectional relationship. However, emerging evidence highlights a significant sex-based disparity in this dynamic relationship, with women disproportionately affected by chronic pain and sleep disturbances. This presentation explores the unique neurobiological, hormonal, and psychosocial mechanisms that underpin this phenomenon in females.

Materials and methods: To elucidate the multifactorial interactions between sleep disruption, pain perception, and the female sex, with a focus on hormonal fluctuations, stress reactivity, and their collective impact on pain modulation. Drawing from current interdisciplinary research, this presentation synthesizes findings from sleep medicine, pain neuroscience, endocrinology, and psychoneuroimmunology. Special attention is given to the role of the menstrual cycle, perimenopause, and stress-induced hormonal changes (e.g., cortisol and estrogen) in modulating pain sensitivity and sleep architecture.

Results: Women are more likely than men to experience sleep disorders such as insomnia and to report heightened pain sensitivity. Hormonal fluctuations across the menstrual cycle and life stages significantly influence both sleep quality and pain thresholds. Chronic stress further exacerbates this relationship through dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, amplifying both

sleep disruption and central sensitization of pain pathways. These factors often coexist with mood disorders, creating a feedback loop that sustains poor sleep and persistent pain.

Conclusions: Understanding the sex-specific interactions among sleep, pain, and hormonal regulation is critical for the development of targeted, gender-sensitive interventions. This presentation calls for an integrative approach that addresses both biological and psychosocial contributors to improve sleep and pain outcomes in women.

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Investigating differential rhythmicity in circadian biomarkers using skin perspiration wearables

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Introduction: With advancements in wearable technologies like smartwatches, there has been growing interest in developing noninvasive sensors that can integrate with wearables for real-time health monitoring. The focus of this research is the detection of melatonin through perspiration, which contains similar biomarkers found in blood at measurable concentrations and develop a sensor algorithm for real-time melatonin monitoring in perspiration. The research aims to analyze circadian patterns in melatonin and cortisol and understand how light exposure impacts melatonin levels and explore whether perspiration can serve as a reliable surrogate for saliva in tracking melatonin.

Materials and methods: Features were extracted from the raw sensor data collected using a continuous, non-invasive wearable biosensor designed to measure circadian biomarkers. The primary objective was to model circadian patterns in circadian biomarkers, melatonin and cortisol. The raw sensor data was pre-processed to remove noise. To train and validate the model, interpolated melatonin levels derived from discrete saliva samples were used as the output variable. A total of 23 participants were included in the study, and strict protocols were implemented to control external variables that could influence cortisol and melatonin secretion. Participants refrained from caffeine, stimulants, and alcohol consumption after 6 p.m. to prevent disruption of the natural circadian cycle. To minimize light exposure, they remained in dim lighting conditions (less than 5 lux) from 10 p.m. to 4 a.m., which was verified using wrist-worn light exposure monitors. Physical activity levels were also monitored using wearable devices to account for potential activity-related effects on melatonin secretion. This controlled environment ensured the collection of consistent, high-quality data for the training and validation of machine learning models.

Results: Perspiration concentrations strongly correlated with salivary levels, with Pearson's coefficients of 0.89 for cortisol and 0.78 for melatonin. Bland-Altman analysis confirmed agreement, with narrow limits for cortisol (-4.68 to 6.13 ng/mL) and moderate variability for melatonin (-11.76 to 18.16 pg/mL). Circadian rhythmicity assessed via CircaCompare and Hedges' g revealed significant trends, with cortisol peaking in the morning ($g = 1.0831$) and melatonin highest at night ($g = 0.7575$). ANOVA showed significant temporal and age-related variations ($p < 0.0001$), with younger individuals exhibiting stronger rhythms. Correlation heatmaps indicated robust intra-age group relationships for melatonin and an age-related decline in light sensitivity in older adults. Machine learning models achieved high predictive accuracy, with R^2 values of 0.95 for cortisol and 0.96 for melatonin and RMSEs of 1.29 ng/mL and 3.12 pg/mL, respectively.

Conclusions: Perspiration-based wearable sensors integrated with machine learning offer a promising solution for real-time, non-invasive monitoring of cortisol and melatonin. This technology lays the foundation for advancing personalized tools for stress and sleep management. The research demonstrates the efficacy of a non-invasive sensor to monitor cortisol and melatonin in perspiration continuously. Utilizing statistical tools and assessing circadian rhythm, significant patterns were identified that aligned with established circadian rhythms and showed how melatonin is affected by environmental factors like light. The rhythmicity data from Circacompare validates that the sensor algorithm effectively captures cortisol's and melatonin's natural cycles.

Investigating the Effects of Pre-Sleep Virtual Reality Relaxation Experiences on Subjective and Objective Sleep Outcomes (Pilot RCT)

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Introduction: Currently, the use of electronic devices before sleep is not advised by health experts due to findings regarding the effects of blue light on the circadian clock and cognitive arousal such devices can produce before sleep. This broad assumption has recently been challenged by recent evidence that the use of electronic devices, in the context of producing relaxation and reducing cognitive arousal, can provide improved sleep outcomes.

Virtual reality (VR) technologies have shown therapeutic benefits for several conditions, including phobias, depression, post-traumatic stress disorder, social anxiety and pain. In many of these studies, improvements in sleep quality are reported as a secondary outcome. The aim of this study was to assess the effects of a purpose-built VR Pre-sleep experience over a traditional pre-sleep relaxation activity (reading) on sleep quality across a week in the home of young adults.

Materials and methods: Thirty-five young adults (9 M, 26 F, mean age 22.6 yrs, SD = 3.6), participated in a randomised crossover study across two weeks. After an initial orientation session, participants engaged in a VR Relaxation Experience (Liminal VR Pty Ltd) or Relaxation Control (reading a self-chosen book) for 10 mins before sleep each night for one week for each condition in a randomised order. For the duration of the experiment, participants wore a wrist actigraphy unit (wGT3X-BT, Actigraph LLC) to record their sleep/wake profiles at home while also using a sleep diary. On the last two nights of each week, participants sleep was recorded using portable polysomnography (PSG; Z-Machine Insight+, General Sleep Corporation).

Results: Statistical analyses of the first 35 participants indicated that on average:

- The VR condition had 3% better PSG recorded sleep efficiency compared to the reading control (82.1% vs 85.1%, $t(34) = 2.49$, $p = .02$).
- The VR condition showed 3.5 minutes shorter PSG recorded sleep onset latency compared to the reading control condition (5.3 mins vs 8.8 mins), trending towards statistical significance, $t(34) = 1.89$, $p = .07$ (NS).
- None of the mean actigraphy measures between conditions were statistically significant.
- Further subgroup analysis of 21 participants with poor initial sleep at baseline (PSQI > 5) showed no difference in results.

Conclusions: Findings from 35 participants indicated initial evidence that VR showed some significant improvements in PSG recorded sleep efficiency but no other sleep measures. VR could be a potential sleep aid. However, further research and refinement of the study design are needed.

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Large-Scale Investigation into Sleep Health: Patterns and Challenges in Chinese Population

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Introduction: Sleep is essential for our physical health, memory, and overall well-being. Understanding how people sleep is essential for public health. Traditional sleep studies often rely on subjective reports or are limited in scale. This study aimed to investigate the basic sleep patterns and common sleep issues in a large sample of the Chinese population.

Materials and methods: Data were collected from 93,640 participants. Objective sleep data—specifically, sleep duration, sleep onset time, and awake time—were collected using commercial wearable devices up to 300 days. Subsamples of participants who completed validated questionnaires, including the Pittsburgh Sleep Quality Index (PSQI) to assess subjective sleep quality, the Athens Insomnia Scale (AIS) to evaluate insomnia symptoms, and the Stop-Bang questionnaire to screen for high risk of obstructive sleep apnea (OSA) were selected for further analyses. Statistical analyses involved descriptive statistics and subgroup analyses. Ethical approval for the study was granted by the Institutional Review Board of Shanghai Medical College, Fudan University.

Results: The survey revealed an average sleep duration of 6.75 ± 1.60 hours. A substantial proportion (36.16%) of participants slept less than 6 hours per night, while 48.56% slept 6-8 hours, and 15.28% slept more than 8 hours. Sleep duration showed slight seasonal variations, being longer in spring (6.78 h) and winter (6.77 h), and shorter in summer (6.67 h) and autumn (6.68 h). The mean sleep onset time was 00:01, and the mean waking-up time was 06:43. Notably, 47.57% of individuals initiated sleep after midnight, and 13.69% after 02:00. Sleep onset time varied across generations, with those born before 1970 averaging at 23:02, compared to 00:33 for those born after 2000. Widespread sleep disturbances were reported, with an average of 1.4 nightly awakenings and common issues including difficulty falling asleep, frequent awakenings/early waking, and nighttime urination, affecting the vast majority and varying with age. PSQI assessments indicated that only 26.99% of participants experienced good sleep quality (PSQI score ≤ 5). Conversely, $52.95\% \pm 5.55\%$ reported mild sleep problems (PSQI score 6-10), $18.17\% \pm 4.29\%$ had moderate problems (PSQI score 11-15), and $1.89\% \pm 1.51\%$ faced severe problems (PSQI score 16-21). The prevalence of insomnia symptoms, as measured by the AIS, was notably high, affecting 73.39% of the surveyed subsample. Furthermore, the Stop-Bang questionnaire identified 17.49% of respondents as being at high risk for OSA.

Conclusions: This survey indicates that a significant portion of the Chinese population experiences insufficient sleep duration, poor sleep quality, and a high prevalence of insomnia symptoms, alongside a considerable risk for OSA. These findings highlight a substantial public health concern and underscore the need for increased awareness and strategies to improve sleep health across the population.

Latent physical activity profiles of people with chronic pain: Associations with pain severity, sleep and accelerometer-measured rest-activity rhythm

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Introduction: Approximately one-third of the global population experiences chronic pain (CP), significantly impacting daily activities and altering patients' engagement patterns. Recent research highlights that individuals with CP exhibit diverse pain-related activity patterns, underscoring the need for profiling-based approaches. Although previous studies have explored differences among activity profiles in terms of pain experiences and physical activity, limited attention has been given to differences in sleep and 24-hour rest-activity rhythms (RAR). This study aimed to apply latent profile analysis (LPA) to categorize individuals with CP by self-reported activity patterns, and subsequently examine differences across these profiles regarding pain experiences, sleep quality, and accelerometer-derived RAR.

Materials and methods: 195 participants with chronic non-cancer pain (CNCP), aged 18–65, were recruited in the UK. Eligibility required experiencing CNCP for ≥ 3 months. Participants completed baseline questionnaires assessing pain-related activity patterns (Patterns of Activity Measure–Pain, POAM-P: subscales of avoidance, overdoing, pacing), insomnia severity (Insomnia Severity Index, ISI), and pain severity and interference (Brief Pain Inventory–Short Form, BPI-SF). Actigraphic sleep quality (Actigraphic Total Sleep Time, A-TST; Sleep Efficiency, A-SE) and 24-hour RAR (MESOR – overall physical activity level; Amplitude – robustness of RAR; Intradaily Variability, IV – fragmentation of RAR) were objectively measured using wrist-worn accelerometers (MotionWatch 8) over a 7-day ecological momentary assessment (EMA). LPA identified distinct subgroups based on the three POAM-P subscales. Between-profile differences in pain, sleep, and RAR were analysed using Analyses of Covariance (ANCOVAs), adjusting for demographic covariates (age, gender, BMI).

Results: LPA identified four distinct profiles based on the three POAM-P subscales: “assorted activity regulation – moderate use” ($n = 101$, 51.8%), characterized by moderate use of all three strategies;

“overdoing” (n = 39, 20%), defined by high overdoing but low avoidance and pacing; “avoidant pacing” (n = 39, 20%), marked by high avoidance and pacing but low overdoing; and “assorted activity regulation – minimal use” (n = 16, 8.2%), showing minimal use of all strategies. ANCOVAs revealed significant differences in pain outcomes: the “assorted activity regulation – minimal use” profile reported the lowest pain severity and interference, while the “avoidant pacing” profile reported the highest. No significant differences emerged in sleep quality (ISI, A-TST, A-SE). However, RAR variables differed significantly: the “avoidant pacing” group showed the lowest MESOR and amplitude but the highest IV, reflecting lower activity and more disrupted rhythms. In contrast, the “assorted activity regulation – minimal use” group exhibited the highest MESOR and amplitude and the lowest IV, indicating more robust, stable daily activity rhythms.

Conclusions: This study highlights that distinct POAM-P profiles are associated with differing pain experiences and 24-hour activity rhythms. Understanding these profiles may enable clinicians to tailor more individualized interventions. Notably, minimal use of activity regulation strategies was linked to better outcomes, suggesting that a less pain-reactive, “non-action” approach may benefit CP management, challenging the contemporary assumption that activity pacing is the core intervention among CP patients.

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Linkages between sleep quality, sleep duration, and physical frailty among Older Adults in India

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Introduction:

The global population is experiencing a significant shift towards aging due to increased longevity and decreased fertility rates. Low- and middle-income countries, like India, are experiencing a rate of ageing three times faster than their wealthier counterparts. Given the rapid increase in India's aging population, it is crucial to identify factors linked to frailty among older Indians. The present study aimed to investigate the relationships between sleep quality, sleep duration, and physical frailty in older adults in India. In addition, it explored whether these associations differed by gender.

Materials and methods: This secondary analysis utilized data from the 2015 Wave 2 of the Study on Global Ageing and Adult Health (WHO-SAGE) in India, including a sample of 6,512 adults aged 49 years and above. Pre-frailty and frailty were measured using a modified version of the frailty phenotype developed by Fried and colleagues. Sleep quality and duration were assessed through self-reports. Multinomial and multivariable logistic regression models were employed to investigate the associations between sleep quality, sleep duration, and physical frailty (as well as its individual components), and to examine whether gender moderated these associations.

Results: About 66.8% were classified as pre-frail and 25.2% as frail. Compared to individuals with good sleep quality, those reporting poor sleep quality had significantly higher odds of frailty (Adjusted Odds Ratio [AOR]: 2.79; 95% Confidence Interval [CI]: 1.37–5.66). Comparing older adults obtaining the recommended 7–8 hours of sleep, those sleeping 9 hours or more exhibited a lower likelihood of both pre-frailty (AOR: 0.73; CI: 0.57–0.93) and frailty (AOR: 0.68; CI: 0.51–0.91). When examining specific frailty components, individuals with longer sleep duration had reduced odds of experiencing exhaustion (AOR: 0.86; CI: 0.73–1.00) relative to those with age-appropriate sleep duration. Additionally, frailty was more evident among older men with poor sleep quality and short sleep duration (<7 hours per night) than women with similar sleep patterns. While inadequate sleep quality was not associated with any frailty components in older women, in older men, it was significantly linked to higher odds of exhaustion (AOR: 4.28; CI: 2.28–8.06), weak grip strength (AOR: 2.31; CI: 1.46–3.67), and low physical activity (AOR: 2.81; CI: 1.10–7.21).

Conclusions: The findings of this study suggested notable associations between sleep quality, sleep duration, and physical frailty among older adults in India. Poor sleep quality was linked to an increased likelihood of frailty, while longer sleep duration was associated with a reduced prevalence of frailty, independent of sleep quality. Furthermore, the impact of poor sleep quality and shorter sleep duration on frailty was more pronounced among older men than women, highlighting the importance of developing targeted interventions to address sleep-related issues within this population.

Liproxstatin-1 Attenuates Chronic Intermittent Hypoxia-Induced Aorta Injury via Metabolic Reprogramming of the Pentose Phosphate Pathway

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Introduction: (1)Obstructive sleep apnea (OSA), a common sleep disorder, is pathophysiologically characterized by chronic intermittent hypoxia (CIH) resulting from recurrent upper airway collapse. (2)OSA-induced endothelial dysfunction serves as the pivotal mechanistic link bridging hypoxia and cardiovascular pathology.

Ferroptosis pathway is particularly relevant to vascular pathophysiology, as evidenced by recent investigations into endothelial dysfunction mechanisms.

(3)Liproxstatin-1 (Lip-1) is a potent ferroptosis inhibitor.

(4)The purpose of this study is to elucidate whether Lip-1 exerts its protective effects against CIH-induced vascular injury through metabolic reprogramming.

Materials and methods: Twenty-four male Sprague-Dawley rats (7-8 weeks old) and rat aortic endothelial cells (RAOECs) were stratified into four experimental cohorts: 1) Normoxic control, 2) CIH exposure (8 hour/day, 6%–21% O₂ cycling, 12 weeks), 3) CIH+vehicle, and 4) CIH+Lip-1. Western blotting quantified protein expression of key ferroptosis regulators—glutathione peroxidase 4 (GPX4), cystine/glutamate antiporter solute carrier family 7 member 11 (SLC7A11), and acyl-CoA synthetase long-chain family member 4 (ACSL4)—using β -actin for normalization. Cellular viability was assessed via CCK-8 assay after 24h hypoxia exposure. Flow cytometry with specific fluorescent probes (DCFH-DA for ROS, FerroOrange for Fe²⁺, C11-BODIPY for lipid ROS) quantified oxidative stress parameters. Commercial ELISA kits measured malondialdehyde (MDA), reduced glutathione (GSH), and NADPH/NADP⁺ ratios following manufacturer protocols. Mitochondrial ultrastructure was evaluated through transmission electron microscopy (TEM). Targeted metabolomic profiling (LC-MS/MS) mapped central carbon metabolism alterations, focusing on PPP intermediates.

Results: Oil Red O staining revealed that CIH treatment dysregulated lipid metabolism in aortic tissues. Western blotting analysis demonstrated that the protein abundance of GPX4 and SLC7A11 were significantly reduced in aortic tissues of CIH-induced rats and RAOECs ($p < 0.05$), whereas ACSL4 expression was markedly upregulated ($p < 0.05$). Consistently, in CIH-exposed RAOECs, cell viability was notably decreased, accompanied by elevated levels of ROS, Fe²⁺, lipid ROS, and MDA ($p < 0.05$). Conversely, GSH content and the NADPH/NADP⁺ ratio was significantly diminished ($p < 0.05$). Notably, transmission electron microscopy (TEM) revealed mitochondrial damage in the CIH group, characterized by ruptured mitochondrial membranes and disorganized matrix components. Furthermore, hierarchical clustering analysis profiling indicated that CIH disrupted metabolites of the pentose phosphate pathway (PPP). Strikingly, co-treatment with Lip-1 reversed the aforementioned pathological alterations.

Conclusions: CIH induces ferroptosis-driven arterial endothelial injury through a PPP-dependent mechanism, characterized by NADPH depletion, redox imbalance, and impaired GPX4-mediated antioxidant defense. The PPP remodeling—manifested as suppressed glucose-6-phosphate dehydrogenase activity and diminished NADPH synthesis—creates a permissive environment for iron-catalyzed lipid peroxidation. Lip-1 exerts multi-modal protection by 1) restoring SLC7A11-mediated cystine uptake, 2) enhancing GPX4 activity to neutralize lipid hydroperoxides, and 3) preserving PPP flux to maintain NADPH pools for glutathione regeneration. These findings position Lip-1 as a promising therapeutic candidate for OSA-related vascular complications and highlight metabolic reprogramming of the PPP as a novel target for endothelial protection in hypoxic conditions. Further clinical translation requires investigation of optimal dosing regimens and long-term safety profiles in OSA models.

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Mapping the Evidence: A Scoping Review of Sleep Health in Community-Dwelling Older Adults

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Introduction: Sleep health is a multifaceted concept including sleep duration, sleep continuity/efficiency, timing, alertness during waking hours, and perceived sleep quality. Among older adults, sleep disturbances are common and linked to adverse health outcomes such as frailty, physical and mental health issues, increased healthcare utilization, and mortality. Despite the high prevalence of poor sleep health among older people, the broader concept of sleep health in community-dwelling older populations has not been comprehensively reviewed. The aim of the study was to synthesize existing knowledge on sleep health among community-dwelling older adults (aged 65 and over), covering all five core dimensions of sleep health. The review also sought to identify key knowledge gaps and future research priorities.

Materials and methods: The review followed a systematic scoping methodology. Literature searches were conducted in Medline, CINAHL, and PsycINFO to identify peer-reviewed studies published in English or Swedish that included participants aged ≥65 years living in community settings. Only studies addressing all five sleep health dimensions were included. Data results on sample size, sleep variables, and health outcomes were extracted and synthesized.

Results: Eight studies met the inclusion criteria, where seven studies originated from USA and one study from Taiwan. Seven studies were based on data from a male and female osteoporosis registry. The studies had sample sizes ranging from 1,413 to 6,485 with a mean age between 76 – 83.6. The findings suggest that multidimensional sleep health is an important indicator of well-being in older adults. Poor sleep health, especially when two or more dimensions are impaired, was associated with higher risks of depression, higher healthcare cost, and mortality. Sex-based differences were notable: women reported poorer sleep and more frequent daytime napping, which itself was linked to higher mortality. In contrast, individuals reporting better sleep health had lower odds of frailty. Very few studies included adults aged 80 and above, limiting generalizability to the oldest-old population.

Conclusions: The scoping review highlights a clear need for more nuanced and inclusive research on sleep health in community-dwelling older populations. Future studies should include diverse samples, particularly the oldest age groups, and account for contextual factors such as care settings and sleep medication use. A more comprehensive understanding of sleep health is essential for developing effective interventions to support successful healthy aging.

Menopausal Hormone Therapy and Cardiovascular Outcomes in Menopausal Women with Obstructive Sleep Apnea

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Introduction: Menopause exacerbate the risk of cardiovascular events in women with obstructive sleep apnea (OSA). The efficacy and safety of menopausal hormone therapy (MHT) in cardiovascular outcomes in this population remain unclear.

Materials and methods: We conducted a propensity score-weighted cohort study using data from 363 menopausal women with OSA from a tertiary medical hospital. Patients were stratified based on MHT use (59 treated vs. 304 untreated). Baseline demographics, comorbidities, and apnea-hypopnea index (AHI) were balanced via overlap weighting. Outcomes included heart failure (HF) and major adverse cardiovascular events (MACE), analyzed using Cox regression with follow-up periods of 3 and 10 years.

Results: After weighting, baseline characteristics including age, AHI, and comorbidities showed no significant differences between groups. At 3 years, MHT was not significantly associated with reduced risk for HF (HR: 0.800, 95% CI: 0.167-3.837, p=0.781) or MACE (HR: 0.815, 95% CI: 0.226-2.932, p=0.754). Similarly, at 10 years, no significant reductions were observed in HF (HR: 0.836, 95% CI: 0.277-2.521, p=0.751) or MACE (HR: 0.902, 95% CI: 0.359-2.265, p=0.826).

Conclusions: Menopausal hormone therapy in menopausal women with OSA did not significantly impact the incidence of heart failure or major cardiovascular events over both short and long-term follow-up periods. Further studies with larger cohorts are warranted to confirm these findings.

Meta-analysis of the studies about smartphone usage time relation to sleep quality among medical students

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Introduction: Smartphone usage has become a part of daily life among medical students, often leading to concerns about its impact on sleep quality. Given the demanding nature of medical education, adequate sleep is crucial for cognitive function, academic performance, and overall well-being. This meta-analysis aims to systematically evaluate the relationship between smartphone usage time and sleep quality among medical students.

Materials and methods: A comprehensive search of electronic databases (PubMed, Google scholar, Science direct, Cochrane review and Clinical trial.gov) was conducted to identify studies published between June 2014 and June 2024. Inclusion criteria were studies that assessed smartphone usage time and its correlation with sleep quality using validated measurement tools among medical students. Data extraction and quality assessment were performed independently by two reviewers. Statistical analyses were conducted to determine pooled effect sizes and heterogeneity among the studies.

Results: A total of 20 studies involving 2,823 medical students were included. The meta-analysis revealed a significant negative correlation between smartphone usage time and sleep quality, overall odds ratio of smartphone addiction to non-addiction for poor sleepers is 3.33 (95%CI = 1.45-7.61), with the high heterogeneity at 91%. The P-value for heterogeneity is below 0.00001, the p-value for overall effect = 0.004.

This indicates that increased smartphone use is associated with poorer sleep quality. Subgroup analyses showed that the relationship was stronger in studies using objective measures of sleep quality compared to self-reported measures. Additionally we analyzed poor sleep quality between genders. The overall odds ratio of poor sleep quality between male to female is 1.87 (95% CI = 1.16-3.01), with the low heterogeneity of 0% , p-value for heterogeneity = 0.90, overall effect p-value = 0.010.

Conclusions: The findings of this meta-analysis suggest that excessive smartphone usage is significantly associated with poor sleep quality among medical students. Future research should focus on differences between pre-clinical student, clinical student and postgraduate students sleep quality

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Metabolic characterization of sleep phenotypes from a multidimensional metabolomics perspective and sleep-metabolic networks

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Introduction: Sleep traits interact extensively with metabolism; different sleep traits can correlate with each other through homologous metabolites, forming a complex sleep-metabolism network. This study will assess the bidirectional relationships between 1091 plasma metabolites and 10 sleep traits, focusing on specific metabolic pathways and shared gene loci, and evaluate the metabolic association between sleep traits.

Materials and methods: We first assessed the causal relationships between plasma metabolites and sleep traits using bi-directional Mendelian randomization analysis. Bayesian network modeling was used to clarify the metabolic associations among sleep traits. We then identified two important

metabolic pathways through enrichment analysis and pathway analysis. Co-localization analysis further elucidated the genetic associations between sleep traits and plasma metabolites.

Results: A total of 145 metabolites significantly influenced sleep traits. The metabolite category most influencing sleep trait is lipids, and the sleep trait most influenced by plasma metabolites is sleep duration. Metabolites affecting both napping and sleep duration are enriched in "Biosynthesis of unsaturated fatty acids" pathway, whereas chronotype-associated metabolites enriched "Caffeine metabolism" pathway. Network analysis positioned napping as the central node connecting 7 other phenotypes. Co-localization analyses finally reveal 7 genetic variants shared across 26 sleep-metabolite pairs, with a shared genetic variant between daytime sleepiness and napping.

Conclusions: This study highlights the plasma metabolites that causally/genetically associate with sleep traits and two important enriched metabolic pathways, as well as metabolic associations between different sleep traits. We hope that will provide valid evidence for unraveling the metabolic mechanisms of sleep health and the metabolic associations between sleep traits.

Modeling Sleep Health Trends among U.S. College Students, 2019–2024: Descriptive Secondary Analysis of ACHA-NCHA III/IIIb

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Introduction: Sleep is foundational to student health and performance, yet multi-semester national trends are rarely synthesized. We summarized publicly available ACHA-NCHA III/IIIb estimates (2019–2024) to describe patterns in five sleep indicators: weeknight duration, weekend duration, sleep onset latency (SOL), daytime tiredness, and days felt well-rested.

Materials and methods: We compiled semester-level percentages and calculated means across 11 terms. Primary analyses were descriptive because observations are repeated cross-sectional aggregates rather than the same individuals over time. As an exploratory step, we conducted repeated-measures ANOVA with Bonferroni-adjusted pairwise comparisons across mutually exclusive response categories (e.g., <7 h, 7–9 h, ≥10 h). Where strata were available, we summarized undergraduate (UG) vs postgraduate (PG) patterns for key categories (e.g., <7 h weeknights; ≥31-min SOL).

Results: On weeknights, the mean proportion reporting 7–9 hours was 49.5%, versus 40.2% for <7 hours and 1.2% for ≥10 hours. On weekends, 63.6% reported 7–9 hours, 19.3% <7 hours, and 8.1% ≥10 hours. Daytime tiredness was frequent: 38.3% reported 3–5 days/week and 29.0% reported 6–7 days; only 3.9% reported 0 days. Feeling well-rested was uncommon most days: 34.7% reported 1–2 days/week, 30.1% 3–5 days, 17.3% 0 days, and 8.8% 6–7 days. SOL means were 34.1% for <15 minutes, 26.1% for 16–30 minutes, and 28.4% for ≥31 minutes. Exploratory pairwise comparisons indicated statistically significant separations among categories for weeknights, weekends, SOL, tiredness, and well-rested days (all $p < .05$), consistent with large descriptive gaps. UG-PG summaries were directionally similar to overall estimates.

Conclusions: College students continue to experience disrupted sleep patterns and widespread fatigue, with parallel trends in stress and psychological distress. These persistent issues suggest systemic misalignments between student wellness needs and academic and institutional demands. Colleges and universities should adopt holistic wellness strategies that target both sleep and mental health such as integrated sleep education, access to mental health resources, brief cognitive-behavioral therapy for insomnia (CBT-I), and the reform of academic structures to support recovery and rest.

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Multidimensional sleep health associates with depression symptoms in university students

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Introduction: Healthy sleep is important for mental wellbeing. Sleep problems frequently emerge in young adulthood and often precede the onset of depression. It is therefore important to identify sleep health metrics that can be used to predict mental health problems. The goal of our study was to determine dimensions of sleep health that are most closely associated with depression symptoms in university students using the Ru-SATED sleep health framework. We hypothesized that multidimensional sleep health scores would be negatively associated with depression scores. Based on prior work, we predicted that sleep satisfaction and alertness would be the sleep health dimensions most closely associated with depression symptoms.

Materials and methods: Sleep behavior was measured over 2 weeks in 547 university students (21.32 y $\pm$ 1.78 y; 63.2% female) using wrist actigraphy devices and daily diaries. Sleep data were analyzed using the Ru-SATED sleep health framework. Actigraphy data were used to determine the number of days that students met daily criteria for healthy sleep duration, timing, regularity, and efficiency. Diaries were used to assess self-rated sleep satisfaction and alertness. Students received a score of 0 to 4 for each sleep dimension based on the number of days they met criteria for healthy sleep. These scores were summed to derive a composite sleep health score (range=0-24). The Center for Epidemiologic Studies Depression Scale-Revised (CESD-R) was used to measure depression symptoms (range=0-80). Linear regression was used to test whether sleep health composite scores predicted depression scores. Multiple linear regression was used to test associations of the 6 sleep health dimensions with depression scores when entered into the model as individual predictors.

Results: Results for simple linear regression showed that higher composite sleep health scores predicted lower depression and explained 15.0% of variance in CESD-R scores ($R^2=0.15$, $P<0.001$). The multiple regression model, which allowed the predictive weights of individual sleep health dimensions to vary, explained 31.4% of variance in CESD-R scores ($R^2=0.31$, $P<0.001$). "Satisfaction" and "Alertness" were the only sleep health dimensions with statistically significant associations with CESD-R score. The CESD-R score decreased by 2.37 points for each additional day of the week that students reported being satisfied with their sleep, and by 3.03 points for each additional day per week that students reported feeling alert.

Conclusions: University students with better multidimensional sleep health had fewer depression symptoms. However, individual sleep health dimensions in the RuSATED framework differed in the strength of their association with depression scores. Sleep health metrics that give more weight to self-rated sleep satisfaction and alertness may perform better at predicting depression symptoms in young adults. Future studies should compare the performance of unweighted and weighted sleep health scores at predicting mental health outcomes.

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My Sleep Recipe: A Bedtime Book to Support Sleep Health in School-Age Children

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Introduction: Reading at bedtime has numerous benefits for child sleep and development, including fostering positive sleep associations, reduced sleep onset latency, and longer sleep duration. Additionally, bedtime reading promotes cognitive development, emotional regulation, and helps to align child and parent expectations around sleep, all of which contribute to better overall sleep quality. Despite these clear benefits, many children's books on sleep are developed for very young children, very rarely portray children from diverse backgrounds, or fail to depict the realities of obtaining healthy sleep while offering clear suggestions to mitigate poor sleep. In this study, we aimed to develop a bedtime book for school-aged children and assess the utility of the book on parent's perceptions of their child's bedtime routines.

Materials and methods: In collaboration with three community centers, we utilized the Reach Out and Read model to distribute the bedtime story book during the well child visit to school-aged children (4-8 years old) comfortable communicating in English and/or Spanish. The bedtime book, "My Sleep Recipe",

was crafted and developed over multiple iterations, with feedback from our advisory board, caregivers, and sensitivity readers to insure content validity for the target population. The book utilizes the "RESTED" framework (Routine and Regularity; Environment; Screens; Timing; Expectations; Duration) to convey basic principles of healthy sleep. Inside of the book, families received study information by scanning a QR code to consent and complete a one-time survey. The survey asked about general demographic questions, perceptions of the book and their child's sleep, and took approximately 5 minutes to complete.

Results: Data collected from October 2024 to May 2025 includes 17 participants (9 Hispanic/Latino), were mostly female (14, 82.3%), with an average age of 35.5 years (range=26-46 years), and the majority (15, 88.2%) received government health insurance. All families reported reading to their child at least twice per week, with a quarter reading daily. Participants reported an average of five bedtime activities per night. The most frequently rated bedtime activities included brushing teeth, reading, and putting on pajamas. Since receiving the book, all participants indicated that they looked at the book with their child at least twice, with 58.8% spending more time reading at bedtime and going to bed earlier or at the same time. The most frequent change in bedtime routine was a reported decrease in electronic use before bedtime (6, 35.3%) and followed a more consistent bedtime, (5, 29.4%).

Conclusions: Incorporating a bedtime book into a sleep routine can be an essential tool for fostering healthy sleep. Given the potential of bedtime books to positively influence sleep and development, further research should incorporate developmentally and culturally appropriate material and examine the use of various bedtime books and other story formats that older children may prefer, and how these tools can be adapted and maximized to help bedtime for school-aged children.

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Neurobehavioral effects of one night of partial sleep deprivation in school-age children and adolescents: a meta-analysis

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Introduction: In adults, one night of restricted sleep may impair alertness and sustained attention. For children and adolescents, some have argued that because of brain immaturity, the effects of sleep deprivation on these neurobehavioral functions may not be as prominent, and they may have a higher ability to compensate for acute sleep loss. This meta-analysis aimed to synthesize findings from experimental studies that investigated the effects of one night of partial sleep deprivation on alertness and cognitive functions in school-age children and adolescents.

Materials and methods: Ninety-one articles were retrieved from databases such as PubMed and PsycINFO, and 11 articles which met the inclusion criteria were included in this meta-analysis. All the analyses were conducted using R, and a random effects model were used to pool the effect sizes from the studies. The neurobehavioral functions investigated include objective and subjective alertness, executive function, complex attention, sustained attention, declarative memory, and processing speed. An intra-study meta-analysis was carried out for those studies that investigated more than one cognitive domain to obtain an overall effect size to be included in the meta-analysis. Effect sizes were coded such that a negative effect size reflects neurobehavioral impairments following partial sleep deprivation.

Results: The mean age of the participants (N = 350) was 13.97 (SD = 0.97) years. The average total sleep time (TST) of the partially sleep deprived group was 4.28 (SD = 1.79) hours, while the control group had an average TST of 8.68 (SD = 4.01) hours. One night of partial sleep deprivation decreased objective alertness ($g = -1.69$, $p < 0.01$), and its impairing effect on subjective alertness was numerically smaller and marginally non-significant ($g = -1.49$, $p = 0.07$). One night of partial sleep deprivation did not have any significant impact on overall cognition ($g = 0.12$, $p = 0.44$) or individual cognitive domains ($|g| = 0.04$ to 0.30 , $p > 0.15$).

Conclusions: Objective alertness is prominently impaired after one night of partial sleep deprivation in school-age children and adolescents; however, they might not perceive such deficit, since a corresponding decrease in subjective alertness was not detected in this meta-analysis. We did not find

any significant impairment in the cognitive functions investigated after a single night of partial sleep deprivation. This finding should not be interpreted as a reason for children and adolescents to curtail their sleep, as cognitive deficits might accumulate over more nights of partial sleep deprivation in these age groups. Lastly, the differences in findings from this age group and adults may be explained by differences in brain development.

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Nocebo Effects on the Duration of First-Night Effect in Insomnia Patients: A Polysomnographic Study

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Introduction: The first night effect (FNE) is a phenomenon where individuals experience sleep disturbances during the first night in unfamiliar environment. This phenomenon may compromise the first night's polysomnography (PSG) results and impede daytime function. Previous studies have demonstrated that placebo administration can mitigate the FNE in healthy individuals but exacerbate sleep in insomnia patients. However, duration of FNE under continuous placebo intervention in insomniacs remains undetermined. This study aims to investigate the variation of the FNE in insomnia patients with continuous placebo administration.

Materials and methods: This study enrolled 68 patients with insomnia disorder (DSM-5 criteria). Participants underwent four consecutive nights of PSG in a sleep laboratory following a 4-day placebo intervention. PSG data were analyzed using the Friedman test for differences across nights, with post hoc comparisons conducted via the Nemenyi method and Bonferroni correction.

Results: Following placebo intervention, significant differences were observed across key sleep parameters between the first and second nights : wake after sleep onset (WASO) decreased from (114.81 ± 78.10) minutes to (81.80 ± 54.34) minutes ($p = 0.001$), sleep efficiency (SE) improved from (69.84 ± 17.95)% to (76.02 ± 15.24)% ($p = 0.005$), N3 sleep duration increased from (42.95 ± 34.13) minutes to (53.63 ± 32.56) minutes ($p < 0.001$), REM sleep duration rose from (64.91 ± 54.79) minutes to (75.43 ± 48.35) minutes ($p = 0.002$), and REM sleep percentage increased from (17.71 ± 13.57)% vs (19.39 ± 11.75)% ($p = 0.018$). Following post-hoc comparison analysis, these parameters stabilized without further significant changes from the second night onward ($p > 0.05$).

Conclusions: The study indicates that placebo intervention may elicit the FNE in insomnia patients but may not impact its duration. Sleep parameters demonstrate stabilization starting from the second night. Future research should examine individual response differences.

Non-Rapid Eye Movement Parasomnias & their Impact on the Academic Performance in Medical University Students: A Cross Sectional Study

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Introduction: Parasomnias are disruptive motor episodes during sleep transitions, classified into rapid eye movement (REM) and non-rapid eye movement (NREM) types. NREM parasomnias (arousal disorders) include confusional arousals, sleepwalking, and sleep terrors. Despite knowing that parasomnias can negatively impact mental health, there is a noticeable dearth of studies on parasomnias among university students. This study aims to ascertain the prevalence of arousal disorders, their association with sleep quality, and their impact on the academic performance of university students.

Materials and methods: A quantitative cross-sectional study was carried out with validated questionnaires to collect online data using stratified random sampling after obtaining ethical approval from the ethical review board of Foundation Medical College. Rao soft was used to determine sample size with a 95% confidence interval and a 5% margin of error. The study included both male and female

MBBS students at Foundation University School of Health Sciences. All descriptive and inferential statistical tests including Pearson chi-square test, t-test, and ANOVA test were applied using SPSS 26, and a p-value of < 0.05 was considered statistically significant.

Results: The sample consisted of $n=175$ participants of ages ranging from 18-25 years [19.82 ± 3.99]. There were $n = 96$ (54.9%) female participants and $n = 79$ (45.1%) male participants in terms of gender distribution. The PSQI (Pittsburgh Sleep Quality Index) score of participants ranged from 0-15 with a mean PSQI score of 6.74 ± 3.15 (PSQI score of ≥ 5 is indicative of poor sleep quality). On assessing the prevalence of NREM parasomnias a total of $n=84$ (48%) had confusional arousals, $n=29$ (16.6%) had sleepwalking, and $n=74$ (42.3%) had sleep terror. The results of the ANOVA test indicate no significant association ($p=0.387$) between academic performance (last exam score) and sleep quality (PSQI score). The t-test suggests a significant association between sleep quality (PSQI score) and the occurrence of confusional arousals ($p=0.006$), sleepwalking ($p=0.03$), and sleep terror ($p=0.04$). The Pearson chi-square test yields a significant association between academic performance (last exam score), and sleepwalking ($p=0.037$).

Conclusions: The study reveals a notable prevalence of NREM parasomnias among medical students. The study concludes that individuals with poor sleep quality (high PSQI scores) are more likely to experience NREM parasomnias. However, the results of the study are not generalizable, and this warrants the need for further large-scale multicenter study, and future work could be done on evaluating awareness, knowledge, and various perceptions related to it.

Objective Analysis of Sleep Quality and Academic Performance Trends in Medical Students Using Wearable Technology

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Introduction: Optimal sleep is crucial for cognitive function, mental health, and academic success. Medical students, due to rigorous schedules, often experience disrupted sleep, impacting scholastic success. This study analyses sleep quantity and quality among international medical students at the University of Georgia using wearable technology, examining correlations between sleep metrics and academic performance, moving beyond subjective self-reports for precise data.

Materials and methods: An experimental study was conducted on 50 medical students (26 females, 24 males) who self-reported sleep deprivation. Sleep data was collected over seven consecutive days using the Huawei Band 3 Pro, which tracks deep sleep, light sleep, REM sleep, sleep continuity, breathing quality, and night-time awakenings. Data was extracted from the Huawei Health app on the eighth day, stored in an Excel sheet, and analyzed using SPSS (Version 26). Pearson correlations were used to assess relationships between sleep variables and academic performance, while t-tests examined gender differences. Ethical approval was obtained, and strict confidentiality was maintained.

Results: Participants had a mean Night Sleep Points score of 78.35, indicating generally good sleep quality. The average deep sleep continuity score was 89.74, suggesting minimal disturbances during deep sleep, which is crucial for memory consolidation. Breathing quality was high, with an average score of 95.24, reflecting stable and efficient respiratory patterns during sleep. A significant positive correlation was observed between Breathing Quality and Deep Sleep Continuity ($r = 0.42$, $p < 0.05$), highlighting the role of proper respiratory function in uninterrupted deep sleep. Additionally, Night Sleep Points correlated moderately with Breathing Quality ($r = 0.34$), reinforcing the link between overall sleep quality and respiratory health.

Regarding academic performance, while the correlation with sleep metrics was weak, a positive trend was observed between deep sleep percentage and perceived academic performance ($r = 0.252$, $p = 0.078$). This suggests a potential relationship that may become clearer with a larger sample size.

A gender-based analysis of breathing quality revealed noticeable differences. Males demonstrated generally higher breathing quality scores, with their median and interquartile range sitting higher on the scale compared to females. This suggests that a larger proportion of males experience better

respiratory efficiency during sleep. Although some overlap was observed, the overall trend indicates superior breathing quality among male participants.

Conclusions: This study highlights the potential role of wearable sleep technology in objectively assessing sleep patterns among medical students. Findings suggest that medical students generally maintain good sleep quality, with high deep sleep continuity and excellent breathing scores. While no strong correlation was found between sleep quality and academic performance, results emphasize the importance of deep sleep and respiratory efficiency for overall well-being. The study also revealed gender differences in breathing quality, suggesting potential physiological or lifestyle influences. Future research should include larger sample sizes, control additional variables, and explore potential gender-based differences further. Universities should consider integrating sleep education and wellness programs to support student mental health and cognitive performance.

Objectively-defined sleep regularity is associated with macrovascular and microvascular complications among individuals with type 2 diabetes – a cohort study

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Introduction: To assess the association of accelerometer-measured sleep regularity with macrovascular and microvascular complications among individuals with type 2 diabetes (T2D).

Materials and methods: A total of 3,862 participants with type 2 diabetes at baseline from UK Biobank (UKB) were included. The sleep regularity metrics measured by wrist-worn accelerometers include sleep regularity index (SRI) and sleep duration SD. Macrovascular complications included coronary heart disease (CHD) and stroke. Microvascular complications included diabetic neuropathy, diabetic kidney disease, and diabetic retinopathy. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for macrovascular and microvascular complications.

Results: During a median follow-up of 8.0 years, 410 composite macrovascular and 615 composite microvascular events occurred. Compared to participants in the highest tertile of SRI (regular sleepers), those in the lowest tertile were at higher risk of composite macrovascular complications (HR 1.29, 95% CI: 1.01-1.66) and stroke (1.97, 1.08-3.58). Compared to participants in the lowest tertile of sleep duration SD (regular sleepers), those in the highest tertile were at higher risk of composite macrovascular complications (1.44, 1.12-1.84), CHD (1.40, 1.07-1.82), and stroke (2.07, 1.13-3.81). For microvascular complications, no significant association of sleep regularity metrics was found (all $P > 0.05$). However, the dose-response analysis suggested a potential nonlinear association between SRI and diabetic neuropathy, with lower SRI consistently associated with higher risk of diabetic neuropathy compared with the median of SRI (HR 1.92, 95%CI: 1.28-2.88, 5th percentile vs. 50th percentile).

Conclusions: An irregular sleep pattern across days is clinically relevant for increasing the risk of macrovascular complications and diabetic neuropathy among individuals with type 2 diabetes.

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Obstructive sleep apnea physiological burdens and cognitive performance in older community dwelling American adults

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Introduction: Obstructive sleep apnea (OSA) is characterized by frequent intermittent hypoxemia, a highly prevalent nocturnal breathing disorder, and a universal public health problem. OSA severity, as defined by apnea-hypopnea index (AHI), is associated with cognitive impairment and a higher risk of Alzheimer's disease. However, oxygen saturation (SpO₂) based metrics such as hypoxic load and

ventilatory burden showed better adverse outcome predictive power than AHI. Thus, this study investigated whether these OSA-related physiological burdens, i.e., hypoxic load and ventilatory burden, are associated with cognitive performance in community-dwelling older adults.

Materials and methods: The study is part of a longitudinal study that included 135 clinically cognitively normal (i.e., clinical dementia rating scale, CDR=0) white non-Hispanic (37.8%) and black African American (56.3%) community-dwelling older adults (median age, 65.9 yr.) who participated in the sleep, aging, and brain health study at NYU. Cognitive performance was assessed using the unified dataset (UDS 3), an extensive neuropsychological battery test assessing various cognitive domains, including global cognition (MoCA), verbal memory, visuospatial, attention, language category fluency, processing speed, and executive function. Total sleep time (TST), ventilatory burden (VB) defined as proportion of abnormal breaths (<50% normalized amplitude), and hypoxic burden (HB) defined as the summation of desaturation areas (>3%) calculated from SpO₂ signal, were computed from an overnight polysomnography (PSG) conducted at Mount Sinai Integrated Sleep Centre. Linear mixed regression models were used to investigate the association between ventilatory and hypoxic burden and cognitive performance. Models were adjusted for age, race, sex, BMI, TST, and slow wave activity.

Results: The average TST for participants was 5.31 (Q1: 4.5 - Q3: 6.8) hr. BMI was 29.4 (Q1: 24.6 - Q3: 32.6), and AHI was 9.6 (Q1: 5.3 - Q3: 11.13). For each unit increase in hypoxic and ventilatory burden, the cognitive performance decreased on the MoCA (HB: β -0.179, VB: -0.0289, $p < 0.001$) and attention (HB: β -0.102 and VB: β -0.761, $p < 0.001$) tasks. Similarly, the elevated hypoxic and ventilatory burden was associated with increased time taken to complete executive function tasks (HB: 0.295 and VB: β 0.834, $p < 0.001$). In contrast, the language fluency test (HB: β 0.163 and VB: β 0.569, $p < 0.001$) and verbal memory test (HB: β 0.128 and VB: β 0.345, $p < 0.001$) scores were higher, indicating a better performance with elevated hypoxic and ventilatory burden. However, AHI had no significant association with decreased cognitive performance. In addition, there was no statistically significant association between the visuospatial and processing speed task-specific performances and hypoxic and ventilatory burden.

Conclusions: In this sample of cognitively normal older community-dwelling adults, OSA-related hypoxic and ventilatory burden were each associated with decreased cognitive performance in global cognition, with domains subserving attention, processing speed, and executive function driving these findings. The relatively better performance noted in language fluency and verbal memory domains in this population may reflect various underlying compensatory mechanisms associated with higher education.

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Obstructive sleep apnea syndrome and prothrombotic markers (alpha 2 antiplasmin a2AP and tissular plasminogen inhibitor 1 PAI-1)

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Introduction: Obstructive sleep apnea (OSA) is a chronic and prevalent condition that is associated with endothelial dysfunction, atherosclerosis and predisposes to a global cardiovascular risk and significant general morbidity and mortality. Despite its high prevalence and the susceptibility of patients with cardiovascular disease to stressors, OSA is still underrecognized and untreated in daily clinical practice. Inflammation is a major factor in the development and progression of cardiovascular disease, and OSA is associated with the excessive release of pro-inflammatory and pro-thrombotic mediators that contribute to the development of atherosclerosis and cardiovascular complications in these patients.

Materials and methods: A prospective observational study was conducted that included 56 patients diagnosed with moderate/severe OSA and 32 healthy patients. The collected data included personal information (sex, age), anthropometric measures (weight, height, BMI), associated diseases (cardiovascular, pulmonary and metabolic), parameters recorded by cardiorespiratory polygraphy (AHI, ODI, number of apneas, number of hypopneas, snoring index, average O₂ saturation, minimum O₂

saturation, T90, maximum pulse, minimum pulse, predominant sleep position), evaluation of the Epworth sleepiness scale at diagnosis. In the morning following the nocturnal cardiorespiratory polygraphy, biological samples were collected for a complete blood count to determine neutrophil to lymphocyte ratio (NLR) and ELISA testing of PAI-1 and a-2-AP.

Results: The present study aimed to investigate the proinflammatory status of patients with OSA quantified by NLR, and they had a higher NLR value compared to the control group, so that, independently of the BMI value, the obesity disposition, the associated comorbidities, they present a low-grade systemic inflammation. The majority of patients had obesity (84%) and severe OSA (93%) with a mean AHI of 66.3 events/hour of sleep and a mean oxygen saturation 88%. The predisposition to the development of cardio- and cerebrovascular diseases is clear, especially since the NLR value was higher in patients with arterial, mixed dyslipidemia, strongly influencing atherogenesis and the evolution of cardiac pathology.

Regarding antifibrinolytic markers, both PAI-1 and a-2-AP had statistically significantly higher values in the group of patients with OSA compared to the control (0.15177 ng/ml vs 0.12926 ng/ml, $p < 0.05$; 0.48325 pg/ml vs 0.34757 pg/ml, $p < 0.05$). In fact, patients with OSA develop a chronic prothrombotic status that may underlie major cardiovascular events.

Conclusions: The present study showed that the NLR value was higher in patients with severe OSA which associated arterial hypertension, mixed dyslipidemia, strongly influencing atherogenesis and the evolution of cardiac pathology. Regarding antifibrinolytic status, OSA patients had statistically significantly higher values of the studied biomarkers compared to the control group. Thus, patients with OSA develop a chronic prothrombotic status, reason why they need to be multidisciplinary evaluated at the time of the diagnosis. This study aimed to find new markers in the evaluation of OSA patients since there are important comorbidities associated with OSA.

Obstructive Sleep Apnea Syndrome, Excessive Daytime Sleepiness and Essential Hypertension – Clinical-Pathogenetic correlations

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Introduction: Obstructive sleep apnea syndrome (OSA) is a chronic respiratory disease characterized by partial (hypopnea) or total (apnea) cessation of breathing associated with a drop in oxygen saturation. The resumption of the physiological respiratory cycle is associated with increased sympathetic activity leading to intermittent hypoxemia $\pm$ hypercapnia, changes in blood pressure and pulse values. The relationship between OSA and arterial hypertension (HTN) is incompletely elucidated, with multiple mechanisms involved, such as alterations in the autonomic nervous system, hormonal and inflammatory changes, changes in intrathoracic pressure, with hemodynamic consequences and alterations in the physiological structure of sleep. In addition to chronic inflammation and intermittent nocturnal hypoxemia, the triggering of mechanical, autonomic, chemical and inflammatory mechanisms, OSA has become an independent risk factor of cardiovascular pathologies.

Materials and methods: We conducted a prospective study which included 126 adult patients diagnosed with moderate or severe sleep apnea and arterial hypertension. They had previously confirmed OSA diagnosis and HTN established following a specialized cardiological evaluation. The data studied included personal information, anthropometric indices, the presence of comorbidities, nocturnal cardiorespiratory polygraphy parameters and Epworth sleepiness scale assessment (at diagnosis and at 6 months). In the evaluation of hypertensive cardiovascular pathology, the duration in months since the diagnosis of HTN was assessed, compliance with the hyposodium diet, the presence of antihypertensive treatment and the mean and maximum value of systolic and diastolic blood pressure (BP) quantified by Holter BP at diagnosis, 3 months and 6 months were monitored. Also, these data were dynamically correlated with the Calgary Quality of Life Index (SAQLI).

Results: The present study demonstrated a positive proportional correlation between the degree of excessive daytime sleepiness and daytime and nocturnal BP values. Excessive daytime sleepiness becomes a predictor for severe OSA, and the increase in BP values at the time of OSA diagnosis is influenced by both OSA severity and obesity.

Patients with indication for home airway positive pressure therapy (CPAP) show a significant reduction in daytime and nocturnal systolic and diastolic BP values at 6 months, under conditions of good

compliance.

We used the Calgary Questionary to assessed the quality of life (QoL) in included patients and we concluded that those with daytime sleepiness had a decreased QoL. However, by implementing positive airway pressure therapy, a significant improvement is achieved, 6 months after initiation.

Conclusions: The present research brings additional information to a major global health problem. Patient associating OSA, HTN and excessive daytime sleepiness had higher BP values and decreased QoL at the moment of the diagnosis with significant improvement 6 months after CPAP initiation. Therefore, sleep apnea syndrome has become a pathology that requires a multidisciplinary, individualized approach, depending on the comorbidities it associates with and the patient's symptoms.

Occupational Exposure to Physical and Chemical Hazards and Sleep disturbance: The Mediating Role of Pre-Sleep Arousal

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Introduction: Occupational exposure to physical and chemical hazards could adversely affect sleep health. However, few studies investigate the role of pre-sleep arousal (PSA) in occupational sleep health. This study investigates the relationship between occupational exposure to physical and chemical hazards and sleep disturbances, focusing on the mediating role of PSA.

Materials and methods: This cross-sectional study used baseline data from the Korean Work, Sleep, and Health Study (KWSHS), including 4,430 wage workers aged 20–65. Occupational exposure (e.g., to noise, vibration, heat, cold, dust, vapors, and environmental tobacco smoke) was measured through structured questionnaires. Sleep disturbances were assessed using the Insomnia Severity Index and the Pittsburgh Sleep Quality Index–Korean version. PSA was evaluated using the Pre-Sleep Arousal Scale, including cognitive and somatic subscales. Logistic regression and causal mediation analyses were performed, adjusting for demographic, occupational, behavioral, and health-related covariates.

Results: Exposure to occupational hazards, including noise, vibration, high temperatures, and environmental tobacco smoke, was significantly associated with increased insomnia symptoms and reduced sleep quality. PSA, particularly somatic arousal, mediated the relationship between these exposures and sleep disturbances, indicating that higher PSA levels partially explain the adverse impact of occupational hazards on sleep.

Conclusions: The findings suggest that occupational exposure to physical and chemical hazards contributes to sleep disturbances among workers, with PSA serving as a significant mediator. Interventions aimed at reducing workplace hazard exposure and managing PSA may be effective strategies for improving sleep health in occupational settings.

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OSA Screening Questionnaires – What's New? Introducing the “GPSS” – General Practice Sleep Scale

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Introduction: Obstructive sleep apnoea (OSA) is a prevalent global health issue, affecting nearly one billion individuals worldwide. Over the past decades, various OSA screening questionnaires have been developed to identify individuals at risk. This study aimed to review the available OSA screening tools and discuss the features of more recent tools, with a focus on the General Practice Sleep Scale (GPSS), which is designed specifically for screening OSA in general practice settings.

Materials and methods: A comprehensive literature search was conducted using PubMed with keywords such as “OSA screening,” “Sleep apnea screening,” and “Sleep apnea questionnaire.”

Additional tools were identified by reviewing the reference lists of retrieved articles. Screening tools were analyzed based on their design features and country of origin.

Results: A total of 22 OSA screening tools were identified, including the Epworth Sleepiness Scale (ESS, 1991) and the Top End Sleepiness Scale (TESS, 2021). Of the remaining 20 tools, three were published in the 1990s, five between 2000–2010, ten between 2011–2020, and two between 2021–2025, with the GPSS being the most recent (2025). The majority originated from the USA (n=6), followed by Brazil (n=4), Canada (n=3), Australia (n=2), and one each from Germany, Belgium, Switzerland, Poland, and Japan. Most tools incorporated variables such as body mass index (BMI), neck circumference, age, sex, and snoring history. Recent tools, particularly the GPSS, were more likely to incorporate comorbidity information and use multiple risk thresholds rather than binary criteria.



Conclusions: The evolving understanding of sex-based differences and metabolic impacts of OSA has informed the design of newer screening tools such as the GPSS. The GPSS represents a promising advancement and warrants further evaluation and adaptation across diverse populations.

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Oscillatory population-level activity of dorsal raphe serotonergic neurons in sleep-wake disorders

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Introduction: The incidence of sleep-wake disorders is increasing, with the core pathological process involving abnormal changes in brain electrical activity related to the regulation of sleep-wake cycles. Studies have shown that 5-hydroxytryptamine (5-HT) neurons in the dorsal raphe nucleus (DRN) play a crucial role in regulating sleep-wake processes by releasing 5-HT to the prefrontal cortex (PFC), a downstream brain region, thereby altering sleep-wake states. However, the role of the DRN 5-HT neuronal pathway to the PFC in sleep-wake disorders and its underlying mechanisms remain unclear.

Materials and methods: Firstly, we performed synchronized electroencephalogram (EEG) recordings with fiber photometry to monitor the activity dynamics of 5-HT neurons in DRN across different sleep-wake phases. Secondly, sleep-wake disorder animal models were established using acute restraint stress (ARS) and chronic restraint stress (CRS). We assessed the effects of restraint stress on total sleep duration and sleep architecture in mice, while simultaneously examining whether the activity of DRN 5-HT neurons was altered during these processes. Next, miniscope was employed to record the activity of DRN 5-HT neurons during restraint stress and to evaluate their reactivation patterns during subsequent sleep periods. Subsequently, fiber photometry was utilized to monitor fluctuations in 5-HT neurotransmitter levels within PFC during sleep in animals exposed to ARS or CRS. Finally, patch-clamp electrophysiology was conducted to investigate the electrophysiological properties of DRN 5-HT neurons and PFC neurons in animals subjected to ARS or CRS.

Results: The population oscillatory activity of DRN 5-HT neurons projecting to PFC exhibited tight coupling with distinct sleep-wake phases. Specifically, DRN 5-HT neurons displayed heightened activity during wakefulness, reduced activity during non-rapid eye movement (NREM) sleep, and nearly ceased firing during rapid eye movement (REM) sleep. Mice subjected to CRS developed significant sleep-wake disturbances, characterized by shortened REM sleep latency, prolonged REM sleep duration, and an increased probability of transitions from NREM to REM sleep compared to controls. Furthermore, CRS mice exhibited distinct activity patterns of DRN 5-HT neurons across sleep-wake phases relative to unstressed controls. Notably, during NREM sleep, the magnitude of DRN 5-HT neuronal activity in CRS mice was significantly greater than that in controls. Importantly, DRN 5-HT neurons activated during restraint stress showed reactivation during subsequent sleep periods, as captured by miniature fluorescent microscopy. This reactivation phenomenon suggests a potential link between stress-induced neuronal activation and sleep dysregulation. Chemogenetic activation of the DRN 5-HT to PFC neuronal circuit mimicked the effects observed in CRS-treated mice. Furthermore, chemogenetic inhibition of the DRN 5-HT to PFC circuit effectively rescued the CRS-induced sleep disturbances. Suppressing the activity of this circuit restored baseline sleep architecture, normalized REM sleep parameters, and reduced aberrant phase transitions.

Conclusions: The DRN-PFC 5-HT pathway critically regulates sleep-wake dynamics and mediates stress-induced sleep disturbances. -CRS disrupts sleep architecture by amplifying DRN 5-HT neuronal activity during NREM sleep, promoting REM sleep abnormalities, and enhancing stress-activated neuron reactivation during sleep. These findings highlight the DRN-PFC 5-HT circuit as a therapeutic target for stress-related sleep disorders.

Parental Sleep Loss: Effects of Parental Bedtime Procrastination on Parental Sleep

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Introduction: Bedtime procrastination (BP) is the intentional delay of sleep to reclaim personal time and is associated with sleep-related difficulties. Parents of young children often report irregular sleep patterns, reduced personal leisure time, and heightened parenting stress, which may contribute to the use of BP as a coping strategy to restore a sense of control. Despite its relevance, there is limited research on BP in parents. This study aimed to explore parental BP and to investigate its associations with parental sleep.

Materials and methods: This study utilized data from a randomized controlled trial targeting parental cognitions about their child's sleep. Participants were 94 parent and child (6–24 months) dyads. Parents completed daily sleep diaries for their own sleep and their child throughout a 4-week intervention period, and for one week at each follow-up assessment (4 weeks and 12 weeks post-intervention). The sleep diaries included scheduled bedtime (SBT; the time each day that parents reported intending to go to bed), light-off time (LO; actual time attempting to sleep), wake after sleep onset (WASO), and parental total sleep time (TST). BP was calculated as the difference between SBT and LO. Child sleep indicators included WASO, TST, nap duration, and nighttime parenting involvement (the total time spent attending to the child during the night). Two multiple linear regression models were conducted to examine the effects of child- and parent-related sleep factors on parental TST. Model 1 included children's nap duration and nighttime parenting involvement as predictors. Model 2 added parental BP to assess its incremental contribution.

Results: Mean age of the parents was 33.61 ± 3.37 years (95.7% female), and the mean age of children was 12.62 ± 5.62 months (53.2% girls). A total of 4,374 sleep diaries were collected. The mean duration of parental BP was 44.52 minutes ($SD = 65.01$ minutes). In Model 1, children's nap duration and nighttime parenting involvement were significantly associated with parental TST (adjusted $R^2 = .044$). Increases in children's nap duration were significantly associated with shorter parental TST ($\beta = -0.042$, $p < .001$). Similarly, each additional minute of nighttime parenting involvement was linked to a 0.692-minute reduction in parental TST ($\beta = -0.050$, $p < .001$). In Model 2, all predictors remained statistically significant. Notably, each additional minute of parental BP was associated with a 0.766 minute decrease in parental TST ($\beta = -0.334$, $p < .001$), indicating Model 2 explained more variance in parental sleep duration (adjusted $R^2 = .30$) compared to Model 1 (adjusted $R^2 = .044$).

Conclusions: These findings suggest that parental sleep is influenced not only by external demands such as child sleep patterns but also by modifiable behavioral factors such as bedtime procrastination. This underscores the potential to improve parental sleep by focusing on bedtime behaviors. Results indicate that interventions aimed at improving parental sleep should address both caregiving-related demands and modifiable behavioral patterns such as bedtime procrastination.

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Pediatric Sleep Assessment Tools: Classification, Comparison, and Applications of Artificial Intelligence

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Introduction: Sleep quality is vital to children's growth, cognitive development, and overall health. Accurate assessment of pediatric sleep is essential for the early detection and intervention of sleep disorders. This paper reviews commonly used subjective and objective pediatric sleep assessment tools worldwide. These tools are categorized and compared based on different age groups, and their advantages, limitations, and applicability are analyzed.

Materials and methods: Subjective sleep assessment tools are found to be simple, convenient, cost-effective, and easy to implement. However, attention should be paid to the potential impact of recall bias on the results. Commonly used tools include sleep diaries, ISAS, BISQ, BISQ-R, TSAS, TCSQ, BEARS, CSHQ, SDSC, ASHS, and ASWS. These instruments assess various aspects such as sleep duration, sleep-onset difficulties, nighttime awakenings, sleep-disordered breathing, snoring, morning wake-up problems, daytime sleepiness, and co-sleeping. Objective sleep assessment tools, such as polysomnography (PSG) and actigraphy, record physiological signals. These tools are used to evaluate wake-sleep states and sleep stages, and PSG is considered the gold standard for assessing pediatric sleep-disordered breathing. Recent studies have explored innovative applications of artificial intelligence (AI) in sleep assessment. Including automated sleep staging based on PSG data and real-time monitoring using wearable devices combined with machine learning. Furthermore, an intelligent assessment system has also been proposed, which covers the entire process of screening, diagnosis, and intervention.

Results: Therefore, when selecting assessment tools, factors such as age appropriateness, assessment content, accessibility, reliability and validity, and cultural adaptability should be comprehensively considered. This helps achieve a more comprehensive and accurate evaluation of pediatric sleep. In addition, this paper introduces localized Chinese versions of assessment scales for infancy (ISAS, TSAS) and adolescence (ASHS, ASWS). These tools provide evidence-based support for clinical tool selection and intervention optimization.

Conclusions: It is suggested that future efforts focus on multi-source data integration, technological ethics, and model generalizability to support the continued advancement of precision and intelligence in pediatric sleep assessment.

Perceived barriers and facilitators to delayed school start times in Dutch and Flemish secondary schools

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Introduction: Sleep is essential for adolescents' mental, cognitive, and physical health. However, many adolescents sleep too little and of poor quality. A key cause is the mismatch between adolescents' delayed biological clock and early school start times, leading to chronic sleep deprivation. Delaying school start times is a potentially effective strategy to improve adolescent sleep. This study aims to explore barriers and facilitators to implementing later school start times in Dutch and Flemish secondary schools as perceived by school leaders.

Materials and methods: Semi-structured interviews (n = 18) were held with key stakeholders (i.e. school leadership or student support staff) from three categories of secondary schools in Flanders and The Netherlands: (1) schools that have implemented later start times, (2) schools that have considered such changes, and (3) schools firmly opposed to it. The interview guide was based on the MIDI (Measurement Instrument for Determinants of Innovation) framework. Interviews were recorded, transcribed, and thematically coded in MaxQDA 24.8.0.

Results: Stakeholders identified both barriers and facilitators across the phases of adoption, preparation, implementation, and continuation of delaying school start times. Adoption was often hindered by logistical concerns, ingrained routines, and perceived scheduling conflicts, though facilitated by awareness of adolescent sleep needs and renewed school vision. Preparation was facilitated by stakeholder communication, participatory planning, and adapting schedules and regulations. Implementation challenges included public transport mismatches and concerns about later end times, but benefits such as calmer school mornings, improved student alertness, and more meaningful interactions were frequently observed. Continuation was facilitated by alignment with broader educational visions, teacher and student satisfaction, and perceived health and performance benefits.

Conclusions: Successfully shifting school start times requires more than overcoming logistical barriers; it depends on strong internal leadership, alignment with pedagogical values, and a culture that allows for experimentation and adaptation. Open communication with staff and families plays a key role in building trust and support. At the same time, system-level actors—such as educational networks or government bodies—have an important role to play.

Perinatal Subjective Sleep Disturbance and Circulating Cytokine Levels: Bidirectional Examinations

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Introduction: Adaptational changes in cytokines across the gestational are essential to a healthy pregnancy. High levels of proinflammatory cytokines may result in systemic inflammation often linked to less favorable delivery and maternal outcomes. Likewise, systemic inflammation in the postpartum period may confer increased mood disorders. Significant sleep disturbance, such as poor sleep quality or efficiency, is associated with increases in inflammatory cytokines. Hence, sleep disturbances may precipitate chronic inflammatory changes which are considered a risk factor for poor delivery or maternal outcomes, such as preterm birth or mood disorders. On the other hand, inflammation is noted to impart disturbed sleep as well as adverse outcomes. This preliminary evaluation assessed whether sleep disturbances were associated with circulating cytokine markers across the perinatal period.

Materials and methods: These data were collected as part of the Healthy Babies Before Birth (HB3) study. Perinatal women ($N = 169$) who had available inflammation and sleep data from 4-times points: 8-16 weeks, 30-36 weeks, 6 months and 1-year postpartum were included. Sleep data were ascertained from the Pittsburgh Sleep Quality Index (PSQI) and cytokines were assayed using a custom V-PLEX human immunoassay plate. Multi-level models using maximum likelihood estimation examined within-subjects and between-subjects effects considering four sleep variables (PSQI total (overall sleep quality), sleep duration, mid-sleep timing, and sleep efficiency (SE)) and the cytokines (INF- γ , IL-6, -8, 10, and TNF- α) as well as the IL-6/IL-10 ratio across the 4 timepoints. Multi-level models were also used to test reverse relationships, whether inflammation predicted sleep variables.

Results: Participants were $M_{age}=31.3$ (5.6) years of age, with $M_{educ}=16.0$ (3.1) years of education. Over 75% were married and White. Between subjects' analyses indicate that poor sleep quality was significantly associated with the IL-6/IL-10 ratio ($\beta=.16$, $p<.05$). Shorter sleep duration was also significantly associated with higher IL-8 ($\beta=-.11$, $p<.05$), IL-6 ($\beta=-.14$, $p<.05$), and the IL-6/IL-10 ratio ($\beta=-.18$, $p<.01$) between-subjects, as well as higher IL-8 at the subsequent timepoint ($\beta=.09$, $p<.05$). Lastly, mid-sleep timing was significantly associated with a higher IL-6/IL-10 ratio at the next time point ($\beta=.07$, $p<.05$). No associations were noted for SE. For the reverse relationships, only one significant result emerged: later mid-sleep timing predicted lower IL-8 levels at the next timepoint ($\beta=0.07$, $p<.05$).

Conclusions: Corroborating the limited literature, sleep disturbances, including poorer sleep quality, shorter sleep duration, and later mid-sleep timing, are associated with greater circulating levels of pro-inflammatory cytokines and a higher ratio of IL-6/IL-10. Addressing the bidirectional nature of these variables, we also tested whether the sleep variables predicted inflammation. Only a single association emerged. Later mid-sleep timing was associated with higher inflammation. While these data suggest that sleep influences inflammation, more so than the reverse, further exploration of these pathways is needed. The data imply that the behavior of sleep may be an ideal candidate for intervention in order to mitigate adverse pregnancy outcomes.

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Persistent Hypoxia in an Apparently Healthy Woman

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Introduction: Hypoxia, a reduction in blood oxygen levels, can result from various factors. Pulse oximetry is a common tool for measuring hemoglobin oxygen saturation and serves as an alternative to invasive ABG analysis. This case report highlights the diagnostic and therapeutic complexities of a rare case of chronic hypoxia on pulse oximetry in an apparently healthy 40-year-old woman who incidentally discovered the condition.

Materials and methods: A 40-year-old female patient with a history of controlled hypothyroidism and thalassemia minor incidentally noted low SpO₂ (79-83%) on pulse oximetry during the COVID-19 pandemic, despite normal initial pulmonary and cardiac evaluations. One year later, during her pregnancy (achieved via IVF), her nocturnal hypoxia worsened, necessitating oxygen therapy. Post-delivery, PSG revealed moderate obstructive sleep apnea. Despite improvement in respiratory events with CPAP, her SpO₂ did not rise above 90%. Concurrent ABG with pulse oximetry confirmed normal arterial oxygen saturation (SaO₂) versus the low pulse oximetry SpO₂ (82%). Cardiovascular shunt evaluation was negative. Ultimately, methemoglobinemia with a level of 1.8% was diagnosed, explaining the discrepancy between pulse oximetry and ABG.

Results: This case underscores the importance of accurate differential diagnosis in chronic hypoxia, especially when pulse oximetry readings are inconsistent with clinical and other paraclinical findings. Differential diagnoses include pulmonary and cardiac diseases, vascular shunts, and methemoglobinemia. Methemoglobinemia, even at low levels (1.8% in this patient), can lead to spuriously low SpO₂ readings by pulse oximetry. The concomitant diagnosis of obstructive sleep apnea also contributed to transient hypoxic events. The impact of pregnancy on the severity of sleep apnea and nocturnal hypoxia was also a notable point.

Conclusions: In the presence of chronic hypoxia on pulse oximetry that does not correlate with initial clinical and paraclinical findings, rare differential diagnoses, such as methemoglobinemia, should be considered. An arterial blood gas (ABG) is essential to confirm true oxygen saturation. Thorough evaluation for sleep-disordered breathing is also crucial in these patients. Concurrent management of both methemoglobinemia and sleep apnea is vital for improving quality of life and preventing long-term complications.

Acknowledgments: We sincerely thank all the medical staff, nurses, and personnel from various departments who participated in the care and monitoring of this patient. Furthermore, we express our sincere gratitude for their contributions and gratitude to the patient for her cooperation and permission to publish this case report.

Personalized Sleep Extension in a Pilot Study: Effects and Moderators

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Introduction: Chronic short sleep is associated with adverse health outcomes, yet effective behavioral interventions remain understudied. This pilot study examined the efficacy of a tailored sleep extension (SE) intervention incorporating behavior change techniques and explored the moderators of treatment response.

Materials and methods: Eleven chronically short-sleeping adults (<6.5 hours; 25±1.5 years) completed a 3-day baseline, 4-day sleep hygiene education (SH), and 7-day 90-min SE protocol. Daily sleep was assessed via actigraphy and sleep diary. We first assessed overall intervention effects on seven sleep parameters, then examined phase-specific changes in sleep duration. Given substantial between-participant variability in sleep response (ICC = 28–54%), we further tested whether baseline individual characteristics moderated SE outcomes using simple slope analysis for significant moderators.

Results:

SE significantly improved sleep duration but showed mixed effects on sleep quality and stability. SH increased time in bed ($\beta = 0.72$ h, $p = 0.019$), SE further increased time in bed ($\beta = 1.49$ h, $p < 0.001$),

and tended to increase actual sleep duration ($\beta = 0.55$ h, $p = 0.059$). However, increased sleep duration was accompanied by greater fragmentation ($\beta = 9.435$, $p = 0.015$) and lower sleep efficiency ($\beta = -5.49$, $p = 0.024$), although no change in subjective sleep quality. And, intervention did not change sleep efficiency, latency, and circadian timing. Exploratory analysis showed that emotional stability, baseline sleep duration, and sleep barrier reduction during interviews would moderate the SE effect on actual sleep duration.

Conclusions: This pilot study supports the feasibility and effectiveness of a personalized SE protocol in extending sleep among short-sleeping adults. While SE increased sleep duration, it also led to greater fragmentation, suggesting a trade-off during adaptation. Importantly, individuals with lower emotional stability, longer baseline sleep duration, and more barriers solved benefited the most. These findings highlight the need to tailor behavioral sleep interventions based on individual psychological and sleep-related characteristics.

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Physical activity, weekend catch-up sleep, and depressive symptoms: Mediating effects of high-sensitivity C-reactive protein

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Introduction: We aimed to examine the effect of physical activity (PA) and weekend catch-up sleep (WCS) on depressive symptoms by evaluating their effects on high-sensitivity C-reactive protein (hsCRP) levels.

Materials and methods: Data were collected from 10,715 adults aged ≥ 19 years. PA and depressive symptoms were assessed using self-report scales. The WCS was calculated by subtracting self-reported average weekday sleep hours from weekend sleep hours, and serum hsCRP levels were measured using immunoturbidimetric methods. Given that depressive symptoms are characterized by their multifaceted nature, we identified specific symptoms associated with hsCRP levels. Path analysis was used to investigate the association between PA, WCS, hsCRP, and depressive symptoms, and that between PA, WCS, hsCRP, and specific symptoms related to hsCRP.

Results: Higher levels of PA and WCS were associated with a decreased risk of depressive symptoms through lowering hsCRP levels. Among various depressive symptoms, sleep problems and appetite changes were associated with hsCRP. In pathway analyses using them as dependent variables, higher levels of PA and WCS were also associated with a decreased risk of sleep problems and appetite changes through lowering hsCRP levels.

Conclusions: Increased levels of PA and WCS may help alleviate depressive symptoms, particularly sleep problems and appetite changes, by mitigating chronic inflammation. Therefore, ensuring adequate exercise time and compensating for inadequate weekday sleep during weekends are crucial for maintaining mental well-being.

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Planned Study Protocol: Sleep Health Among Older Adults – A Register-Based Cross-Sectional Study within NEAR-Aging

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Introduction: Sleep disturbances are common among older adults and are often associated with physical and mental health issues, as well as reduced quality of life. However, the relationship between various dimensions of sleep health and factors such as lifestyle, health status, quality of life and demographics remains insufficiently explored. The National E-infrastructure for Aging Research (NEAR) is a Swedish research consortium that gathers extensive registry data from older adults, providing a unique opportunity to investigate these associations. The aim is therefore to explore the associations between sleep health dimensions and lifestyle habits, physical and mental health, quality of life, and demographic factors in individuals aged 65 and older.

Materials and methods: A retrospective cross-sectional design will be used to enable objective conclusions from the collected registry data. The study population consists of individuals aged 65 and older who have responded to questions related to the sleep health dimensions. Data will be extracted from NEAR-aging studies that include variables related to the five sleep health dimensions: sleep duration, sleep continuity/efficiency, sleep timing, daytime sleepiness, and subjective sleep quality. Related variables will include physical activity, somatic and mental health conditions (e.g., depressive and anxiety symptoms), subjective memory function, self-rated health and quality of life, lifestyle habits (alcohol and tobacco use) as well as demographic data (age, sex, marital status, educational level). Statistical analyses will include descriptive statistics, group comparisons, and correlation analyses. The study is approved by the Swedish Ethical Review Authority and financed by the Medical Research Council of Southeast Sweden.

Results: The study is expected to reveal significant associations between different dimensions of sleep health and various factors related to physical and mental health, quality of life, lifestyle, and demographics in older adults in a Swedish context. Individuals with poorer sleep health are likely to report more mental health symptoms, reduced physical and cognitive functioning, lower quality of life, and less healthy lifestyle habits. Also, the results is also expected to reveal beneficial health outcomes associated to individuals reporting good sleep health. Reported poor sleep health or good sleep health dimensions, may also be prevalent in specific demographic groups, such as by age, sex, or educational level. Moreover, each sleep dimension may show distinct patterns of association with health and behavior.

Conclusions: The study conclusion is anticipated to highlight the complex interplay between sleep health and multiple domains of well-being in older adults. The findings may support the importance of holistic health assessments in aging populations and promote the integration of sleep health evaluations into routine geriatric care. Ultimately, this study could contribute to the development of targeted, multidimensional interventions aimed at improving sleep and overall health for older persons.

Polysomnographic comparison of sleep architecture between patients with disorders of consciousness and healthy controls

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Introduction: Disorders of consciousness (DoC) involve prolonged impairments in awareness and wakefulness. Sleep architecture, particularly the presence of deep and REM sleep, has been suggested as a potential indicator of residual brain function and recovery potential. However, systematic comparisons between DoC patients and healthy individuals using polysomnography (PSG) are limited.

Materials and methods: In the current prospective study, patients diagnosed with DoC (more than one month post-injury) and their age- as well as sex-matched healthy controls were recruited. All DoC patients underwent 24-hour PSG monitoring in a hospital setting, while healthy controls underwent 12-hour standardized PSG in our sleep lab. Key parameters included total sleep time (TST), sleep efficiency, proportions of N1, N2, N3, REM sleep, and the presence of sleep-disordered breathing (SDB), evaluated by the apnea-hypopnea index (AHI).

Results: Five DoC patients (mean age 60.6 ± 13.4 years) and three healthy controls (mean age 54.2 ± 11.2 years) were included in this preliminary analysis. Average sleep efficiency in the DoC group was 67.1%, which was comparable to 68.3% in controls. In the patient group, the average proportions of sleep stages were: N1 at 5.9%, N2 at 13.9%, N3 at 69.5%, and REM at 10.7%, with an AHI of 2.9. In the control group, N1 accounted for an average of 7.8%, N2 for 44.7%, N3 for 31.5%, and REM for 16.0%, with an AHI of 0.9. These preliminary results suggest that DoC patients showed significantly reduced N2 and REM sleep, while a markedly increased proportion of N3 sleep, and more frequent SDB compared to healthy individuals.

Conclusions: Sleep architecture differs substantially between DoC patients and healthy individuals. PSG-based assessment may provide objective markers of residual brain function and support the development of sleep-informed approaches for consciousness evaluation and neurorehabilitation.

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Poor sleep behaviour from childhood to adolescence is associated with polycystic ovary syndrome in adolescence: Findings from the Raine Study

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Introduction: Poor sleep behaviour is highly prevalent in females with polycystic ovary syndrome (PCOS), but its relationship with PCOS during childhood and adolescence is unclear. This study compares the longitudinal sleep behaviour trajectories and specific sleep behaviours from childhood to adolescence in those with and without PCOS.

Materials and methods: Caregivers of index participants (Gen2) of the Raine Study completed the Child Behavior Checklist (CBCL) questionnaire at ages 5-, 8-, 10- and 14-years. The CBCL includes six sleep behaviour items, each rated as '0' (not true), '1' (somewhat/sometimes true) or '2' (very/often true), which were summed to generate a composite score. A higher score indicates poorer sleep behaviour. PCOS status was assessed at 14-year using the 2018 adolescent Rotterdam criteria. Sleep behaviour composite scores were analysed longitudinally using generalized estimating equations at each time point and across time from 5-, 8-, 10- to 14-years. Prevalence of each sleep behaviour item from ages 5- to 14-years were also determined.

Results: N=187 participants with fully completed sleep behaviour and PCOS data were included, consisting of 29 (15.5%) diagnosed with PCOS. After adjusting for age of menarche, body mass index percentiles, family income, and symptoms of anxiety/depression, participants with PCOS exhibited poorer sleep behaviour trajectory compared to participants without PCOS that worsened over time from ages 5- to 14-years (mean difference (MD)=0.65, 95% confidence interval (CI)=0.23 to 1.07, $p=0.003$). Poor sleep behaviour trajectories did not differ significantly between participants with and without PCOS at age 5 (MD=0.09, 95% CI= -0.39 to 0.58, $p=0.71$), but diverged significantly from age 8 (MD= 0.76, 95% CI=0.14 to 1.37, $p=0.016$) until age 14 (MD=1.04, 95% CI=0.36 to 1.72, $p=0.003$). Specifically, compared with participants without PCOS, those with PCOS had a higher prevalence of several poor sleep behaviours during childhood, including trouble sleeping (24.1–69.0% vs. 7.0–43.7% at ages 5, 10, and 14), being overtired without good reason (34.5–79.3% vs. 20.3–53.8% at ages 5, 8,

and 14), and sleeping less than most kids (24.1–48.3% vs. 11.4–31.0% at ages 10 and 14). Other sleep problems such as nightmares, talking or walking in sleep, and sleeping more than most kids showed smaller or inconsistent differences between groups.

Conclusions: Our findings suggest that participants with PCOS diagnosed at adolescence have poorer sleep behaviour patterns during childhood compared to participants without PCOS. In children with diagnosed PCOS at adolescence, poor sleep may worsen hormonal imbalances and metabolic issues, potentially increasing insulin resistance and obesity, and further sleep problems in a vicious cycle. Future research should identify and address childhood sleep problems, leading to better interventions and support.

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Poor sleep quality in students with good academic performance in a medical school in Venezuela

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Introduction: The demands of the medical career can affect the quality of sleep of students, which could affect their academic performance, however, those who sleep less dedicating night hours to their studies, could have better grades. The objective of this study was to determine the sleep quality of medical students at a university in Venezuela and its relationship with academic performance.

Materials and methods: Observational, descriptive, cross-sectional study. All first, second, and fourth year medical students at the University of the Andes in San Cristóbal, Venezuela, were invited to participate. After signing the informed consent, the Pittsburgh Sleep Quality Index was applied and was related to their academic performance. Statistical analysis was performed with SPSS 22 and significance was considered less than 0.05. For categorical variables, Chi-square was used and for numerical variables, Pearson's correlation. The study was approved by the Ethics Committee of the Universidad de Los Andes.

Results: A total of 90 students were included. The mean age was 23.70 years (SD: 3.17; min: 20 and max: 35), 57.8% were women. The average grade point average was 15.75 out of 20 (SD: 2.20; min: 10 and max: 20). The average PSQI was 8.46 (SD: 3.47; min: 2 and max: 17), (23.3% good, 56.7% moderate, and 20% poor). Sleep latency was 21.94 minutes (SD: 17.21; min: 1 and max: 90) and mean nighttime sleep was 5.23 (SD: 1.04; min: 2 and max: 8). Students with better academic performance had higher PSQI scores (Pearson 0.027; P=NS). None of the students with excellent academic performance scored for good sleep quality, while 26.7% of them scored for poor sleep quality, compared to students with regular academic performance, of whom 33.3% scored for good sleep quality and 20% for poor sleep quality (P=NS). No significance was found in any of the other study variables.

Conclusions: The sleep quality of medical students at the University of the Andes in Venezuela tends to be poor overall, but those with better academic performance have an even worse sleep quality, probably because they dedicate more hours to their study and responsibilities, at the expense of their sleep hours.

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Poor subjective sleep quality independently predicts greater disability and functional decline in older adults at-risk of dementia

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Introduction: Dementia is characterised by progressive cognitive and functional decline, and sleep disturbance is an early prodromal feature, occurring years before formal dementia diagnoses. It is unclear if the presence of sleep disturbance in older adults with cognitive concerns is also linked to disability and functional decline. This study aims to determine if sleep quality is predictive of these features in a well-characterised cohort of community-dwelling older adults at-risk of dementia.

Materials and methods: Baseline data were drawn from the larger longitudinal Healthy Brain Ageing (HBA) cohort (total N = 1469), comprising community-dwelling older adults aged ≥ 50 years (mean $\pm$ SD age, 67.5 ± 8.9 ; 59.5% female) with new-onset cognitive concerns. Subjective sleep quality was measured with the Pittsburgh Sleep Quality Index (PSQI). Disability and functional decline were assessed using the 36-item WHO Disability Assessment Schedule (WHO-DAS Global Score) and the HBA-Functional Assessment Questionnaire (HBA-FAQ), respectively. Key covariates included age, depression (Geriatric Depression Scale, GDS-15), and comorbidity (Cumulative Illness Rating Scale, CIRS). Two multiple linear regression analyses were conducted to determine the unique variance in WHO-DAS ($n = 507$) and HBA-FAQ ($n = 828$) scores explained by PSQI, after statistically controlling for age, GDS-15, and CIRS.

Results: Two multiple linear regression models examined the independent contribution of subjective sleep quality (PSQI) to disability and functional impairment. In the first model predicting WHO-DAS global disability scores ($N = 507$; Adjusted $R^2 = .455$, $p < .001$), poorer PSQI scores significantly predicted greater disability ($\beta = 0.154$, $sr^2 = 2.0\%$, $p < .001$), even after controlling for age, depressive symptoms (GDS-15), and comorbidity (CIRS). In this model, GDS-15 ($\beta = 0.533$, $sr^2 = 23.6\%$) and CIRS ($\beta = 0.195$, $sr^2 = 3.4\%$) were also significant predictors (both $p < .001$), while age was not. In the second model predicting HBA-FAQ functional impairment scores ($N = 828$; Adjusted $R^2 = .378$, $p < .001$), poorer PSQI scores again significantly predicted greater functional impairment ($\beta = 0.175$, $sr^2 = 2.6\%$, $p < .001$), independent of covariates. GDS-15 ($\beta = 0.551$, $sr^2 = 25.5\%$) and older age ($\beta = 0.097$, $p = .001$) were also significant predictors in this model, while CIRS was not.

Conclusions: Poorer subjective sleep quality consistently and independently predicted both greater overall disability and increased functional impairment in community-dwelling older adults at risk of dementia, even after accounting for depressive symptoms, age, and comorbidity. While depressive symptoms were also strong predictors, the distinct contribution of PSQI across different functional measures underscores its importance. These findings suggest addressing subjective sleep disturbances may be a valuable target for interventions to mitigate functional decline in this vulnerable population.

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Postpartum maternal sleep disruption is associated with perception of infant temperament: Findings from a 6-month longitudinal study

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Introduction: Accumulating evidence links postpartum sleep disruption to adverse infant outcomes, including deficits in infant-maternal bonding. Infant temperament, or individual differences in infant reactivity and self-regulation, represents a combination of heredity, maturation, and context. For example, mothers with higher postpartum depression and anxiety perceive their infants as having more difficult temperaments. Maternal perception of infant temperament is likely also influenced by maternal sleep. We examined the associations between maternal postpartum sleep and maternal perception of infant temperament and the moderating effect of maternal depression and anxiety over 6 months following delivery.

Materials and methods: Postpartum women with a history of depression ($n=166$) completed self-report measures of their sleep (Pittsburgh Sleep Quality Index, PSQI), depression (Edinburgh Postnatal

Depression Scale), and anxiety (Generalized Anxiety Disorder Scale-7), and a parent-report measure of infant temperament (Infant Behavior Questionnaire, IBQ) once per month for 6 months following delivery. The IBQ includes 3 temperament factors: surgency/extraversion (e.g., smiling, activity level), negative affectivity (e.g., sadness, recovery from distress), and orienting/regulation (e.g., duration of oriented attention, low intensity pleasure). The sleep duration and sleep efficiency components and PSQI total score were examined as predictors. Concurrent associations between maternal sleep and infant temperament and interactions with maternal anxiety and depression were tested via 2-level multilevel models. Predictors were person-mean centered at level 1 (month level) and grand-mean centered at level 2 (person level).

Results: Maternal reports of infant surgency/extraversion, negative affectivity, and orienting/regulation significantly increased over time (p 's < .001), and maternal self-reported sleep duration, efficiency, and quality significantly increased over time (p 's < .001). Months with shorter sleep duration and lower sleep quality were significantly associated with higher maternal-reported infant negative affectivity (p 's < .01), and months with shorter sleep duration, lower sleep quality, and lower sleep efficiency were associated with significantly lower maternal-reported infant orienting/regulation (p 's < .05). Mothers who reported lower sleep efficiency and lower sleep quality on average also reported significantly higher infant negative affectivity (p 's < .05). Depression symptoms moderated the effects of sleep efficiency and quality on maternal-reported infant negative affectivity at the person level, such that lower infant negative affectivity was reported by those with lower depression symptoms and higher sleep efficiency (p = .05) and quality (p < .05). Anxiety symptoms also moderated the effect of sleep efficiency on maternal-reported negative affectivity at the person level, such that higher infant negative affectivity was reported by those with higher anxiety and lower sleep efficiency (p < .05).

Conclusions: Maternal perception of infant negative affectivity and orienting/regulation was associated with postpartum maternal sleep disruption. Maternal perception of infant orienting/regulation may be specifically sensitive to acute disruptions in postpartum sleep, whereas maternal perception of infant negative affectivity is linked to both acute and more trait-like maternal sleep disruption. Lower depression symptoms may buffer trait-like effects of maternal sleep disruption on perception of infant negative affectivity, whereas higher anxiety symptoms may be sensitizing. These findings highlight the importance of maternal sleep health for infant outcomes.

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Postpartum Sleep Health as a Network: Mapping Multidimensional and Contextual Dynamics

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Introduction: In the postpartum period, women experience significant sleep disruptions, affecting not just sleep quality but also how rested, alert, and satisfied they feel. Sleep health is a multidimensional construct encompassing sleep satisfaction, alertness, sleep timing, efficiency, and duration. Despite its multidimensional nature, prior research has largely focused on individual domains, with little attention to the interactions between domains. Moreover, sleep, particularly during the postpartum period, is embedded within a complex interplay of psychosocial contexts. This study aims to model interrelations among sleep health domains and their maternal, infant, and psychosocial correlates.

Materials and methods: Participants were a community sample of nulliparas 4–12 months postpartum. Sleep health was assessed using five domains: (1) Sleep Satisfaction was assessed using two items from the Insomnia Severity Index: sleep dissatisfaction and distress related to sleep. (2) Alertness was assessed using Fatigue Severity Scale, Epworth Sleepiness Scale, and Karolinska Sleepiness Scale. (3) Sleep Timing was calculated via bedtime deviation and rise deviation, which quantified the misalignment between participants' preferred and actual sleep/wake timing. (4) Sleep Efficiency was assessed using sleep onset latency and wake after sleep onset. (5) Sleep Duration was assessed by total sleep time. Maternal cognitive sleep factors included Glasgow Sleep Effort Scale and Dysfunctional Beliefs and Attitudes about Sleep; Infant sleep factors included infant daytime/nighttime total sleep time, sleep onset latency, and wake after sleep onset; Social-support factors included emotional and instrumental support, and proportion of nighttime support.

Network structures were estimated using Gaussian Graphical Model, where nodes represent variables

and edges represent conditional associations after controlling for all other variables in the network. To identify influential variables, strength centrality, bridge centrality, and expected influence were computed.

Results: The study included 329 participants (Mean_{age} = 31.76, SD_{age} = 4.67), with infants averaging 7.04 months old (SD = 2.60). For the sleep health network, the strongest connection was observed between sleep dissatisfaction and sleep-related distress (Satisfaction domain), followed by the association between distress and fatigue (Satisfaction and Alertness), and sleep onset latency and total sleep time (Efficiency and Duration). Nodes ranked highest in both strength centrality and expected influence were distress, fatigue, and dissatisfaction. For the integrated network with sleep health and contextual factors, maternal cognitive sleep factors showed the most extensive associations, particularly with satisfaction, alertness, and efficiency. Infant-related variables were linked primarily to efficiency and alertness, while social support factors had fewer direct connections. Maternal sleep effort demonstrated the highest bridge strength.

Conclusions: Postpartum sleep health is not only multidimensional, but the domains are interconnected. During the first postpartum year, distress with sleep and fatigue played central roles in overall sleep health. Further, amongst maternal, infant, and psychosocial correlates of sleep health examined, sleep effort emerged as a modifiable factor that exerted a strong influence on maternal sleep health. These findings contribute to a growing shift toward an integrated, multidimensional approach to postpartum sleep health. Distress with sleep, fatigue, and sleep effort may be prioritised in as therapeutic targets in sleep health interventions.

Predicting Insomnia Symptoms in University Students Using Machine Learning: The Roles of Stress, Dietary Intake, and Nature Connectedness

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Introduction: University students are particularly vulnerable to stress and sleep disturbances as a result of the psychological and adaptive challenges that come with transition to adulthood. The study aims to advance understanding of sleep problems among young people taking into account key risk factors, including stress, dietary intake and nature connectedness.

Materials and methods: A cross-sectional survey was conducted among 420 university students in Hong Kong. The Insomnia Severity Index (ISI) was used to assess the symptoms of insomnia disorder. The Perceived Stress Scale 4 (PSS-4) was used to measure perceived stress. The Short Food Frequency Questionnaire (FFQ) was used to measure dietary intake. Nature Relatedness Scale (NR-6) was used to assess the level of nature connectedness. Additional data on demographics, chronic conditions, alcohol use, smoking, and screen time were also collected. Participants were categorized into two classes: (i) those with clinical insomnia of moderate severity or above (ISI ≥ 15), and (ii) those without clinical insomnia (ISI < 15). To identify key predictors of clinical insomnia, the Extreme Gradient Boosting (XGBoost) machine learning algorithm was applied using Python. The dataset was split into training and validation sets in a 7:3 ratio with stratification. Given the imbalance class distribution within the dataset, the Synthetic Minority Oversampling Technique (SMOTE) was applied to the training data.

Results: Of the 420 participants, 8.6% (*n* = 36) were identified as having moderate or severe clinical insomnia. The mean age of participants was 20.7 years (standard deviation = 1.93), 28.3% were male, and 22.6% reported having a chronic condition. The XGBoost model achieved a balanced accuracy rates of 82% for predicting moderate severity or above clinical insomnia. The most predictive factors, in order of importance, were perceived stress level, whole milk intake, nature connectedness, fresh fruit consumption, and intake of seafood and shellfish.

Conclusions: These findings offer valuable insights into the complex interplay between insomnia, stress, dietary intake, and nature connectedness. The results also highlight the potential of machine learning models to identify individuals at elevated risk of insomnia based on the factors of stress level, dietary intake, and nature connectedness in the future research.

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Predictive and prognostic markers in the complex screening and diagnosis of Obstructive Sleep Apnea Syndrome

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Introduction: Obstructive sleep apnea syndrome (OSA) is a common but often underdiagnosed sleep disorder characterized by repeated interruptions in breathing during sleep, followed by intermittent decreases in oxygen saturation. Consequently, people with OSA experience fragmented sleep, multiple nocturnal and daytime symptoms, with a significant negative impact on their general health and quality of life.

Given the important complications of this pathology and its increased prevalence in the general population, the developed diagnostic methods and the difficult access to them, it is necessary to create preventive models by identifying the predictive factors of this pathology, in order to increase awareness and expand the possibilities of investigation of this pathology.

Materials and methods: The study group included a number of 30 consecutively selected patients, with an increased risk of sleep apnea quantified by the STOP-BANG questionnaire and the Epworth Sleepiness Scale (ESS). The data studied included: anthropometric measurements, the presence of comorbidities, nocturnal cardiorespiratory polygraphy parameters, the level of fractional nitric oxide in exhaled air (FeNO) and the mean and maximum level of End Tidal CO₂ (EtCO₂) assessed by continuous nocturnal capnography.

Results: The majority of patients had at the diagnosis excessive daytime sleepiness (ESS > 10 points). In the analyzed group, the mean age at the time of diagnosis was 55.60±10.55 years, with a predominance of male gender and 63.3% had at least one associated cardiovascular pathology. The mean level of FeNO in the studied group was 26.03±17.387 ppb, without being influenced by the presence of comorbidities, SASO severity or body mass index (BMI). The mean level of EtCO₂ was 44.70 ±3.879 mmHg, 43% of the subjects having values above the physiological limit.

There was a statistically significant correlation between BMI and ESS (p=0.001) and also between apnea-hypopnea index (AHI) (p=0.001) and the presence of cardiovascular comorbidities (p=0.004). In addition, it was observed that patients with severe OSA had higher EtCO₂ levels compared to those with moderate OSA (p=0.001), and there was a statistically significant correlation between Desaturation Index (ODI), Time spent at oxygen saturation ≤90% (T90%) and EtCO₂ level (p=0.001 and p=0.001, respectively). Following the study, statistically significant relationships between anthropometric indices and OSA severity were reported in the group of patients diagnosed with OSA, and as a predictive and severity marker, EtCO₂ plays a central role, having higher levels in patients with severe OSA and important desaturations which associated obesity.

Conclusions: Nocturnal monitoring of CO₂ levels can play a crucial role in the complex evaluation of patients with obstructive sleep apnea syndrome, especially in those with identified risk factors (obesity, associated cardiovascular pathology). The use of this parameter in current clinical practice can facilitate the adjustment of an appropriate, individualized treatment and reduce the risk of associated complications.

Detailed analysis is required, on large groups of patients, in order to study the complex relationships between these identified markers (FeNO, EtCO₂) and the severity of obstructive sleep apnea syndrome, the presence of comorbidities with the aim of developing effective screening and diagnostic models.

Preliminary Efficacy of Transdiagnostic Intervention for Sleep-Circadian dysfunction adapted for common mental disorders: A case series

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Introduction: Sleep and common mental disorders contribute to global public health challenges. Sleep has been established as a modifiable transdiagnostic contributor in the onset and maintenance of psychopathology. The role of sleep in influencing the illness trajectory, with effects on frequency of relapses, severity, and duration of episodes, calls for interventions targeting sleep across mental health conditions. The Transdiagnostic Intervention for sleep-circadian dysfunction (TranS-C) adopts a sleep health promotion perspective and was adapted in individuals with common mental disorders to reduce the dilemma of sequentially or concurrently targeting sleep. While previous studies have looked at sleep through the lens of Cognitive behavioural therapy for insomnia with individuals with primary insomnia and associated comorbidities, the TranS-C operates from a transdiagnostic preventative lens rather than a medical model. Previous research suggests that apart from behavioural symptoms, maladaptive cognitive processes—such as dysfunctional beliefs about sleep, repetitive negative thinking (RNT), and perfectionistic tendencies—play a key role in the bidirectional relationship between sleep and mood.

Materials and methods: The feasibility and preliminary efficacy of an adapted TranS-C protocol are displayed through a case series of five adults with common mental disorders (CMD), recruited from outpatient services at a tertiary mental health hospital. Individuals with a CMD meeting a cut-off score of > 5 (indicating sleep disturbances) in the Pittsburgh Sleep Quality Index and who had stabilisation of medication for four weeks were recruited. Outcome measures included sleep quality, mood (depression and anxiety symptoms), RNT, dysfunctional beliefs about sleep, and self-efficacy. Participants received 10-12 weekly sessions incorporating cognitive-behavioural strategies and psychoeducation targeting shared sleep and mood mechanisms. The outcomes were measured at pre-, post-, and follow-up of 3 months.

Results: The individuals recruited had primary diagnoses of health anxiety, recurrent depressive disorder, generalised anxiety disorder, PTSD in remission, and chronic insomnia. Negative affect and rigid perfectionism were common personality domains observed in the sample. The findings indicate a significant change in mood and sleep disturbance severity post-intervention. Additionally, there was a reduction of repetitive negative thinking, dysfunctional beliefs and an increase in cognitive flexibility and self-efficacy that was seen post-intervention.

Conclusions: These findings provide preliminary evidence for the utility of the modular, transdiagnostic intervention for individuals with CMDs and comorbid sleep-circadian dysfunction. The promising outcomes underscore the importance of targeting shared cognitive-affective mechanisms and support the need for future controlled trials to establish efficacy and generalizability. Moreover, addressing sleep-circadian dysfunction as a modifiable factor may enhance treatment outcomes and illness trajectories for individuals with comorbid and complex mental health challenges.

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Preliminary Findings on Sleep Patterns in Working Women of Menopausal Generation in Japan

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Introduction: Currently, approximately 40% of working women in Japan are in their mid-40s to 50s, which corresponds to the menopausal age group. This demographic also shows a high rate of labor force participation. Therefore, supporting the health and well-being of this population is considered crucial to maintaining overall workforce productivity. However, many women experience difficulties balancing menopausal symptoms with work, and sleep-related issues in particular have been reported to affect job performance. In this study, we present our interim findings from a project funded by the

Japan Agency for Medical Research and Development, which investigates the impact of menopausal symptoms on work productivity. Specifically, we report on the measurement of sleep status among working women in the menopausal age group. The objectives of this investigation are to assess sleep disturbances as menopausal symptoms and to clarify their impact on work productivity.

Materials and methods: The study aims to include 50 working women in their 20s to 30s as a comparison group, and 50 working women in the menopausal age group (40s to 60s) as the primary study population. Participants put on a wearable, simplified electroencephalogram device. The SmartSleep™ device (Philips, Koninklijke Philips N.V., the Netherlands) used in this study was placed on the women's heads during sleep for approximately three weeks, from bedtime to wake-up time. The device is connected to a smartphone, which collects sleep data such as sleep depth and sleep duration. One week after the start of the measurement and again at the end of the two-week measurement period, participants completed web-based questionnaires regarding their subjective sleep quality, sleep duration, and work productivity. The study commenced in December 2024 and is scheduled to be conducted over five terms. To date, two waves have been completed.

Results: A total of 16 participants were included in the first wave and 19 participants in the second wave. In the first wave, 44% were in their 40s and 56% in their 50s. In the second wave, 46% were in their 40s, 34% in their 50s. The self-reported average sleep duration was 359 minutes in the first wave and 383 minutes in the second wave. However, the actual measured sleep duration was 281 minutes in the first wave and 283 minutes in the second wave, indicating a discrepancy between perceived and actual sleep duration. The proportion of deep sleep was 37.5% in the first wave and 31.3% in the second wave. The presenteeism score, assessed using the WHO-HPQ (World Health Organization Health and Work Performance Questionnaire), was 59.4 in the first wave and 61.6 in the second wave.

Conclusions: These results provided an overview of the sleep conditions, including deep sleep, among women in the menopausal age group. We plan to complete the remaining study waves and accumulate further data to compare menopausal and younger women. We also aim to clarify the relationship between menopausal symptoms, sleep conditions, and work productivity.

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Prenatal Parental and Partner Sleep Predict Coparenting Quality Across the First Year Postpartum

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Introduction: Linkages between poor sleep and impairment of individuals' daily functioning are well-established. However, research examining the impact of sleep on family functioning is limited. Building upon previous work linking sleep with parenting (Bai et al., 2020, 2025; King et al., 2020), and the ecological model of coparenting (Feinberg, 2003), the current study investigated how prenatal parental and partner sleep predicts coparenting during the first year postpartum, with infant sleep and other relevant variables statistically controlled. Adopting a family systems approach (Cox & Paley, 1997), both parents' and partners' sleep patterns were considered in the examination. By focusing on prenatal sleep, we aim to document prenatal markers that providers can use to identify and support families vulnerable to coparenting challenges before delivery.

Materials and methods: 210 First-time expectant mothers (≥18 years) and their partners participated in an NIH-funded randomized controlled trial evaluating coparenting interventions. Parental prenatal sleep across 7 consecutive days was assessed using AW-64 actiwatches in the 3rd trimester. Because sleep is multi-faceted, several sleep indicators were considered, including *fall asleep time*, *wake minutes after sleep onset* (WASO; total awake minutes from fall asleep time to wake time), *total sleep time* (TST; the elapsed time from fall asleep time to wake time subtracted by WASO) averaging across 7 days, and *variability in sleep duration* (VSD, the standard deviation of TST across 7 days). At 1, 3, 6, and 12 months postpartum, mothers and fathers separately reported their coparenting perceptions via the Coparenting Relationship Scale (Feinberg et al., 2012), with higher scores indicating better perceived overall coparenting.

Results: Longitudinal actor-partner interdependence models within a multilevel modeling framework were conducted to examine the interactive effects of parental and spousal prenatal sleep on postnatal coparenting perceptions. Fathers reported higher coparenting quality than mothers on average ($p <$

.05), and coparenting satisfaction decreased over time in both parents. After controlling for infant TST, prenatal coparenting expectations, prenatal depression, race, family sociodemographic risk, and intervention status (control vs. intervention), parental and partner TST interacted to predict change in coparenting across 1 to 12 months ($p = .01$). Specifically, families where both parents had longer prenatal TST reported higher initial coparenting quality, and this advantage persisted over time. In contrast, families where both parents had shorter prenatal TST reported lower 1-month coparenting that remained consistently lower over time. Notably, families where only one parent had short TST showed significant decreases in coparenting quality over time. Additionally, greater prenatal VSD in parents but not partners was independently predictive of poorer postnatal coparenting experiences, with the effect remaining stable across time. No effect of prenatal WASO, fall asleep time, or any infant sleep variable on coparenting was obtained.

Conclusions: Our findings suggest that parental sleep patterns can be an easily assessed marker for identifying families at risk for coparenting difficulties before delivery. Our results suggest that coparenting transition-to-parenthood interventions can benefit from targeting prenatal sleep health in parents before they transition to first-time parenthood.

Prevalence and Psychological Profiles of Comorbid Obstructive Sleep Apnoea and Post-Traumatic Stress Disorder in a UK General Population Sample

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Introduction: Post-Traumatic Stress Disorder (PTSD) impacts 4% of UK and 5.6% of adults worldwide. PTSD is strongly linked to sleep disorders, including Obstructive Sleep Apnoea (OSA). Emerging evidence suggests a bidirectional relationship between OSA and PTSD, with overlapping hyperarousal mechanisms exacerbating both conditions. Evidence also suggests the risk of OSA in people with PTSD may have a differential profile to developing OSA. This study examines the prevalence and psychological profiles of comorbid OSA and PTSD in a UK general population sample.

Materials and methods: Three-hundred-eighteen adults (75.8% female; 29.9% aged 34-44 years) completed validated online questionnaires, including the STOP-BANG (OSA risk), PCL-17 (DSM-5 PTSD symptoms classification), PSAS (pre-sleep arousal), ESS (daytime sleepiness), HADS (depression and anxiety), B-PSQI (sleep quality), and EQ-5D-5L (quality of life). Participants were grouped into OSA-only risk (low, intermediate, and high) and OSA+PTSD categories. Chi-square tests were used to examine associations between group classifications and key demographic or psychological factors.

Results: Prevalence: 87.7% of participants were PTSD-symptomatic. High OSA risk (STOP-BANG ≥ 5) occurred in 13.3% of PTSD-symptomatic individuals whereas 5.1% non-symptomatic ($\chi^2=7.899$, $P=0.019$).

Demographic profile:

Males predominantly belonged to (OSA+PTSD), particularly in the high-risk OSA and symptomatic PTSD (35.3% of males), ($\chi^2=79.80$, $P < 0.001$, $ES = 0.354$). Additionally, 77.8% of high-risk OSA and symptomatic PTSD participants were <45 years vs. 50% >45 in OSA-only ($\chi^2=79.04$, $P < 0.001$). Median BMI was significantly higher in (OSA+PTSD) (36.41 kg/m^2) vs. OSA-only (25.71 kg/m^2 ; $P < 0.001$).

Psychological characteristics:

Pre-sleep arousal: Somatic arousal affected 98.1% of (OSA+PTSD) in contrast to 73.3% OSA-only ($\chi^2=43.989$, $P < 0.001$).

Daytime sleepiness: Among those with severe excessive daytime sleepiness, 25.0% were classified in the high-risk OSA symptomatic PTSD, while no participants with this level of sleepiness were in the OSA-only group, ($\chi^2(20) = 37.79$, $P = 0.009$, $ES = 0.172$).

Psychological Distress: Individuals with both anxiety and depression were predominantly classified in the (OSA+PTSD) (44.5%), while those with no anxiety or depression were more likely to be in the OSA-only group (30.6%), ($\chi^2(15) = 72.98$, $P < 0.001$, $ES = 0.277$).

Sleep Quality: Poor sleep quality (B-PSQI > 5) was more prevalent in the (OSA+PTSD) group,

particularly in the high-risk OSA symptomatic PTSD subgroup (13.1%) and the intermediate- OSA risk symptomatic PTSD subgroup (29.8%), ($\chi^2(5) = 15.68, P = 0.008, ES = 0.222$).

Quality of Life: “Poor” quality of life was reported exclusively by individuals in the (OSA+PTSD) group (20.0% in both intermediate- and high-risk symptomatic subgroups), while no participants in the OSA-only group reported poor quality of life, ($\chi^2(15) = 43.81, P < 0.001, ES = 0.314$).

Conclusions: Individuals with comorbid OSA and PTSD represent a distinct psychological and health profile, marked by younger age, male predominance, elevated BMI and heightened somatic arousal. They also exhibit greater psychological distress, excessive daytime sleepiness, and significantly poorer quality of life. findings underscore the urgent need for comprehensive screening protocols to go beyond traditional OSA risk factors, particularly in individuals with PTSD. Early identification and integrated treatment approaches targeting both conditions are essential to reduce the cumulative burden of this complex phenotype and improve health outcomes.

Prevalence, profile and perioperative outcomes of patients with Obstructive Sleep Apnea in a Low-resource center

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Introduction: OSA is a major but under-recognised public health disorder in Africa.^{1,2} Genetic and cultural factors make Blacks to be susceptible. OSA is associated with significant perioperative morbidity.² Useful data from LRCs are scarce, leading to sub-optimal care.

Objectives: To determine the OSA prevalence among surgical patients, associated factors, cultural variables, and perioperative outcomes, in a low-resource center.

Materials and methods: Methods: This mixed-methods study was conducted at a level-3 teaching hospital in Nigeria. Through convenience sampling, we retrieved 264 records of surgical patient. Data were cleaned, sorted, and summarised using the IBM SPSS 25.0. These include demographics, socioeconomic status, BMI, co-morbidities, STOP-BANG questionnaire score, PSG or HSAT OSA diagnosis, access to CPAP device, history of corrective surgery e.g., UPPP, anaesthesia technique, and surgical outcomes e.g., difficult airway, delayed recovery, postoperative hypoxia, and unplanned ICU admission. Quantitative analysis employed descriptive statistics i.e., frequencies, and mean, inferential tests i.e., chi-square test was used for categorical associations, and logistic regression was used for outcome predictors. Qualitative data included cultural beliefs, sleep patterns, duration and other profile, feeding practices, and use of traditional medicine. Thematic analysis involved manual coding. Mixed-methods integration summarised quantitative and qualitative data. The strength of the study is methodological triangulation, while limitations are convenience sampling bias and retrospective design.

Results: This retrospective analysis of 264 surgical cases revealed a 28.8% (n=76) OSA prevalence via STOP-BANG questionnaire screening. No patient had PSG or HSAT sleep study for OSA diagnosis. OSA was statistically associated with obesity (p=0.001, aOR 3.2, 95% CI 2.1-5.0), low socioeconomic status (p=0.001, aOR 2.6, 1.5-4.3), hypertension (p=0.001, aOR 1.9, 1.2-3.1), and sedentary lifestyle (p=0.001, aOR 2.2, 1.3-3.6), while smoking showed no association (p > 0.05, aOR 1.1, 0.8-1.5). Strikingly, 72% of screened patients prefer traditional medicine, resulting in delayed presentation (mean symptom period: 4.2±1.8 years). Surgical management was limited to tonsillectomy in 15.5% (n=41), with no patients receiving UPPP, MMA, or perioperative CPAP use. Among OSA patients (n=76) undergoing non-OSA surgeries, general anaesthesia (35.5%, n=27) showed statistically higher complication rates vs regional anaesthesia (63.2%, n=48): difficult intubation (12.9% vs 0%, p<0.001), postoperative hypoxia (21.2% vs 3.8%, p=0.002), and unplanned ICU admission (9.1% vs 2.3%, p=0.018).

Conclusions: This study highlights critical gaps in OSA care Nigeria. Lack of access to sleep studies suggest system failure. STOP-BANG is used for OSA screening and diagnosis. Strong association with obesity, and hypertension underscores need for integrative screening programs. Increased community education, access to sleep studies, and CPAP device will transform surgical outcomes in resource-limited settings.

Keywords: obstructive sleep apnea, surgical complications, Nigeria, sleep study

Acknowledgments: Reference

1. Komolafe MA, et al. Sleep medicine in Africa: past, present, and future. *J Clin Sleep Med*. 2021; 17 (6): 1317 – 21.
2. Ojo AK, et al. Review of Obstructive Sleep Apnea and the perioperative management of patients in a resource-limited setting. *West Afr J Med*. 2024; 41 (10) :1066 – 78.

Abbreviation

OSA: obstructive sleep apnea
LRCs: low-resource countries
PSG: polysomnography
HSAT; home sleep apnea testing
CPAP: continuous positive airway pressure

Prevalence, Risk Factors, Harm Perception, Attitude and Effect on Sleep Quality Towards Sugar Consumption Among University Students in Lebanon: A Cross-Sectional Study

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Introduction: Sleep has been a major concern among university students and may be influenced by dietary factors. With increased ready-made foods and sugar dense meal consumption, students are more frequently exposed to high levels of added sugars which has been linked to poor sleep outcomes and health. This study aims to assess the prevalence, risk factors, harm perception, and attitude of sugar consumption and its correlation with sleep quality among Lebanese university students.

Materials and methods: In a cross-sectional study of 404 Lebanese university students age range from 18 to 34, sleep quality was measured using Pittsburgh sleep quality index (PSQI), a 16-item questionnaire (score range 16–65, where higher scores indicated better sleep). Food Frequency Questionnaire (FFQ) and Beverage Questionnaire (BEVQ-15) were used to assess dietary sugar intake via a composite score derived from cereals, sweets, snacks, and sweet beverages (score range 24–195, where higher scores indicated greater sugar intake).

Results: Data normality was confirmed with skewness and kurtosis assessments, and Pearson correlation analysis revealed a significant inverse relationship between sugar consumption and sleep quality ($r = -0.256$, $p < 0.001$). Moreover, simple linear regression analysis indicated that each one-unit increase in the sugar consumption score corresponded to a 0.09 point decrease in sleep quality, with the model accounting for approximately 7% of the variance.

Conclusions: These findings suggest that higher intake of added sugars is independently associated with poorer sleep quality among Lebanese university students, identifying dietary sugar as a modifiable risk factor for sleep disturbances and supporting the need for targeted nutritional interventions and further longitudinal research using objective sleep measures.

Process evaluation of the implementation of a participatory developed school-based healthy sleep intervention in adolescents

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Introduction: Insufficient sleep among adolescents negatively impacts their mental and physical health. This study evaluates the process (delivery, participation, experience, context, maintenance and perceived impact) of a participatory developed healthy sleep intervention to provide insight into the underlying mechanisms of intervention effects and to formulate recommendations for future healthy sleep interventions in adolescents.

Materials and methods: After implementation in three secondary schools, questionnaires were administered in students ($n = 1075$), teachers ($n = 13$) and parents ($n = 55$). In addition, 14 focus group interviews with students ($n = 92$) and three individual interviews with school management were conducted. SPSS and NVivo were used for descriptive and thematic content analyses.

Results: Participants were generally satisfied with the intervention. Intervention components that were visible within the school context (i.e. kick-off event, posters, gadgets, class competition with Fitbits) were considered most successful since they sparked conversations about sleep. Opportunities for social comparison (e.g., class discussions, polls on Instagram) and tailoring of materials to the school context (e.g., picture of a teacher on poster) were appreciated by students. Contextual factors, including staff workload and lack of structural support, negatively affected implementation.

Implementers reported a lack of adequate information to implement intervention components, which resulted in low dose delivered for some intervention components (e.g., mobile application, classes about sleep). For sustained integration, clear roles, adequate support, and motivated staff are essential.

Conclusions: The intervention was generally well received. The participatory approach ensured that intervention components matched adolescents' living environment and the school context, but involving implementers earlier in the participatory process of implementation planning could optimize implementation.

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Proposal of a Novel Sleep Evaluation Index Utilizing Metabolic Dynamics During Sleep

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Introduction: Recent studies have highlighted the impact of sleep quality on physical performance and quality of daily life (QOL). High-quality sleep, in particular, is essential for muscle repair, fatigue recovery, health maintenance, and enhancement of athletic performance (Charest J et al., 2020). However, conventional sleep research has mainly assessed sleep quality through sleep depth measured by polysomnography, leaving actual metabolic processes and concrete degrees of physical recovery largely unexplored. This study focuses on metabolic change as a core indicator of bodily recovery, aiming to quantitatively analyze metabolic dynamics during sleep and to propose metabolic indices that complement conventional sleep evaluation.

Materials and methods: Nine healthy adult men participated. Two mattress types—selected for their potential influence on sleep quality and physical recovery—were tested: (i) the FACET mattress, manufactured by INOAC Corporation and featuring a hexagonal-slit structure reported to promote efficient rolling, improve pressure distribution, and maintain posture during sleep (FACET condition); and (ii) a control mattress of identical material but without slits (standard condition). Each participant underwent two nights of sleep experiments under each condition. The measured parameters were heart rate, autonomic nervous system indices, metabolic rate, and body movement; we compared the effects of mattress type on each parameter and on the interrelationships among these parameters.

Results: Under the FACET condition, heart rate and metabolic rate decreased and body movement was suppressed during N3 sleep. The reduction in metabolic rate was especially pronounced, and both decreases were statistically significant according to the Mann-Whitney U test ($p < 0.01$). During N2 sleep, heart rate was comparable to the standard condition, whereas metabolic rate fell significantly ($p < 0.01$) and body movement increased significantly ($p < 0.01$). In REM sleep, where bodily activity is commonly suppressed, heart rate rose significantly ($p < 0.01$), while metabolic rate and body movement both decreased significantly ($p < 0.01$). Autonomic nervous system indices—often used as conventional sleep indicators—showed no substantial differences between mattress conditions.

Conclusions:

Under the experimental condition of using different mattresses, metabolic indices captured changes in sleep state during the N2 and N3 stages more sensitively than heart-rate or autonomic nervous-system indices. The simultaneous reduction in metabolic rate and body movement during REM sleep under the FACET condition likely reflects better posture maintenance and reduced antigravity muscle activity afforded by the hexagonal-slit structure. The accompanying rise in heart rate and the absence of change in autonomic indices suggest that conventional bio-signal-based metrics may overlook certain metabolic responses. These findings indicate that integrating metabolic indices with traditional

methods could enable more direct evaluation of recovery processes, offering a new perspective for assessing factors—such as mattress mechanical properties—that physically interact with the body.

Proposing a definition for sleep disorders

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Introduction: To establish an overarching definition of what constitutes a sleep disorder, it is essential to know which health conditions should be included in the classifications of sleep disorders and to better distinguish the normal from the pathological in sleep medicine. This would bring together several professional organizations in their understanding of this hitherto heterogeneous concept. However, no consensus regarding a general definition of a sleep disorder currently exists.

Materials and methods: We explore two of the main frameworks used in medical epistemology that could be used to define sleep disorders rigorously: harmful dysfunction analysis (HDA) and symptom network theory.

Results: For each framework, we detail the conceptual background, the method for applying it to the establishment of a general definition of a sleep disorder, the application to main sleep disorders of the ICSD-3-TR (with an emphasis on insomnia disorder) and a discussion of the main aspects of these two general definitions in the context of sleep medicine.

Conclusions: The complementarity between the two definitions could then be considered as an "epistemic hub" which could serve to clarify the debate about what sleep disorders are, so that our understanding of them and their clinical management improve.

Acknowledgments:

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Psychosocial determinants of sleep health among university students: a structural equations modeling approach

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Introduction: Students are more at risk to develop sleep difficulties which could impact their health, mental health and academic performances. To address sleep issues before they reach clinical threshold, studying sleep health, an emerging concept in the literature, seems relevant. It considers sleep as a multidimensional construct which varies along a continuum, bringing nuance to the interpretation of individual sleep. This study aims to explore psychosocial determinants of sleep health among university students, using a socioecological approach.

Materials and methods: An online survey was sent to students (aged from 18 to 30 years old) registered at Laval University during the autumn semester. Those with a major medical condition or using medication to help them sleep were excluded from the study. The data were collected outside exam periods. This survey included questionnaires collecting information about sociodemographic, sleep health, sleep hygiene, sleep beliefs (using the Theory of Planned behavior), mental health (i.e. anxiety, perceived stress), health literacy, and social support. Prior to the statistical analyses, the data were weighted to be representative of the student population. Statistical analyses were then carried out to verify the goodness of fit of the proposed theoretical model, as well as a more in-depth analysis of the predictive and moderating factors.

Results: Valid data were provided by 524 participants. The model demonstrated a good overall fit to the data, and several hypothesized trajectories were supported. Specifically, poor sleep hygiene significantly predicted sleep health ($\beta = -.29, p < .01$), anxiety predicted sleep health as well ($\beta = -.26, p < .01$), behavioral control predicted both behavioral intention ($\beta = .30, p < .01$) and poor sleep hygiene ($\beta = -.28, p < .01$), behavioral intention predicted poor sleep hygiene ($\beta = -.13, p < .05$), and attitude predicted behavioral intention ($\beta = .14, p < .01$). Conversely, some expected associations were not confirmed: perceived norms and their importance did not predict behavioral intention; and perceived stress was not a direct predictors of sleep health. However, three unexpected significant pathways emerged: behavioral intention directly predicted sleep health ($\beta = .18, p < .01$), perceived stress predicted behavioral intention ($\beta = .25, p < .01$), and anxiety predicted poor sleep hygiene ($\beta = .39, p < .01$). In addition, moderation effects were observed. Employment status moderated the relationship between anxiety and sleep health, with stronger effects among students who had a job. Health literacy moderated the model with stronger perceived stress and anxiety effects for students with low literacy and stronger behavioral control effect for students with high literacy.

Conclusions: The psychosocial determinants examined in this study play a key role in students' sleep health. Anxiety has both direct and indirect effects, particularly among students combining work and studies, while perceived stress mainly strengthens intentions without directly improving sleep. Behavioral control strongly shapes intentions and sleep hygiene, whereas attitude and social norms play a limited role. Health literacy enhances the protective role of behavioral control and reduces the negative impact of stress and anxiety, especially among students with lower literacy. These findings highlight the relevance of interventions targeting both anxiety and sleep hygiene, while promoting students' perceived control. Finally, as intention poorly predicted sleep hygiene, futures studies should focus on specific sleep-related behaviors.

Quadratic Effects of Harsh Parenting on Changes in Children's Sleep During the Transition to Early-Adolescence

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Introduction: The family context is proposed to play a critical role in creating an optimal sleep environment (high levels of security, low arousal) (Worthman & Melby, 2002). Although harsh parenting has been identified as a risk factor for children's sleep problems, this work has strictly examined linear associations (Bell & Belsky, 2008; Kelly et al., 2014). Emerging work in the broader family risk literature indicates that effects of harsh parenting may be nonlinear (Hidalgo et al., 2023). Risk saturation (Morris et al., 2010) and family risk models (Davies et al., 2022) suggest prolonged exposure to intense levels of harsh parenting may activate processes designed to prevent sustained arousal in ways that decouple risk and development. Advancing this area of research, we utilized a two-wave longitudinal design to examine linear and quadratic effects of harsh parenting on change in children's actigraphy-derived sleep during the transition to early-adolescence.

Materials and methods: Children ($N=339$; Wave1: $M_{age}=9.44$ years, 48% girls, 65% White, 35% Black) and their parents, from socioeconomically diverse backgrounds in the southeastern USA, participated in two waves of data collection spaced two years apart. Harsh parenting was assessed via mothers' and fathers' report on the well-established Parent-Child Conflict Tactics Scale (Straus, 1999). Sleep is a multifaceted construct and while sleep parameters may overlap (Buysse, 2014; Sadeh, 2015), they represent distinct facets with differing developmental and clinical implications (Boatswain-Jacques et al., 2023; Park et al., 2019). Accordingly, we assessed several well-recognized sleep parameters. Sleep was measured objectively with actigraphy over one week to derive measures of sleep minutes (total number of minutes scored as sleep between sleep onset and wake time), efficiency (percentage of sleep time between onset and wake time), and activity (percentage of epochs during the night with activity). Children also self-reported on sleep-wake problems over the past two weeks (School Sleep Habits Survey; Wolfson & Carskadon, 1998).

Results: We examined effects of harsh parenting on changes in children's sleep over two years controlling for race, sex, body mass index, family income, and marital problems. No linear effects of harsh parenting emerged. There were significant quadratic effects of harsh parenting on sleep minutes

($p=.05$), efficiency ($p=.02$), and activity ($p=.04$). Increases in harsh parenting from low to moderate levels corresponded with decreases in sleep minutes and efficiency. As harsh parenting reached high levels, declines in sleep minutes and efficiency plateaued. Increases in sleep activity corresponded with increases in harsh parenting from low to moderate levels. Negative effects on sleep activity plateaued as harsh parenting reached high levels.

Conclusions: Novel findings illustrate that prospective relations between harsh parenting and children's sleep may be quadratic. At low to moderate levels of harsh parenting, sleep worsened. At high levels of harsh parenting, associations with less-optimal sleep attenuated; this pattern is consistent with risk saturation perspectives suggesting that prolonged exposure to intense levels of familial risk may activate processes designed to prevent chronic arousal. Findings highlight the importance of considering nonlinear associations in investigations between family risk and sleep.

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Racial Disparities in Perceived Social Support and Sleep Quality Among College Students

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Introduction: Insufficient sleep is a public health problem among college students. Approximately 71% of college students sleep less than eight hours per night, and one-third of students have trouble falling asleep at least once a week. Social support has been posited as a contributor to sleep quality. This study aims to determine whether perceived social support correlates with sleep quality among college students and whether these relationships differ by racial group.

Materials and methods: This is an observational, cross-sectional survey study. Traditional college-age students (18-23 years) who attend a large, public university were recruited in the lobbies of classroom buildings and student centers, Sunday through Saturday. Participants completed the Personal Resource Questionnaire (PRQ) and Pittsburgh Sleep Quality Index (PSQI) on a tablet. Higher scores on the PRQ indicate stronger social support while lower scores on the PSQI indicate better sleep quality. Descriptive statistics, chi-square tests, and Spearman's rho correlations were conducted.

Results: A total of 296 participants were enrolled in this study (51.7% White, 24.3% Asian, 24.0% Black). The mean age was 19.6 (SD=1.3). Most participants were female (63.8%), non-Hispanic (88.2%), and lived on campus (55.7%). Most participants shared a room (58.4%), were on financial aid (59.8%), and were unemployed (51.9%). Black and Asian students had lower perceived social support compared to White students (mean scores=136.1, 134.5, and 141.6, respectively, $p=0.04$), with no significant differences between Black and Asian students. Among the entire sample, perceived social support correlated with sleep quality such that higher perceived social support was associated with better sleep quality ($r=-0.28$, $p<0.001$). Black students had the strongest negative correlation between perceived social support and sleep quality ($r=-0.38$, $p<0.005$) compared to the correlation among White students ($r=-0.33$, $p<0.001$) and Asian students ($r=-0.20$, $p<0.11$). Black students were significantly less likely to report sleeping at least 7 hours/night than Asian or White students (25.7% vs 40.0% vs 47.9%, respectively; $p=0.002$).

Conclusions: This study highlights significant racial disparities in perceived social support and its association with sleep quality among college students. Colleges should consider offering programs to increase social support, particularly for Black students, as one way to potentially improve sleep quality.

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Real-World Observation of a Multi-Modal Smart Sleep Wellness Device: Sleep Quality Changes in a Consumer Population

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Introduction: This observational study evaluated the real-world effects of a smart sleep wellness device from Japan, developed by AmLife. The device, referred to as an Electric Potential Therapy (EPT) Device, integrates three key modalities—electric potential therapy, thermal therapy, and natural environmental sounds (such as ocean waves and bird calls)—along with calming audio frequencies, all embedded within a mattress designed to naturally enhance sleep comfort and overall well-being. The study was sponsored by AmLife and conducted in natural home environments.

Materials and methods: Sixty adults with mild sleep disturbances (PSQI > 5) were enrolled through rolling recruitment cycles, with each participant using the device nightly for 10 consecutive days. Subjective outcomes included the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Perceived Stress Scale (PSS). Objective outcomes were obtained from the Go2Sleep wearable device, with sleep efficiency analyzed as the primary parameter.

All data were anonymized and securely stored. Trend and correlation analyses will be conducted using paired t-tests or generalized linear mixed models (GLMM), implemented in Python 3.11.9 or SAS 9.4.

Results: Participants reported notable improvements in specific areas of their sleep experience as captured by the Pittsburgh Sleep Quality Index (PSQI). These included feeling less cold at night, experiencing fewer bad dreams, rating their overall sleep quality more positively, and having less difficulty staying awake during daily activities (all $p < 0.01$). ESS scores decreased significantly (from 9.74 to 8.76, $p = 0.044$), particularly in passive or sedentary contexts such as reading, watching television, taking an afternoon rest and after lunch. PSS scores also declined significantly (from 23.7 to 22.4, $p = 0.03$), especially in domains related to emotional regulation and coping with unpredictability. Mean sleep efficiency on day 10 was 98.43% (SD, 0.92), compared with 97.84% (SD, 2.35) on day 1 ($p = 0.07$), with notable inter-individual variability.

Conclusions: This real-world user observation study demonstrated that the EPT device improved selected aspects of sleep experience, including greater thermal comfort, fewer night-time disturbances, and better overall sleep ratings. Users also experienced a significant reduction in daytime sleepiness (ESS) and a notable decrease in stress levels (PSS), especially in terms of emotional balance and coping with daily challenges. These findings highlight the potential role of multi-modal non-pharmacological interventions in enhancing sleep, emotional stability, and well-being in daily life.

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Reduced sleep quality and decreased executive performance in patients with psoriasis

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Introduction: Psoriasis is a widespread dermatological disease with frequent multiple comorbidities. In its pathogenesis and maintenance, sleep impairments seem to play a crucial, albeit underestimated, role. Here, our main aim is to provide an in-depth analysis of psoriatic patients' objective sleep features - whose clear and full description is still lacking - also addressing their association with cognitive functioning.

Materials and methods: Psoriatic patients were recruited from Dermatology Units based on the following criteria: 18–65 years, mild symptom severity (PASI < 10; DLQI < 5), no systemic treatment (topical only), absence of comorbid medical conditions (including psychiatric and sleep disorder diagnoses), no history of drug or alcohol abuse, limited caffeine (no more than 150 mg/day) and alcohol (no more than 250 mL/day) consumption. Control participants were recruited via social media and advertisements following the same inclusion criteria except for the presence of psoriasis.

All participants underwent 7 days of actigraphy (Camtech, UK). Sleep during the final two nights was also monitored using SomnoArt (PPRS, FR), a validated wearable device. Cognitive performance was assessed with the Rey-Osterrieth test, Rey Auditory Verbal Learning Test (RAVLT), Finger Tapping Test (FTT), 2-back test, and Go/No-Go task.

Results: Nineteen patients (12M, 7F; age = 37.89 ± 12.93) and 53 controls (14M, 39F; age = 28.33 ± 13.29) were recruited. Psoriatic patients showed reduced total sleep time ($p=.013$), higher sleep latency ($p=.023$), NREM ($p=.050$) and REM sleep duration ($p=.024$) compared to control participants. In addition, patients' sleep showed reduced number of sleep cycles ($p=.041$) and frequency of short awakenings (< 2 minutes; $p=.049$), as well as a higher number ($p=.005$) and frequency (per hour of sleep) ($p=.003$) of functional uncertainty periods (FUP; i.e. periods with three or more state transitions, separated by no more than 90 seconds). As for the cognitive assessment, patients committed more errors on the Go/No-Go Task ($p=.041$), obtained higher scores at the Rey Figure immediate test ($p=.004$) and less correct responses on the 2-back test ($p=.043$).

In the overall sample, positive correlations emerged between sleep efficiency and the number of correct responses on the FTT ($p=.353$; $p=.003$) and total responses to the 2-back test ($p=.242$; $p=.042$). Sleep cycle number correlated positively with performance at the Rey Figure Delayed Recall ($p=.301$; $p=.011$) and RAVLT ($p=.257$, $p=.012$) and negatively with Go/No-Go response time ($p=-.338$; $p=.004$).

Conclusions: Despite the mildness of symptom severity, psoriatic patients display significant impairments in their sleep features. Specifically, patients' sleep turns out to be shorter and more fragmented and notably shows reduced organization in NREM-REM cycles, a well-established indicator of sleep quality. Psoriatic patients' sleep also appears less stable than controls, as reflected by data on FUPs. These changes are negatively correlated with performance at executive tasks, highlighting an interesting interplay between sleep and cognitive functioning. The present data suggest that specific interventions to improve sleep quality could have an impact on patients' psychophysiological state and even on the very same course of psoriatic disease.

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Reducing Evening Screen Time with REST-O: A Randomised Pilot Trial to Address Bedtime Procrastination

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Introduction: Bedtime procrastination, the voluntary delay of going to bed without external reasons, is increasingly recognized as a contributor to insufficient sleep and associated health risks. Formative work indicates that pre-sleep electronic device use, a ubiquitous bedtime procrastination behaviour, may be targeted using a behaviour change approach. This pilot study aimed to examine (1) the acceptability and feasibility of the Reducing Evening Screen Time online program (REST-O) in new career starters, and (2) the preliminary effect of the program on daily pre-sleep electronic device use and sleep duration, as well as weekly measures of bedtime procrastination, excessive device use, and sleep quality and duration.

Materials and methods: A total of 59 participants (mean age: 23.3 years) were randomly assigned to one of three conditions: (1) self-compassion intervention, (2) sleep hygiene intervention, or (3) waitlist control. Each intervention consisted of a single 45-minute online session, followed by a one-week period during which participants were encouraged to apply the strategies learned. Assessments were conducted at baseline and after the one-week intervention period, measuring bedtime procrastination, sleep quality and sleep hygiene behaviors.

Results: All groups experienced a reduction in daily pre-sleep device use ($M = 23.4$ min per day) and an increase in daily sleep duration ($M = 12.7$ min per day) post-intervention. Continued reductions in bedtime procrastination, excessive device use, and improvements in sleep quality and duration were observed at followup. Improvements in sleep quality and sleep hygiene behaviors were also observed in the control group. The program appears feasible and acceptable to participants with a high daily completion rate ($M = 84.7\%$).

Conclusions:

Reductions in habit strength and hedonic motivation suggest that changes in automatic routines and the desire for short-term rewards may explain the improvements in bedtime behaviour. These findings offer early evidence that brief, self-guided behaviour change interventions can help reduce pre-sleep screen use and bedtime procrastination—behaviours linked to poor sleep. Participants found the

interventions practical and easy to follow, reporting high satisfaction and strong engagement. This study shows that targeting sleep hygiene in simple, accessible ways may support better sleep routines. Larger studies are needed to confirm these results and to better understand how these interventions work over time.

Acknowledgments: We would like to acknowledge all the participants who took part in this trial.

Relationship between stress, depression, anxiety, coping strategies, and sleep hygiene practice among Chinese employed adults: A cross-sectional study

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Introduction: As the current economic environment gets worse and worse, the pressure faced by employed adults is also increasing. The different ways employed adults deal with mental status may affect their sleep health. However, the interactions of these variables were scarcely examined in the cultural context of China. This study aims to explore the relationship between coping strategies, mental health, and sleep hygiene practice among Chinese employed adults.

Materials and methods: A total of 192 employed persons from Physical Examination Center of a tertiary hospital were recruited in this study from August 2024 to February 2025. An online questionnaire survey was conducted using the general information questionnaire, Sleep Hygiene Practice Scale (SHPS), Depression Anxiety Stress Scales (DASS), and Simplified Coping Style Questionnaire (SCSQ). SPSS was applied to perform descriptive and regression analysis.

Results: This study found that Chinese employed adults suffered from medium level of sleep hygiene practice, 41.7% experienced depression, 40.6% for anxiety, 22.4% for stress, and 45.3% applied positive coping strategies. Sleep hygiene practice was negatively related to coping strategies ($r=-0.275$, $P<0.001$), and positively associated with depression, anxiety, and stress ($r=0.598$, 0.695 , 0.662 , respectively, all $P<0.001$). Multiple line regression analysis found that stress ($\beta=0.239$, $P=0.024$) and anxiety ($\beta=0.487$, $P<0.001$) were the positive predictor of poor sleep hygiene practice.

Conclusions: Chinese employed adults are experiencing mixed psychological emotions and have poor sleep hygiene behaviors. To enhance the sleep health of adults, it is necessary to take measures to reduce their anxiety and personnel stress, so as to promote the sleep health of patients.

Relationship of sleep duration and sleep quality with Cardio metabolic Health, Inflammation, Oxidative stress and Antioxidants in night shift workers

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Introduction: Human circadian rhythm is naturally aligned with the day-night cycle, promoting wakefulness during daylight hours and sleep during the night. However, night shift work forces individuals to sleep during the day, often in suboptimal conditions, resulting in shorter sleep duration, increased sleep fragmentation, and decreased sleep efficiency. Night shift workers often experience disrupted sleep patterns, leading to compromised sleep quality and associated health risks. Poor sleep quality among night shift workers has been linked to various adverse health outcomes, including increased risk of cardiovascular disease, metabolic disorders, and impaired cognitive function. The purpose of this study is to explore the relationship of sleep quality and duration with inflammation, oxidative stress, and antioxidants and cardio metabolic health in night shift workers.

Materials and methods: After approval from institutional ethics committee, 110 adults, were recruited and were divided into day workers and night shift workers. The volunteers were subject to anthropometric, chronobiological and sleep evaluations (by a questionnaire based on Pittsburgh sleep quality index), as well as to blood collection. Cardiometabolic health markers which were assessed by evaluating Blood pressure, Fasting triglyceride (TG) level, Fasting high-density lipoprotein (HDL)

cholesterol level and Fasting blood glucose. Markers of inflammation- C-Reactive Protein (CRP), IL-6, IL-1 β and TNF- α); marker for oxidative stress- γ Glutamyl Transferase (GGT) and markers for antioxidant status- Bilirubin, Uric acid, Vitamin A, C, D and E were measured in blood samples.

Results: This study found significant health differences between adults working day and night shifts, particularly regarding sleep quality, inflammation, and cardiometabolic health indicators. Key results include: 1. **Cardiometabolic Indicators:** Night shift workers exhibited higher body weight, systolic blood pressure, and triglycerides compared to day workers. Poor sleep quality was associated with increased diastolic blood pressure. 2. **Inflammation:** Elevated C-reactive protein (CRP) levels were observed among night shift workers, suggesting a link to chronic inflammation. However, other inflammatory markers did not show significant differences. 3. **Oxidative Stress and Antioxidants:** Surprisingly, individuals with poorer sleep quality had significantly lower GGT levels (16.72 ± 6.59) compared to those with better sleep quality (31.86 ± 15.58 ; $p < 0.001$), indicating that GGT may not reliably reflect oxidative stress in this context. Additionally, vitamin A levels were higher in night shift workers, suggesting a potential compensatory response to oxidative stress. 4. **Correlation Analysis:** Longer sleep duration positively correlated with serum bilirubin levels and negatively correlated with IL-1 β levels, indicating that adequate sleep may help reduce inflammation. Notably, poor sleep quality was associated with lower uric acid levels, reflecting a potential relationship between antioxidant levels and sleep quality. 5. **Ethnic Considerations:** The study also highlights the need for further exploration of ethnic differences in sleep health and its impact on health outcomes, as this could influence the observed relationships.

Conclusions: These findings underscore the complex interplay between sleep quality, health indicators, and shift work, emphasizing the need for targeted public health strategies to address the unique health challenges faced by night shift workers.

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Relationships between childhood sleep health and mental health at 12-years: Findings from the *Growing Up in New Zealand* study

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Introduction: Poor sleep health is associated with poor mental health, however limited research has focused on these relationships in late childhood, and examined independent contributions of multiple facets of sleep health, or explored potential influences of sleep at earlier ages. Using survey data from the *Growing Up in New Zealand* longitudinal study, we aimed to investigate how sleep at multiple timepoints across childhood relates to mental health at 12-years of age.

Materials and methods: Child-reported depression symptoms (CES-DC-10) and anxiety symptoms (PROMIS Pediatric Anxiety-SF8a) at 12-years were outcome variables in multiple linear regression models. Model 1 (cross-sectional) concurrently included 12-year sleep measures (maternally-reported sleep duration weekdays, sleep duration weekends, sleep problem; sleep consistency [weekday-to-weekend sleep duration difference]; child-reported sleep quality) as predictor variables, adjusted for sociodemographic variables at 12-years (child ethnicity, area-level socioeconomic deprivation, material hardship, rurality, gender). Model 2 (longitudinal) additionally included sleep at 8-years (maternally-reported sleep duration, night wakings, sleep problem), 4-years (maternally-reported sleep duration, night wakings, sleep problem), and 2-years (maternally-reported sleep duration, night wakings) as predictors.

Results: The sample ($n = 3,715$) included 22% Māori (Indigenous peoples of Aotearoa New Zealand), 14% Pacific, 13% Asian, 4% 'other' ethnicities and 56% European 12-year-old children. Cross-sectional (Model 1) independent associations were identified between short sleep (<9 hrs) on weekdays, inconsistent sleep patterns (weekday-to-weekend duration difference >1 hr), poor quality (fairly/very bad), and problematic (small or moderate/large problem) sleep at 12-years and higher depression symptoms; and between short sleep on weekdays, poor quality, and problematic (small or moderate/large problem) sleep at 12-years and higher anxiety symptoms. Additional adjustment for sleep health at earlier ages (Model 2) fully attenuated associations (β [95% CI]) between

moderate/large sleep problems and anxiety symptoms (Model 1 1.63 [0.27-3.00], Model 2 0.85 [-0.79-2.49]) but there was minimal attenuation for associations between sleep problems and depression symptoms (small problem: Model 1 0.49 [0.13-0.86], Model 2 0.46 [0.06-0.86]; moderate/large problem Model 1 0.97 [0.36-1.58], Model 2 0.84 [0.16-1.52]), short sleep and anxiety symptoms (Model 1 1.27 [0.29-2.25], Model 2 1.17 [0.11-2.23]) and small sleep problems and anxiety symptoms (Model 1 1.19 [0.37-2.01], Model 2 1.16 [0.28-2.05]).

Conclusions: Results provide evidence of concurrent independent relationships between multiple facets of sleep health at 12-years and depression and anxiety symptoms at 12-years, indicating that sleep and mental health are tightly connected in late childhood. Strengths of association were greatest for sleep quality, the one child-report measure, highlighting the importance of asking children about their sleep experiences which may differ from caregiver perceptions. Findings suggest that the relationship between sleep at younger ages and mental health at 12-years of age is likely complex. This warrants further investigation, alongside exploring sleep and mental health relationships over time as children continue to develop.

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Relationships between sleep and daily step count examined using large-scale, home-based, health monitoring data

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Introduction: Sleep and physical activity are two vital health behaviours, though the relationship between them remains poorly understood. Furthermore, previous research on this topic is often limited by relatively small or geographically constrained samples and an over-reliance on cross-sectional or self-reported data. To help advance knowledge of the sleep-activity relationship, we explored non-linear bidirectional associations between objective sleep parameters and daily step count in approximately 28-million person-days ($N = 70,963$; 244 regions) of large-scale health monitoring data.

Materials and methods: Data were attained using two FDA-cleared consumer health devices. Sleep parameters (sleep duration [mins], sleep onset latency [mins], and sleep efficiency [%]) were derived from the Withings Sleep Analyser, a validated under-mattress sleep sensor. Daily step count was measured using tri-axial accelerometry from the Withings ScanWatch. First, we performed a descriptive analysis to determine the proportion of the sample that routinely attained the National Sleep Foundation's sleep duration recommendations (adults 7-9hrs; older-adults 7-8hrs) alongside research-informed daily step count thresholds (adults 8,000 steps/day; older-adults 6,000 steps/day). Generalised additive mixed models (GAMMs) were used to produce exposure-response curves for the temporal association between sleep parameters and next-day step count, and vice versa. GAMMs were adjusted for demographic, temporal, and geographical factors.

Results: Only 12.9% of the sample routinely achieved 7-9 hours of sleep per night and >8,000 steps/day. 16.5% of participants slept <7 hours per night on average and lead a sedentary lifestyle (i.e., <5,000 steps/day). An inverted-U-shaped exposure-response curve indicated the optimal sleep duration for next-day step count was approximately 6 hours per night (e.g., +339 steps vs 8 hrs/night), though this increased to around 7 hours per night when adjusting for the duration of the wakefulness period. Greater sleep efficiency was associated with increased next-day step count in an exposure-dependent manner (25th to 75th sleep efficiency percentile: +282 steps/day). The association between sleep onset latency and next-day step count was inverse and near-linear (25th to 75th sleep onset latency percentile: -209 steps/day). Conversely, associations between step count and next-night sleep parameters were small and likely lack practical significance. All effect sizes were reduced when accounting for duration of wakefulness.

Conclusions: These data provide a novel insight into the relationship between sleep and physical activity at a multi-national level. Poor routine attainment of sleep recommendations alongside prominent step count thresholds highlights the need for public health initiatives that reduce barriers to both adequate sleep and physical activity, perhaps by better considering their interrelatedness.

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Relaxation of social time pressure affects subjective sleep quality and its associations vary depending on chronotype

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Introduction: Modern societal factors frequently impede the attainment of good sleep quality by many healthy adults. We investigated the chronotype-specific predictors of changes in subjective sleep quality following the relaxation of social time pressure during COVID-19 pandemic social restrictions in Japan.

Materials and methods: The internet-based Global Chrono-Corona Survey (GCCS) study received approval from the Ariel University Human Research Ethics Committee, Faculty of Health Sciences (AU-HEA-MK-20200629). A total of 1,649 participants completed the Japanese version of this study during the initial COVID-19 social restrictions. The final sample for analysis were 1,252 (34.6 ± 13.8 years, 67% female). Logistic regression analyses were used to assess changes under modified social time pressure in sleep quality by chronotype group (early, intermediate or late) from changes in patterns of daily behaviors.

Results: During social restrictions, subjective sleep quality deteriorated with decreased sleep duration and delays in sleep timing in the intermediate chronotype, while late chronotypes' reduction in sleep quality was associated with delayed sleep timing. Improved subjective sleep quality was associated with increased sleep duration and minimal sleep timing delay in the early and intermediate chronotypes. In late chronotypes, improved sleep quality was also associated with longer outdoor light exposure. These findings indicate that the determinants of changes in subjective sleep quality under modified social time pressure are at least partially chronotype-specific. Maintaining sleep timing may universally enhance subjective sleep quality during perturbations of social schedules. Moreover, in late chronotypes, the exposure to daylight may improve sleep quality, regardless of changes in sleep behaviors.

Conclusions: These insights may contribute to the development of effective strategies for promoting better sleep quality in modern societies where insufficient sleep is becoming increasingly widespread.

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Reliability and validity of the Chinese version of Global Sleep Assessment Questionnaire in adult patients with sleep disorders

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Introduction: Global Sleep Assessment Questionnaire(GSAQ) is a comprehensive screening tool to assess the presence of sleep disorders in the general population. Nowadays, Sleep disorders are estimated to affect 40% of adults worldwide, estimated nearly the same in China. This, in combination with a consistent association between lower or poor sleep quality and higher burden of multi-morbidity, underscores the need for translation and validation on the Chinese version of GSAQ to screening sleep disorders in China.

Materials and methods: We first translated GSAQ by two native Chinese speakers independently and back translated by two native English translator who had no access to the original English version of GSAQ. Secondly, we recruited a convenience sample of 55 patients complained with sleep disorders to assess the Chinese GSAQ scale's internal consistency and split-half reliability. Then, additional 55 patients were collected for exploratory factor analysis (EFA). Moreover, we obtained more 91 fulfilled questionnaires to perform confirmatory factor analysis (CFA) with total 201 samples. Finally, The Chinese version GSAQ were tested for criterion validity.

Results: The Chinese version of the GSAQ exhibited a Cronbach's α of 0.718 and a split-half reliability of 0.747. The KMO and Bartlett test confirmed that it was fit for applying this technique to this sample (KMO=0.601, Bartlett's Test of Sphericity $\chi^2=395.142$, $p<0.01$), EFA analysis defined four components of the GSAQ items considering the method of the eigenvalues >1 with 68.893% explained variance.

The CFA showing the goodness of fit of the GSAQ: $\chi^2=77.559$, $P<0.001$, $\chi^2/df=2.041$, $RMSEA=0.072$, $GFI=0.932$, $IFI=0.916$, $CFI=0.913$, indicating an acceptable model fit.

To verify criterion validity in the OSA population, correlations between GSAQ and Apnea Hypopnea Index (AHI) were analyzed. The results showed that the overall GSAQ had positive correlation with AHI ($r=0.312$, $p<0.001$). For insomnia, positive correlation was observed between the total GSAQ score with PSQI ($r=0.340$, $p<0.027$).



Conclusions: Chinese version of the GSAQ is a reliable tool for screening sleep disorders, especially for the most common ones, such as insomnia and OSA.

Restless Nights, Troubled Bodies: The Impact of Sleep Quality and Insomnia on Somatic Complaints in Psychosomatic Rehabilitation Patients

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Introduction: Sleep disturbances, particularly insomnia, are highly prevalent amongst patients in psychosomatic rehabilitation clinics. Impaired sleep quality or insomnia is not only a frequent comorbidity but also a potential aggravator of somatic symptoms, including pain, fatigue, and gastrointestinal complaints. Research suggests a bidirectional relationship between insomnia and somatic symptom complaints. However, this association has not been investigated in patients in psychosomatic rehabilitation clinics.

Materials and methods: From a total of 2,179 admissions to a psychosomatic rehabilitation clinic, a randomized sample of 356 patients (mean age = 49.04 years, SD = 9.96; 51.2% female) was selected. Patients completed standardized questionnaires assessing sleep quality, insomnia symptoms, somatic complaints, and a medical history form. Furthermore, ICD-10 diagnoses for mental and somatic disorders were determined using structured clinical interviews conducted by trained clinicians.

Results: Impaired sleep quality was significantly associated with more somatic complaints ($r = .337$, $p < .001$), and marginally significant with a greater number of somatic diagnoses ($r = .100$, $p = .09$), indicating a broad link between subjective sleep disturbance and somatic symptoms. Poor sleep quality was correlated with decreased general well-being, less appetite, more irregular bowel movements, problems urinating (including frequent urination in small amounts and increased nocturnal urination), and respiratory difficulties at rest and under exertion. Additionally, associations were found with nausea, excessive sweating, chills, and allergies.

Patients who met criteria for insomnia reported significantly more somatic complaints compared to those without insomnia ($t = -4.051$, $p < .001$); however, no significant differences were found regarding the number of somatic diagnoses. Patients who met criteria for insomnia reported significantly reduced general well-being, less appetite, frequent urination in small amounts, respiratory issues, excessive sweating, and chills.

Conclusions: The findings highlight the association between impaired sleep quality, insomnia, and somatic complaints in patients in psychosomatic rehabilitation clinics. Consistent with existing research, our results suggest that sleep quality and insomnia are linked to different somatic symptoms. While insomnia was associated with more self-reported symptoms, it did not correspond with a higher number of somatic diagnoses, suggesting that the quality rather than the quantity of somatic symptoms might have more impact. The results of this study highlight the importance of systematically assessing and treating sleep disturbances in psychosomatic settings, as doing so may improve both psychological and somatic outcomes.

Role of Deglycation molecules,ammino acid,phytonutrients,vitamin and mineral in Good quality sleep management

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Introduction: Sleep quality are global health concerns. Poor sleep quality has significant adverse health outcomes. Sleep quality is defined as an individual's self-satisfaction with four attributes as sleep efficiency, sleep latency, sleep duration, and wake after sleep onset. Antecedents include physiological as age, circadian rhythm, body mass index, NREM, REM, psychological (e.g., stress, anxiety, depression), environmental factors (e.g., room temperature, television/device use), and family/social commitments. Good sleep quality has positive effects such as feeling rested, normal reflexes, and positive relationships. Poor sleep quality consequences include fatigue, irritability, daytime dysfunction, slowed responses, and increased caffeine/alcohol intake.

The recent study was conducted to systematically review the effect of the melatonin on sleep quality. Many nutritional supplements have been used trying to benefit sleep wellness. There was no clinical study in this field. This study provides clinical study in patients with insomnia and normal patients after taking combined nutritional supplements as Rosmarinic acid, Fish oil (Omega 3), L-theanine, Glycine, Tryptophan, GABA, Magnesium, Calcium, Iron, B -complex Vitamins (e.g., B1,2,3,5,6,12,) Vitamin D and Vitamin E. Awake and sleep EEG were performed for clinical evaluation in sleep latency, sleep duration, NREM, REM and wake after sleep onset.

Materials and methods: The clinical trial prospective study in insomnia patients and normal patients compare pre and post taking combined nutritional supplements as Rosmarinic acid, Fish oil (Omega 3), L-theanine, Glycine, Tryptophan, GABA, Magnesium, Calcium, Iron, B -complex Vitamins (e.g., B1,2,3,5,6,12,) Vitamin D and Vitamin E for duration of 1 month. Awake and sleep EEG were performed for clinical evaluation in sleep latency, sleep duration, NREM, REM and wake after sleep onset.

Results: There were 20 cases in this study, 10 cases with normal sleep and 10 cases with insomnia. Awake and sleep EEG were performed pre and post taking combined nutritional supplements as Rosmarinic acid, Fish oil (Omega 3), L-theanine, Glycine, Tryptophan, GABA, Magnesium, Calcium, Iron, B -complex Vitamins (e.g., B1,2,3,5,6,12,) Vitamin D and Vitamin E for 1 month.

There were significant decrease sleep latency in both normal sleep and insomnia ($p < 0.01$), significant increase of duration of sleep in both normal sleep and insomnia ($p < 0.01$), significant increase NREM and REM in both normal sleep and insomnia ($p < 0.01$), significant decrease number wake after sleep in insomnia. But there were not significant decrease number of wake after sleep in normal sleep. The positive effect as feeling rested and fresh up were reported in both groups.

Conclusions: Combined nutritional supplements as Rosmarinic acid, Fish oil (Omega 3), L-theanine, Glycine, Tryptophan, GABA, Magnesium, Calcium, Iron, B -complex Vitamins (e.g., B1,2,3,5,6,12,) Vitamin D and Vitamin E could be the major role for good quality sleep management.

Acknowledgments: I would like to express their sincere gratitude to all of patients who participated in this research. I also extend our appreciation to staff of our clinic for providing the necessary facilities and advocacy message to all patients. More over my parents who have been provided a guidance, encouragement and private fund for this study.

Role of preoptic area thermo transient receptor potential vanilloid type II (TRPV2) channel in sleep and thermoregulation

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Introduction: The maintenance of body temperature is the major homeostatic function of the hypothalamus. The preoptic area of the anterior hypothalamus is one of the most crucial sites of body temperature regulation and sleep. The present study reveals the role TRPV2 ion channel in the regulation of sleep and temperature regulation.

Materials and methods: The study was conducted in 12 male Wistar rats. Surgical procedures were performed for implantation under thiopentone sodium anesthesia (40 mg/kg body weight, i.p.). Bilateral 24G guide cannulae with indwelling styli were implanted, targeting 2 mm above the preoptic area (POA) as outlined in De Groot's atlas. A radio transmitter (TA10TAF-40, Data Science International, USA) was implanted abdominally to telemetrically record body temperature. A K-type thermocouple wire was inserted near the hypothalamus to measure brain temperature, which was recorded at 15-second intervals using a Fluke digital thermometer. Body temperature was recorded telemetrically at the same interval. Temperature measurements were collected from 10 AM to 4 PM, with capsaicin or saline injections administered at noon. Temperature data was averaged over 15-minute epochs. Bilateral injections of 0.2 μ l (TRPV2 agonist) or saline control were delivered at a rate of 0.1 μ l/min via

an injector cannula aimed at the POA. Injection sites were histologically verified. Statistical comparisons were conducted between pre- and post-injection periods, as well as between capsaicin- and saline-treated groups.

Results: The body temperature recorded in 6 rats ranged between 37.00 ± 0.3 °C and 37.46 ± 0.2 °C and brain temperature 36.7 ± 0.3 °C and 37.2 ± 0.4 °C. The injection of TRPV2 agonist ($0.2 \mu\text{g}/0.2 \mu\text{l}$) into the preoptic area produced a prompt increase in body and brain temperature. Tbr significantly increased from 37.1 ± 0.3 °C to 37.8 ± 0.2 °C, 12:15 to 12:30 h, ($p < 0.05$), 36.9 ± 0.2 °C to 38.1 ± 0.5 °C, 12:45 to 13:0 h, ($p < 0.05$), 36.9 ± 0.3 °C to 38.2 ± 0.3 °C, 13:0 to 13:15 h, ($p < 0.05$) and Tb significantly increased from 37.2 ± 0.2 °C to 37.9 ± 0.6 °C, 12:30 to 12:45 h, ($p < 0.05$). In rats, the injection of capsaicin ($0.2 \mu\text{g}/0.2 \mu\text{l}$) into the preoptic area of the anterior hypothalamus produced a prompt increase in body and brain temperature. TRPV2 agonist ($0.2 \mu\text{g}/0.2 \mu\text{l}$) increases REM sleep.

Conclusions: The TRPV2 channel agonist injection in the POA brings about an increase in body and brain temperature by stimulating cold-sensitive neurons and increasing REM sleep.

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Rotating shifts change gut microbiota and sleep in shift workers: an observational study

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Introduction: Shift work can adversely impact workers' sleep conditions and change gut microbiota composition. Meanwhile, a bidirectional relationship exists between gut microbiota and sleep regulation via the brain-gut axis. This study aimed to determine the associations between gut microbiota and sleep alterations in shift workers.

Materials and methods: A total of 31 shift workers and 44 controls were recruited from June 2018 to July 2021 (mean age= 27.71 ± 4.38 years, female%=77%). Shift work was defined as workers involved in 8-hour rotations for more than 3 years. Subjective and objective sleep were assessed via questionnaires and polysomnography (PSG), respectively. Poor sleep efficiency (SE) was defined as $\text{SE} < 85\%$ assessed by PSG. The fecal samples were collected during the PSG recording day and immediately stored at -80°C until 16S rRNA sequencing. Linear and logistic regressions were used to examine the relationship between shift work, microbiota and sleep. All statistical analyses were performed using IBM SPSS 27.0. A p -value < 0.05 was used to determine statistical significance.

Results: Compared to controls, shift workers exhibited lower subjective ($87.27 \pm 11.31\%$ vs. $93.72 \pm 6.00\%$, $p=0.004$) and objective ($86.07 \pm 11.01\%$ vs. $91.66 \pm 4.33\%$, $p=0.013$) SE. Furthermore, we found that the reciprocal-transformed abundance of *Collinsella* was significantly lower in shift workers compared with controls (0.82 vs. 0.93 , $p=0.029$). After adjusting for age and sex, shift work was associated with both the reciprocal-transformed abundance of *Collinsella* ($\beta=-0.11$, $p=0.033$) and poor objective SE ($\text{OR}=9.30$, $p=0.005$), while the reciprocal-transformed abundance of *Collinsella* was significantly correlated with poor objective SE ($\text{OR}=0.05$, $p=0.018$). The association between shift work and poor objective SE was diminished by the reciprocal-transformed abundance of *Collinsella* ($\text{OR}=7.70$, $p=0.012$), though the mediating effect was insignificant.

Conclusions: Shift workers showed changes in gut microbiota composition and lower sleep efficiency. *Collinsella* may be the potential key microbiota linking the relationship between sleep and shift work. Microbiota might be a beneficial therapeutic targeting of sleep disturbances in shift workers.

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Self-Injury-Related Psychosocial Characteristics and Sleep Health in Adults

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Introduction: Self-injury is linked to various sleep problems, such as short sleep duration, difficulty maintaining sleep, and poor subjective sleep quality. This study aimed to investigate how sleep health differs among adults aged 20 to 69 based on their history of self-injury, and to explore four psychosocial factors of self-injury—perceptual (pain perception), situational (being alone), behavioral (latency from urge to action), and volitional (desire to stop)—linked to sleep health.

Materials and methods: A total of 124 adults with a history of self-injury were age- and gender-matched with 248 controls (N=372). Insomnia Severity Index (ISI), Sleep Health Index (SHI), Inventory of Statements About Self-Injury (ISAS), Depressive Symptom Inventory–Suicidality Subscale (DSI-SS), Generalized Anxiety Disorder-7 (GAD-7), and Patient Health Questionnaire-9 (PHQ-9) were assessed. The Sleep Health Index (SHI) is a 14-item self-report questionnaire designed to assess overall sleep health, including three subscales (sleep quality, sleep duration and sleep disorders). In this study, the behavior section of the ISAS (7 items) was used to assess self-injury methods and frequency. Correlations explored associations between self-injury and sleep health indices. Group differences between the self-harm group and controls were analyzed using ANCOVA adjusting for age, gender, suicidal ideation, anxiety, and depression. Additionally, four psychosocial characteristics relevant to self-injury – pain perception, being alone, latency from urge to action, and desire to stop – were assessed as separate variables.

Results: The sample consisted of 372 adults (mean age = 41.6 ± 13.8 years, 48.9% male). Among the self-injury group (n = 124), the most common methods were hitting oneself (16.7%), hair pulling (15.1%), and cutting (14.1%). Most engaged in self-injury alone (75%), within one hour of the urge (70%), and 80.6% expressed a desire to stop. Compared to matched controls, the self-injury group showed significantly poorer outcomes of overall sleep health and associated domains (all $ps < .01$) – even after controlling for covariates. Among the self-injury group, self-injury characteristics (pain perception, being alone, latency from urge to action, desire to stop) were significantly associated with multiple sleep health difficulties measured by the SHI ($r = .20-.30, p < .01$).

Conclusions: Compared to controls, individuals with self-injury reported greater insomnia and poorer sleep health across all sleep health domains. Self-injury psychosocial characteristics—pain perception, being alone, latency from urge to action, and desire to stop—were also associated with increased sleep disruption and greater reliance on medical support for sleep problems. These findings suggest that self-injury is linked not only to poor sleep outcomes but also to psychosocial characteristics that interact with multiple aspects of sleep health.

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Sensationalising sleep: A research agenda for understanding and interpreting sleep-related discourses in the media

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Introduction: The importance of sleep is well recognised, yet around a third of adults report suboptimal or disordered sleep. Common medicalised approaches to sleep seldom align with the reality of people's lives. Sociological perspectives acknowledge how (in our modern accelerated society) sleep is quantified, digitalised, and commercialised. Familial sleep arrangements and the regulation of sleep within the constructs of school and/or work are also key concerns which are shaped by social and cultural expectations regarding rest and productivity.

Sleep-related research has predominantly been from clinical and physiological perspectives. However, more recent epidemiological work has highlighted social disparities in sleep health including by age, gender, economic status, and ethnicity. Nevertheless, nuanced sociological considerations of sleep have seldom been explored. This is particularly important for bicultural countries such as Aotearoa New Zealand where mainstream discourses and health promotion have been colonised and Indigenous Māori are underrepresented.

Materials and methods: Media provides a platform for shaping beliefs and attitudes concerning sleep. Media messaging contributes to definitions of 'normal sleep' and sensationalised messages around sleep(lessness) and disease. These seldom account for nuanced differences across the lifespan or Indigenous knowledge and practices concerning sleep and wellbeing. How sleep-related messages are

delivered, interpreted, and resisted varies and warrants exploring - particularly among populations predisposed to sleep disturbances.

This presentation will outline a suite of research and preliminary findings from a sociological sleep enquiry in New Zealand. This includes the sleep-related themes and discourses present in freely accessible media sources. Followed by an investigation into the beliefs and practices of key groups/audiences in response to such discourses. Including studies using focus groups and interviews as well as creative writing and arts workshops.

Results: Discourse and responses are covered from key groups. For example, in the news media, adolescents sleep issues were presented as both 'a phase' and 'serious business'; pregnant women's sleep was presented as 'doomed' alongside instructions for becoming a safe sleeper and 'perfect mother'; and for older adults - sleep was presented as a 'magic bullet' for avoiding dementia or early death, alongside being something that would inevitably decline with ageing and also challenging to remedy. Finally, sleep was represented via Māori media as a time for communal and cultural connection as well as spiritual wellbeing. Preliminary findings from the audience response phase will be presented to help platform the reality of their sleeping lives and inform sleep messaging that is relevant and appropriate for contemporary New Zealand.

Conclusions: Ultimately, this work is contributing to new and innovative theories on sleep and society. Including, for example, perceptions of sleep as an experience; understandings of sleep disorders and treatments; as well as broader constructs of time, and the role of Māori knowledge in relation to the discourses, practices, and influences of sleep.

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Serial Mediating Effects of Insomnia and Nightmare in the Relationship between Self-Compassion and Non-Suicidal Self-Injury Among Hong Kong Adolescents

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Introduction: Non-suicidal self-injury (NSSI) has been increasingly gaining attention in adolescent mental health due to its association with mental health disorders, such as depression and anxiety disorders and a higher overall mortality rate when compared to their peers, particularly in relation to suicide. While much research has explored the association between self-compassion and NSSI in Western contexts, this association in Chinese culture remains underexplored. Meanwhile, despite growing evidence linking the two variables, the underlying mechanism remains unclear. In particular, notwithstanding the high co-occurrence of self-compassion, sleep disturbances, and NSSI, the potential roles of sleep disturbances remain largely unexamined. Further investigation is warranted to better understand their associations with each other. Thus, it is crucial to explore the abovementioned associations among Hong Kong adolescents. To the best of our knowledge, this is the first study investigating insomnia severity and nightmare distress as sequential mediators in the association between self-compassion and NSSI. We hypothesized the following: 1) Self-compassion is negatively associated with NSSI (H1); 2) Insomnia severity and then nightmare distress serially mediate the association between self-compassion and NSSI (H2).

Materials and methods: A total of 176 adolescents (73% female, $M_{age} = 16.9$, $SD = 1.18$) aged 12 to 18, living in Hong Kong and without a diagnosis of mental illness or a suicide attempt in the past month participated in the study. Participants completed online surveys on QuestionPro, which was disseminated via social media. The survey included socio-demographic information and published scales: the Self-Compassion Scale for Youth, the Insomnia Severity Index, the Nightmare Distress Questionnaire, and the Functional Assessment of Self-Mutilation Questionnaire.

Results: Pearson or Spearman rank correlation analyses indicated a negative correlation between self-compassion and NSSI ($r_s = -0.42$, $p < 0.001$), supporting H1. A serial mediation analysis (model 6) revealed a significant indirect effect of self-compassion on NSSI through the sequential pathway of insomnia severity and nightmare distress ($\beta = 0.02$, $logit = 0.02$, $OR = 1.02$, $SE = 0.01$, $BCa\ 95\% CI = 0.01, 0.03$), giving support to H2.

Conclusions: The present study highlights the significance of self-compassion to NSSI behaviors among Hong Kong adolescents, demonstrating a consistent association between the two variables across different cultural contexts. Nevertheless, due to cultural differences, the contributing factors underlying this association among Hong Kong adolescents warrant further investigation. Additionally, our findings suggest that self-compassion potentially plays a protective role in reducing NSSI engagement, especially in the presence of insomnia and nightmares. The present study shows that adolescents with lower self-compassion may be at greater risk for more severe insomnia, accompanied by nightmare distress, which then possibly increases their NSSI engagement. Future research could explore how self-compassion influences different stages of NSSI, particularly in the context of sleep disturbances, to gain a more comprehensive understanding of this complex interplay.

Acknowledgments: We would like to express our gratitude to all the participants who generously contributed their time to participate in this study.

Sex differences in bidirectional associations between dimensions of Fitbit-derived sleep and emotional health across one year in American Life in Realtime, a nationally representative sample of U.S. adults

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Introduction: We examined sex differences in within-person bidirectional and between-person associations between dimensions of Fitbit-measured sleep and multiple self-reported emotional health measures among a large sample of U.S. adults across ~1 year.

Materials and methods: Data were from American Life in Realtime (ALiR), a probability-based cohort representative of U.S. adults. Participants wore Fitbits to measure nighttime sleep and answered monthly questionnaires on depression, anxiety, and stress symptoms. Linear mixed models examined bidirectional associations of Fitbit sleep measures [mean and SD of total sleep time (TST), sleep onset, and sleep efficiency] across 14-day intervals that immediately preceded or succeeded each monthly report of emotional[WT1] health and between-person associations. Analyses adjusted for sociodemographic variables and examined gender differences.

Results: The analytical sample (n=733-754) had mean age of 47.1±14.6 and 48.7% female. Generally, within-person findings indicated that shorter and longer TST, poorer sleep efficiency, and greater variability in both sleep onset and efficiency than one's average predicted higher depression, anxiety, and stress scores in the subsequent monthly report. In reverse, worse than average emotional health predicted poorer sleep health in the succeeding 14 days, but findings were more consistent with sleep predicting emotional health. In consistent and strong between-person results, those with later sleep onset and more sleep variability had poorer average emotional health. Findings were generally stronger in females.

Conclusions: Poor sleep predicts worse emotional health and vice versa in a large representative sample, particularly among females, highlighting the need for tailored intervention strategies that consider gender-specific patterns in sleep-emotional health dynamics.

Sharper Minds Better Sleep: Effectiveness of a sleep focussed educational and skills building program for improving sleep and mental health in university students

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Introduction: The transition to university is a critical period often marked by significant changes in living circumstances, academic demands, and social relationships. These shifts often lead to elevated stress and disrupted sleep, placing students at heightened risk for psychological distress. Sleep and mood share well-established bidirectional links, suggesting that improving one may positively influence

the other. University-led mental health promotion programs offer a key opportunity to equip students with skills and knowledge to proactively manage wellbeing. This study evaluated the effectiveness of a sleep-health focused, skills-building educational prevention program, called *Sharper Minds Better Sleep*, on improving sleep and mental health outcomes in university students.

Materials and methods: A quasi-experimental, between-groups, pre-post design was used. Participants were young adult university students enrolled in *Sharper Minds Better Sleep* (intervention group), or a control group (students completing surveys only). The intervention included 4x45 minute weekly online group learning sessions (6-8 people per session) delivered via Zoom by trained Provisional Psychologists. Sessions focussed on sleep and circadian health principles, and encouraged practical behaviour change through 'homework' tasks between sessions. All participants completed standardized questionnaires on sleep (duration, disturbance, daytime impairment, regularity), and mental health, while intervention participants also wore an actigraph for 7 days pre- and post-program, and completed additional sleep-related questionnaires (i.e., insomnia severity, bedtime procrastination).

Results: 81 students participated in the intervention group (71% female; $Mage=21.1$, $SD = 4.6$), and 149 in the control group (69% female; $Mage = 19.9$, $SD = 4.03$). Mixed repeated-measures ANOVA's revealed a significant Group $\times$ Time interaction for sleep disturbance [$F(1, 86) = 6.77$, $p = .01$, $\eta^2 = .073$], with the intervention group reporting greater reductions in sleep disturbances than controls from pre-to post-program. In contrast, no significant differences were found for sleep duration [$F(1, 77) = 1.815$, $p = .182$], daytime impairment [$F(1, 78) = 2.318$, $p = 0.132$], or subjective sleep regularity [$F(1, 77) = 3.378$, $p = 0.070$]. A Mann-Whitney U test indicated a significant difference in mental health change scores between groups ($U = 3260.00$, $Z = 2.03$, $p = .042$), with the intervention group demonstrating greater improvement. Within-group analyses of actigraphy data from the intervention group showed significant improvements in actigraphy-derived sleep regularity (Cohen's $d = -.75$), intradaily variability (Cohen's $d = .37$), as well as self-reported insomnia severity (Cohen's $d = .40$) and bedtime procrastination (Cohen's $d = .38$).

Conclusions: Participation in the *Sharper Minds Better Sleep* program was associated with significant reductions in sleep disturbance and improvements in sleep regularity, insomnia symptoms, and bedtime procrastination. These changes were accompanied by greater overall improvements in mental health reports compared to controls. While not all sleep metrics showed significant between-group differences, the results suggest that a skills-focussed sleep intervention can support meaningful changes in student wellbeing. University-delivered preventive programs targeting modifiable behaviours like sleep may offer a scalable pathway to reduce psychological distress and promote resilience in young adults.

Acknowledgments:

Shotgun metagenomics reveals alteration of gut microbiota and metabolic pathways in adults with poor sleep quality

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Introduction: Emerging evidence suggests that the gut microbiome plays a role in sleep disturbance. This study explored the characteristics of the gut microbiome and the functional metabolic pathways related to sleep quality.

Materials and methods: A total of 588 participants were recruited. Sleep quality was assessed using the Pittsburgh Sleep Quality Index, employing a cutoff score of 8.5. Based on this criterion, 42 individuals with poor sleep quality (PSQ) and 546 healthy controls with good sleep quality (GSQ) were identified. The fecal microbiome was analyzed using shotgun whole-metagenome sequencing, and groups were compared based on diversity metrics, differentially abundant species, metabolic pathways and metabolites.

Results: No significant differences in alpha and beta diversity indices were observed between individuals experiencing subjective sleep disturbances and those who did not. *Klebsiella pneumoniae* was more abundant in the PSQ group ($b = 0.476$; $q = 0.017$). Additionally, the following metabolic pathways were enriched in the PSQ group: octane oxidation (coefficient = 0.495, $q = 0.033$), the superpathway of acetyl-CoA biosynthesis (coefficient = 0.377, $q = 0.025$), superpathway of (Kdo)₂-lipid A biosynthesis (coefficient = 0.367, $q = 0.026$), petroselinic acid biosynthesis (coefficient = 0.353, $q =$

0.034), and superpathway of histidine, purine, and pyrimidine biosynthesis (coefficient = 0.349, $q = 0.042$). When metabolites levels associated with poor sleep quality were inferred using MelonnPan, higher xanthine levels were observed in the PSQ group (coefficient = 0.018; $q = 0.025$).

Conclusions: In summary, this study poses significant questions regarding the relationship between the gut microbiome and poor sleep quality.

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Should School Start Times Be Delayed? A Narrative Review

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Introduction: Adolescent sleep deprivation has emerged as a significant public health issue worldwide. The American Academy of Sleep Medicine recommends that adolescents aged 13–18 years obtain 8–10 hours of sleep each night to support optimal health (Paruth. However, many middle and high schools commence before 08:30 AM, conflicting with adolescent circadian rhythms. These early start times contribute to insufficient sleep, impairing academic performance, mood, and overall wellbeing.

Materials and methods: A narrative review methodology was used to synthesize current literature from high- and low-resource settings regarding adolescent sleep patterns and the impact of school start times. Sources included peer-reviewed journals, expert consensus guidelines, and public health data, with particular attention to circadian biology, school operations, and sociocultural contexts.

Results: Adolescents naturally experience a delay in their sleep-wake cycles due to hormonal influences on circadian rhythms. External factors such as screen use, academic demands, and caffeine intake exacerbate delayed sleep onset. Studies from high-income countries have shown benefits of delayed school start times, including longer sleep duration, improved academic performance, and reduced absenteeism. However, most studies are observational, and implementation challenges—such as transportation, scheduling conflicts, and climate considerations—limit generalizability, especially in countries like Sri Lanka.

Conclusions: Delaying school start times aligns with adolescent circadian physiology and has the potential to improve sleep health, academic outcomes, and overall wellbeing. However, implementation must be context-sensitive, especially in resource-limited settings. Complementary strategies such as sleep hygiene education, screen-time regulation, and exploration of dual-shift models aligned with chronotype may enhance effectiveness.

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Sleep and Arousal in Adult Survivors of Chronic Childhood Trauma

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Introduction: Childhood trauma survivors often report sleep disturbances, but the nature and characteristics of their sleep disturbances are understudied, especially in individuals without posttraumatic stress disorder (PTSD) (Kajeepeeta et al., 2015). Chronic trauma affects the autonomic nervous system, which could lead to altered arousal and subsequent sleep disturbances. However, previous studies examined sleep disturbances primarily in trauma survivors in clinical populations, making it difficult to evaluate whether altered sleep and arousal were consequences of trauma exposure or concomitants of current distress. This study investigated subjective and objective sleep and arousal parameters in chronic childhood trauma survivors without PTSD. Specifically, given the lack of previous data on both the sympathetic (SNS) and parasympathetic nervous system (PNS) activity, this study examined skin conductance levels (SCL) and high-frequency heart rate variability (HF-HRV) to fully understand arousal regulation in trauma survivors.

Materials and methods: Fifty survivors of chronic childhood trauma and 50 age-and-gender-matched controls with no history of childhood trauma were recruited (66% women; age = 26.09 ± 5.53). Participants completed the Pre-Sleep Arousal Scale and sleep diaries for 7 days. On the eighth day, they completed psycho-physiological assessments at the laboratory, including Pittsburgh Sleep Quality Index and Depression Anxiety Stress Scale. Three sets of SCL and HF-HRV recordings were obtained at baseline: when participants were at rest for 5 minutes; neutral: when participants read a neutral news story (2 minutes) and listened to a clip of relaxing music (2 minutes); and under distress: when participants read a news story about child abuse (2 minutes) and listen to a clip of child crying (2 minutes). Then, participants' sleep was measured by polysomnography.

Results: Relative to controls, trauma survivors had lower sleep quality (SQ) ($F = 24.70, p < .001, \eta^2 = .34$), longer diary-assessed sleep onset latency and wakefulness after sleep onset (WASO) ($F = 2.90, p = .026, \eta^2 = .11$) even after controlling for psychological distress. Objective differences were not significant in multivariate analyses ($F = 1.24, p = .30, \eta^2 = .05$), although univariate results showed that trauma survivors had greater WASO ($F = 4.54, p = .04$) and lower sleep efficiency ($F = 4.92, p = .03$). Trauma survivors reported higher pre-sleep arousal [$F(1, 82.3) = 31.1, p < .001, \eta^2 = .31$]. They also exhibited lower HF-HRV across all conditions [$F(1, 98) = 3.42, p = .05, \eta^2 = .03$], but SCL of the two groups was comparable. Finally, HF-HRV was associated with subjective SQ, total sleep time, and WASO and objective WASO.

Conclusions: This study found evidence for subjective but not objective sleep disturbances in childhood trauma survivors. Trauma survivors exhibited hyperarousal, indicated by heightened pre-sleep arousal and reduced HF-HRV. Our findings added to the literature that hyperarousal in trauma survivors was substantiated by decreased PNS rather than increased SNS activity, suggesting impaired autonomic downregulation. Finally, correlational findings underscored the potential mediating role of compromised PNS activity in the relationship between childhood trauma and sleep. Future research should explore how altered arousal may play a role in understanding and treating sleep disturbances in childhood trauma survivors.

Sleep and circadian knowledge in Australian undergraduate university students

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Introduction: University students are particularly vulnerable to sleep loss and circadian disruption. Although 7-9 hours of sleep are recommended, up to 11 hours may be required and appropriate for young adults aged 18-25 years. However, sleep is often curtailed by the need to juggle study, paid employment including shift work, and social obligations. This is exacerbated by the circadian delay of adolescence, which continues to the mid- to late-20s. University students are also often engaged in shiftwork. Understanding students' levels of knowledge around sleep and circadian health is critical for designing effective sleep education and health promotion programs.

Materials and methods: Undergraduate students enrolled in an introductory elective subject on sleep and circadian rhythms at the University of Sydney during 2020 to 2025 were asked to complete a pre-course survey as a participation activity. Knowledge was assessed using: 5 multiple-choice questions (MCQs) aligned with key learning outcomes of the subject; a 15-item Sleep Knowledge Questionnaire (SKQ) developed by Gallasch & Gradisar (2007); and the 15-item Sleep Alertness & Fatigue Education in Residency (SAFER) Knowledge Questionnaire from the American Academy of Sleep Medicine. Demographic data, reasons for enrolment, stage of behavioural change, and previous sleep education was also collected.

Results: N=7,287 students responded (67% response, 63% female, mean age 20.2 years, SD 2.5 years). Students endorsed goals of enrolment as increasing knowledge of sleep (88%), improving or changing sleep habits (88%), in addition to completing degree requirements (87%). Consistent with this, most students were in the contemplation (35%) and preparation (42%) stages of behavioural change around

making lifestyle changes to improve sleep. Most students (69%) reported no previous sleep education.

Students scored 2.5 (SD 1.1) out of 5 on MCQs testing key learning outcomes, indicating a lack of understanding of the two-process model of sleep regulation, the circadian delay in adolescence, and the use of light for circadian phase shifting. Mean score on the SKQ, was 10.9 (SD 2.4) out of 15, indicating some understanding of sleep hygiene but a lack of knowledge around bed restriction for insomnia. On the SAFER, students scored 8.2 (SD 2.4) out of 15 demonstrating a lack of practical knowledge around managing fatigue and sleep loss, the use of naps, and shift work. No significant differences were observed for students with and without previous sleep education on any of the knowledge scores (MCQ $t_{7285}=0.95$, $p=0.34$; SKQ $t_{6347}=1.20$, $p=0.23$; SAFER $t_{6175}=0.01$, $p=0.99$).

Conclusions: Undergraduate students possess a basic understanding of sleep hygiene but lack practical knowledge around circadian rhythms and how to manage shift work and sleep loss. Results from this self-selected sample (together with enrolment numbers in this elective subject) indicates a high level of interest in learning about and improving sleep, and points to areas that should be taught more widely. Future research should evaluate the effectiveness of targeted education and health promotion programs for improving knowledge and changing sleep and circadian behaviours.

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Sleep and longevity: insights from sleep macroarchitecture and nocturnal heart rate variability

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Introduction: Healthy aging is priority in the international public health (Bassetti et al., 2022). Emerging evidence indicates that sleep-wake disorders and alterations are causally linked to adverse health outcomes, suggesting that sleep represents a key preventive target for longevity (Mander et al., 2017; Sun et al., 2024). As such, low electroencephalographic delta and sigma power during sleep was linked to cardiovascular risk (Berger et al., 2022), whereas altered sleep spindle amplitude and high theta, alpha, and sigma power were associated with cognitive decline (Djonlagic et al., 2019). Considering the paucity of the current evidence, we aimed to identify sleep phenotypes associated with selected incident comorbidities using real-world data from a university sleep center.

Materials and methods: This is an analysis of the Bernese Sleep-Wake Registry ($n \approx 11000$). Using clinical polysomnography, we quantified sleep macroarchitecture according to AASM criteria and nocturnal heart rate variability (HRV; 21 parameters representing time domain, frequency domain, and non-linear measurements) as the marker of autonomic functioning. Per study participant, we identified incident comorbidities (i.e., a diagnosis was not mentioned at the time of polysomnography but was mentioned at the later assessment point) from the clinical records. 36 incident comorbidities were classified into eight major groups (incident proportion [IP]: neurologic, 24.58%; psychiatric, 16.32% [i.e., depression in 92% cases]; cardiovascular, 19.24%; endocrine, 9.78%; metabolic, 8.49%; pulmonary, 3.71%; infectious, 11.91%; neoplastic, 4.81%). Associations between incident comorbidities and sleep parameters were explored with multiple logistic regression adjusted for age and sex. Only significant ($p < 0.05$) associations were reported.

Results: 4170 participants were included in the analysis (age: 48 ± 19 years; 63% men; total sleep time: 339.34 ± 91.79 minutes; cumulative observation time: 13217 person-years). Sleep macroarchitecture showed limited associations with incident comorbidities, with sleep-disordered breathing being moderately associated with cardiovascular, endocrine, and metabolic diseases and with low duration of slow-wave sleep being weakly associated with endocrine diseases. In contrast, HRV was associated with many of the incident comorbidities. Specifically, neurologic diseases were related to high and complex HRV. In a subanalysis focused on neurologic diseases, stroke (IP: 6.60%) was strongly associated with high and complex HRV, whereas cognitive dysfunction (IP: 10.06%) was moderately associated with a high very low frequency component. Neurodegeneration and neuroinflammation (IP: 1.63%) were strongly associated with low HRV with high sympathetic drive. Psychiatric diseases were strongly associated with low HRV, accompanied by reduced complexity and parasympathetic dominance. Metabolic diseases were moderately linked to high HRV with a high very low-frequency component. Neoplastic diseases were moderately associated with high HRV predictability.

Conclusions: These findings highlight the association of specific aspects of sleep physiology with incident comorbidities in a longitudinal analysis. Notably, nocturnal HRV seemed to provide stronger predictive value compared to sleep macroarchitecture, suggesting that altered autonomic functioning, reflected in HRV, may represent a prodromal phase preceding more overt changes in sleep macroarchitecture. These results underline the potential of nocturnal HRV for early risk stratification and targeted interventions, particularly for neurologic and psychiatric diseases, emphasizing its relevance for brain health. We will further explore the link between health outcomes and sleep microarchitecture.

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Sleep and Nap habits within professional rugby club: SoSleep® Program. From prevention and coaching to performance optimization

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Introduction: Elite Athletes are susceptible to sleep inadequacies especially poor sleep quality and short sleep habits. Poor Sleep and sleep habit are associated to decreased athlete performance, increased injuries and less team success. 2021 expert consensus and clubs medical department were searching for assessment, program and more research on this field. We assessed a 360° sleep program on club request in prospective follow-up upon individual volunteer athlete to sensitize, evaluate and coach for sleep goals to improve individual and collective player's sleep for recovery and performance optimization upon elite rugby team.

Materials and methods: 72 rugby players athletes from professional teams were proposed for educational and voluntary sleep program (SoSleep®) over last 3 seasons in prospective study. The program was consisting in 360° sleep's evaluation directly at club's training field area with education briefing, sensibilization programs, on-line questionnaires, individual sleep assessment, in-board nap room, wearable polysomnography (Dreem® head band), medical sleep clinic evaluation with full home polysomnography test on requirements of club medical department.

Results: We had 47 sensibilization program forms, 36 players with several medical interviews, 106 questionnaire sets, 29 head band nights, 6 medical assessment pathways. Sensibilization program results showed that 52% were exposed to bad sleep prior to program then 89% to individual sleep better knowledge and 98% better sleep management intention after completion. Nap's habits results found that 46% to 91% of all players between 5 specific time period outcomes. We showed also that 91% of athletes will have nap habit during training week more than 75% during rest week (p-value = 0.0625) or 46% during day after match (p-value = 0.002569). Wearable polysomnography results showed 7h52 mean sleep time (26% REM-sleep, 17% deep-sleep, 49% light-sleep, 8% WASO). Average satisfaction program level was 4,53/5.

Conclusions: Sleep education program and our results with specific follow-up and polysomnographic evaluation at training field bedside seem of great interest and very promising. Results deserve to be discussed and confirmed subsequently, notably the low polysomnography deep sleep's proportion. Main explanation up to date would be that evaluations were made during the regular or final phase season when physical training is adjusted, likely different from pre-season trainings with modified sleep needs. Point of interest was the players' napping habits within week preparation and on day match. Player nap results indicate that this behavior seems more associated with an element of preparation and optimization than recovery. Sleep banking usefulness may also be considered and recommended. More data and specific outcome are needed for this specific population.

By the way, associated with competition results over the last 3 seasons with 3 consecutive victories in main national ligue TOP14 and 2 continental victories in European Champions cup, sleep optimization within a sports club seems a required element both for the individual recovery and performance for the player and the collective performance for the team.

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Sleep and Scuba Diving: Prevalence of Sleep Disorders and Their Potential Links with Decompression Illness in Recreational Divers

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Introduction: Scuba diving requires sustained cognitive and physical performance and carries inherent risks. While fatigue and sleep disorders are known contributors to errors in high-risk environments, their impact on diving safety remains underexplored. Data linking sleep disorders to decompression illness (DCI) are scarce, particularly among recreational divers. This study aimed to assess the prevalence of sleep disturbances and their possible association with DCI in a large cohort of civilian recreational divers.

Materials and methods: We conducted a descriptive, cross-sectional study using anonymous, self-administered questionnaires distributed to recreational divers across metropolitan and overseas France, as well as Belgium. All questionnaires were disseminated institutionally via affiliated diving clubs. Professional and military divers were excluded. Data included demographics, diving history (number of dives and certification level), medical and accident history, and sleep-related factors. We used validated instruments: the Berlin questionnaire for OSA risk, the Pichot fatigue scale (cut-off >14), and a general sleep disorders questionnaire. Participants also reported insomnia, habitual snoring, and sleep quality the night before dives. DCI was defined as any incident with neurological, vestibular, or cardiopulmonary symptoms self-reported as a prior diving accident.

Results: A total of 572 complete responses were analyzed. The mean age was 49 ± 13 years, and 363 participants (65%) were male. The median number of lifetime dives was 250 [90–800]. Regarding certification level, 167 divers (29%) were level 1–2, 200 (35%) were level 3–4, and 189 (33%) were certified instructors. A total of 75 divers (13%) reported a prior diagnosis of obstructive sleep apnea (OSA), and 331 (58%) habitual snoring. The Berlin questionnaire identified 160 participants (28%) as high risk for OSA. Among the 75 divers with diagnosed OSA, 43 (57%) were untreated, 9 (12%) used a mandibular advancement device, and 23 (31%) were treated with continuous positive airway pressure (CPAP). Thirty-nine divers (7%) reported at least one episode of DCI. Among all divers, 486 (85%) reported having previously dived after a poor night's sleep, compared to 379 out of 533 divers without DCI (71%) ($p=0.07$). Among the 39 divers who had experienced DCI, 20 (53%) reported sleeping poorly the night before the incident. A positive Berlin score was found in 14 out of 39 divers with DCI (36%), compared to 128 out of 533 without DCI (24%) ($p = 0.1114$). Insomnia was reported by 74 divers (13%), and 35 (6%) had significant fatigue based on the Pichot scale (score >14).

Conclusions: Sleep-related risk factors are frequent among recreational divers. Trends suggest a possible link between poor sleep and DCI vulnerability. The proportion of untreated OSA and reported pre-dive fatigue underlines the value of including sleep screening in diver medical evaluations. These findings pave the way for future prospective studies and call for the integration of sleep health into diver medical assessments.

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Sleep Apnea Monitoring with a Consumer-Grade Wearable: Performance of the Samsung Galaxy Watch

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Introduction: Obstructive sleep apnea (OSA) is a common but significantly underdiagnosed sleep disorder associated with various adverse health outcomes, including cardiovascular disease, cognitive impairment, and reduced quality of life. The gold standard for diagnosing OSA is in-laboratory polysomnography (PSG), which, despite its diagnostic accuracy, presents challenges in terms of

accessibility, cost, and user burden. Wearable devices have emerged as promising alternatives for sleep apnea screening due to their convenience and potential for continuous, at-home monitoring. The Samsung Galaxy Watch (GW), a wrist-worn wearable device equipped with optical sensors for SpO₂ measurement, recently received FDA approval as a Software as a Medical Device (SaMD) for sleep apnea screening. This study aims to validate the AHI estimation performance of the Galaxy Watch6 and Watch7 models in comparison to PSG.

Materials and methods: A total of 326 valid sleep datasets were collected from participants undergoing overnight PSG at Samsung Medical Center. Each participant wore two identical Galaxy Watch devices—either GW6 or GW7—on both wrists during sleep to assess device and wrist-based variability. The devices collected multi-wavelength photoplethysmography (PPG) signals at 25 Hz and calculated SpO₂ values every second. AHI was estimated using a machine learning algorithm applied to one-minute epochs of SpO₂-derived features. Only sleep sessions with $\geq 70\%$ SpO₂ coverage and ≥ 4 hours of duration were included. PSG AHI values served as the reference standard for evaluation. Agreement metrics included Pearson correlation, intraclass correlation coefficient (ICC), Bland-Altman analysis, and diagnostic accuracy using AHI ≥ 15 as the clinical threshold.

Results: The estimated AHI from the Galaxy Watch showed strong correlation with PSG AHI (Pearson $r = 0.9$; ICC = 0.87; 95% CI: 0.84–0.90). Bland-Altman analysis revealed a mean bias of -1.9 events/h, indicating slight underestimation. For detecting moderate-to-severe OSA (AHI ≥ 15), the Galaxy Watch achieved 80% sensitivity, 87% specificity, 92% positive predictive value (PPV), and 70% negative predictive value (NPV). AHI estimation error varied by OSA severity: slight overestimation in normal cases and increasing underestimation in mild, moderate, and especially severe OSA groups (-4.77 events/h in severe cases). A significant negative correlation was found between AHI error and the PSG hypopnea index ($r = -0.47$), suggesting that errors were primarily driven by hypopnea detection, whereas no correlation was observed with the apnea index. SpO₂ coverage and estimation performance were similar between GW6 and GW7 (92.82% vs. 94.21%). Wrist-to-wrist AHI variability was minimal overall, but greater in severe OSA cases and under low SpO₂ coverage conditions, emphasizing the need for high-quality signal acquisition.

Conclusions: The Galaxy Watch demonstrates high accuracy in estimating AHI and effectively identifies moderate-to-severe OSA, aligning with previously reported FDA performance claims. Despite some limitations in hypopnea detection, the device offers a reliable and accessible screening solution for sleep apnea, supporting its broader use in home-based sleep health monitoring. High SpO₂ signal coverage is essential for optimal performance, especially in severe OSA cases. These findings highlight the potential of wrist-worn wearables as scalable tools for public health screening of sleep-disordered breathing.

Sleep Apnea Syndrome in Cardiology: Inaugural Experience of a Sleep Laboratory in Sub-Saharan Africa

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Introduction: Les laboratoires du sommeil sont quasi inexistants en Afrique subsaharienne, malgré la prévalence croissante du syndrome d'apnée du sommeil (SAS), un facteur de risque cardiovasculaire indépendant. Nous rapportons la première expérience d'un laboratoire dédié au sommeil à Dakar, au Sénégal, en nous concentrant sur les caractéristiques cliniques, paracliniques et polysomnographiques des patients évalués pour un syndrome d'apnée obstructive du sommeil suspecté (SAOS) dans un cadre de cardiologie.

Materials and methods: We retrospectively analyzed 186 patients (October 22, 2020 – January 15, 2025) who underwent overnight polysomnography: attended video-polysomnography (n=139) or ambulatory recording (n=47). Standardized questionnaires (Epworth Sleepiness Scale, Pichot Fatigue Scale) were administered. Demographics, cardiovascular risk factors, clinical symptoms, and polysomnographic indices were assessed. OSAS was defined as an apnea-hypopnea index (AHI) $> 5/h$.

Results: Mean age was 48 ± 28 years; 54% male (sex ratio 1.18), mean BMI 27 kg/m^2 . Cardiovascular risk factors were common: hypertension 52%, type 2 diabetes 21%, dyslipidemia 19%. Predominant symptoms were snoring (81%) and morning fatigue (71%). Frequent cardiology referral reasons included recurrent malaise (n=90) and nocturnal palpitations (n=96). Epworth score > 10 occurred in

66% (n=123), mean Pichot score was 12. OSAS was diagnosed in 177 patients (95%): mild (n=43), moderate (n=60), severe (n=91, 49%). Obstructive predominance was noted in 66% (n=123), mixed with central predominance in 34% (n=63). Mean polysomnographic parameters: AHI 29/h, oxygen desaturation index 17/h, microarousal index 61/h, snoring events 222/h, periodic limb movements 47/h. Severe OSAS patients had reduced sleep efficiency (49% vs. 81% overall). Associated findings included periodic limb movements (n=130), Cheyne–Stokes respiration (n=2), obesity hypoventilation syndrome (n=1), and restless legs syndrome (n=3). **Figure 1** presented the main results.

Conclusions: In this inaugural Sub-Saharan African sleep laboratory, OSAS prevalence among cardiology referrals was extremely high (95%), predominantly in middle-aged, non-obese men with cardiometabolic comorbidities. Our data highlight the urgent need to integrate sleep diagnostics into cardiovascular care pathways in the region.

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Sleep characteristics and predictors of their disturbances in the Russian population: preliminary data from the large-scale SLEEPSTUDYRU project

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Introduction: Sleep disturbances are a significant public health concern, linked to diminished quality of life and various somatic and mental disorders. Despite high prevalence, systematic data on sleep in Russia's vast, geographically diverse population remain limited. The SleepStudyRU project, encompassing 11 time zones and diverse climatic regions, offers unique scale and fundamental significance for sleep epidemiology in such a heterogeneous environment. Our objective was to examine sleep characteristics, ascertain disturbance prevalence, and identify associated factors among the Russian population.

Materials and methods: This multicenter SleepStudyRU project surveyed 3,529 adults across all Russian Federal districts, ensuring robust sample representativeness. Data were collected via a custom questionnaire covering demographic, somatic, somnological, and chronobiological profiles. Analysis used frequency characteristics (proportion, %), median, and interquartile range (IQR). Multivariate logistic regression identified associated factors, calculating adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs)

Results: Our sample comprised 3,529 respondents (66.2% women; 33.8% men) from diverse age groups (14–60+ years) and socioeconomic strata across all Federal districts. A striking 67.0% reported sleep quality disturbances. Primary issues included difficulties with sleep onset (38.6%), early morning awakenings (19.8%), and sleep maintenance challenges (13.9%). Daytime sleepiness was reported by 68.1%. Median self-assessed sleep quality was 7 (IQR 5–8) out of 10. For duration, 31.5% slept 7

hours, 25.9% slept 6 hours, and 15.2% slept under 5 hours.

Multivariate regression identified these independent factors significantly associated with increased likelihood of sleep quality disturbances: female sex (aOR 1.26; 95% CI 1.08–1.47); age over 60 years (aOR 1.49; 95% CI 1.07–2.08), presence of comorbidities (aOR 2.15; 95% CI 1.82–2.54), mobile phone use before sleep (aOR 1.56; 95% CI 1.32–1.85), watching TV before sleep (aOR 1.27; 95% CI 1.06–1.51), divorced or widowed marital status (aOR 1.90–1.91; 95% CI 1.38–2.63 and 1.19–3.07), residence in Volga (PFD), Siberian (SFD), or Southern (YFD) Federal Districts (aOR 1.62–2.52 vs. Central (CFD)), suggesting regional specificities. Conversely, moderate regular physical activity (1–2 times/week) was associated with reduced disturbance likelihood (aOR 0.74; 95% CI 0.62–0.89).

Conclusions: These preliminary SleepStudyRU data confirm an exceptionally high prevalence of sleep quality disturbances (67.0%) in Russia. Identified modifiable factors like pre-sleep gadget/TV use and comorbidities indicate promising targets for preventive/therapeutic interventions. Results spanning 11 time zones and diverse climatic zones critically underscore their importance for future investigations into geographical/chronobiological influences on national-scale sleep. Developing large-scale educational programs on sleep hygiene and behavioral impact is unequivocally necessary for improving Russian public health. Further research will clarify regional specificities.

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Sleep Concordance and Discordance in Dyads of Cancer Patients and Bed-Partner Caregivers: A Systematic Review on Patterns, Health Impacts, and Dyadic Interventions

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Introduction: Optimal sleep is composed of adequate sleep duration (seven to eight hours) that is easily initiated (less than 20 min of sleep onset latency [SOL]) and maintained without disruptions (less than 20 min of wake after sleep onset [WASO]). Non-optimal, disturbed sleep has been seen at an alarming high level in cancer patients and caregivers. The context of coping with cancer together as a relational system makes the cancer patient-partner dyads unique in the phenomenon of sleep and sleep disturbance. Therefore, this systematic review aimed to synthesize evidence on sleep concordance and discordance in the dyads of cancer patients and bed-partner caregivers.

Materials and methods: We conducted the systematic review following the JBI Manual for Evidence Synthesis on conducting systematic reviews of effectiveness. Searches were conducted the four medical databases, including PubMed, CINAHL Plus, Web of Science, and EMBASE. Studies were included if they focused on sleep in adult cancer populations, and included the perspectives on dyadic patterns, health impacts, and interventions of sleep among cancer patient-caregiver dyads. A narrative synthesis was conducted based on our three research questions: Dyadic patterns (sleep concordance and discordance), Health impacts (actor and partner effect on physical and psychosocial health), and Dyadic interventions. Meta-analyses were performed to determine the pooled effect of dyadic intervention on sleep outcomes.

Results: A total of 3810 studies imported for screening. Twenty-eight studies were included in the narrative synthesis with 19 observational studies and 9 interventional studies. Majority of caregivers reported the relationships with patients as spouses or partners. Observational studies identified significant actor and partner effects between sleep and health outcomes, including physical functioning, anxiety and depression, quality of life, and relationship satisfaction. Mindfulness practices were the most used intervention strategies in dyads. Psychological interventions, including family resilience therapy and acceptance and commitment therapy, have been applied in cancer patient-caregiver dyads. Eight studies reported the effectiveness of dyadic interventions on cancer patients' and caregivers' sleep disturbances. Dyadic interventions yielded a significant effect on decreasing patients' sleep disturbances (SMD=-0.53, 95%CI [-0.91, -0.15]) with a medium level of heterogeneity indicated by $I^2=48\%$ as well as a significant effect on decreasing caregivers' sleep disturbances (SMD=-0.52, 95% [-0.84, -0.19]) with a low heterogeneity indicated by $I^2=0\%$.

Conclusions: This review acknowledged the interdependent nature of sleep among cancer patients and caregivers. Our results could have significant implications in sleep management for healthcare professionals working with dyads impacted by cancer, particularly bed-sharing couples.

Sleep disorders after mild traumatic brain injuries in young male patients

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Introduction: Aim of this study was to present cases of sleep disorders after mild traumatic brain injuries in young male patients(<30 years old).

Materials and methods: 10 cases are presented. 10 young male patients. Range of age 18-30 years old. Some common symptoms were: 3 of patients have insomnia, 3 patients have sleep apnea, 2 have hypersomnia, and 2 have narcolepsy.

Results: All of them received :Cognitive behavioral therapy (CBT), Natural sleep-inducing remedies, Pharmacotherapy and continue Neurological, Psychological and Psychiatric Support. Good results in 8 patients (80%) and moderate in 2 (20%).

Conclusions: Multidisciplinary approach is essential to achieve optimal results for our patients.

Sleep Disorders in Chronic Kidney Disease Patients

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Introduction: Chronic kidney disease (CKD) is associated with a variety of comorbidities, including sleep disorders, which significantly impact patients' quality of life. Sleep disturbances in CKD patients are underreported and poorly managed, despite their potential to exacerbate CKD-related complications.

Aim of the study: This study aims to assess the prevalence and types of sleep disorders among CKD patients and explore their clinical characteristics

Materials and methods: A cross-sectional study was conducted on 50 CKD patients at conducted at the Department of Nephrology, Medical College for Women& Hospital, Dhaka Bangladesh. During 1 year from January 2024 to December 2024.

Sleep disorders were evaluated using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS).

Clinical and demographic data were also collected.

Results: The study revealed that 40% of participants experienced insomnia, 30% had obstructive sleep apnea (OSA),

20% suffered from restless legs syndrome (RLS), and 10% reported excessive daytime sleepiness. A total of 80% of the participants exhibited poor sleep quality based on the PSQI score, and 30% showed excessive daytime sleepiness according to the ESS. The majority of patients were in advanced stages of CKD (stage 5D), with a high prevalence of comorbidities such as hypertension and diabetes mellitus

Conclusions: In our study, sleep disorders were highly prevalent in CKD patients, significantly affecting their quality of life. The findings underscore the need for routine screening and management of sleep disturbances in this population. Further research is needed to explore the mechanisms linking CKD and sleep disorders, as well as the efficacy of targeted interventions to improve sleep quality in these patients.

Sleep Disturbance and Stressor-Specific Cortisol Dysregulation in Temporomandibular Disorder

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Introduction: Nearly 60% of individuals with temporomandibular joint disorders (TMD), chronic pain conditions affecting the jaw joint and muscles, report sleep disturbances and daytime sleepiness. Further, sleep disruption alters hypothalamic-pituitary-adrenal (HPA) axis functioning in chronic pain. Salivary cortisol reactivity to pain-related (quantitative sensory testing; QST) and social-evaluative (Trier Social Stress Test; TSST) stressors in TMD patients and healthy controls was measured. We hypothesized that sleep disturbance would differentially influence cortisol trajectories, with TMD patients showing impaired regulation and healthy individuals exhibiting more flexible responses.

Materials and methods: TMD patients ($N=33$; $M_{age}=33.5\pm10.1$ years, 70% female, 64% white) recruited from a facial pain clinic and matched pain-free community controls ($N=20$; $M_{age}=27.9\pm7.7$ years, 60% female, 55% white) underwent QST and TSST on separate afternoons, with testing order randomized. Salivary cortisol was collected at baseline, immediately post-testing, and 15-, 20-, 25-, 30-, and 45-minute intervals post-testing. Participants completed psychosocial measures, including the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), at baseline. Separate linear mixed-effects models evaluated log-transformed cortisol trajectories after each task in R, testing 3-way interactions between group (healthy vs. TMD), collection time, and sleep variables (PSQI total and subscales, ESS total), controlling for baseline cortisol. Natural splines modeled cortisol trajectories across time (spline 1=early phase up to 20 minutes post-stressor; spline 2=recovery phase). Likelihood ratio tests supported using 2 degrees of freedom for modeling time.

Results: After QST, significant 3-way interactions emerged for PSQI total (spline 1: $b=0.17[0.00, 0.34]$, $t(324)=1.99$, $p=.047$), sleep quality (spline 1: $b=1.23[0.53, 1.93]$, $t(324)=3.44$, $p<.001$), sleep latency (spline 1: $b=0.69[0.12, 1.26]$, $t(324)=2.37$, $p=.019$), sleep duration (spline 1: $b=0.89[0.15, 1.63]$, $t(324)=2.37$, $p=.019$), sleep disturbance (spline 2: $b=0.58[0.04, 1.12]$, $t(324)=2.12$, $p=.035$), daytime dysfunction (spline 1: $b=-0.68[-1.34, -0.02]$, $t(324)=-2.01$, $p=.045$), sleep efficiency raw score (spline 1: $b=-0.05[-0.09, -0.01]$, $t(324)=-2.68$, $p=.008$), and ESS total score (spline 1: $b=0.10[0.01, 0.19]$, $t(318)=2.10$, $p=.036$). Overall, greater sleep dysfunction was associated with elevated early cortisol responses in TMD patients and steeper early declines in healthy controls.

After TSST, significant 3-way interactions were found for PSQI total (spline 2: $b=-0.15[-0.25, -0.05]$, $t(318)=-2.86$, $p=.004$), sleep latency (spline 2: $b=-0.35[-0.70, -0.01]$, $t(318)=-2.02$, $p=.045$), sleep disturbance (spline 1: $b=-1.41[-2.21, -0.61]$, $t(318)=-3.48$, $p<.001$), daytime dysfunction (spline 2: $b=-0.59[-0.98, -0.19]$, $t(318)=-2.93$, $p=.004$), sleep efficiency raw score (spline 1: $b=0.05[0.01, 0.09]$, $t(318)=2.55$, $p=.011$; spline 2: $b=0.03[0.01, 0.06]$, $t(318)=2.83$, $p=.005$), and ESS total score (spline 1: $b=-0.10[-0.19, -0.01]$, $t(312)=-2.29$, $p=.022$). Overall, greater sleep dysfunction was associated with blunted cortisol in TMD patients and stronger cortisol increases in healthy controls.

Conclusions: These findings suggest stressor-specific HPA axis patterns. Following pain-related stress, sleep-disturbed healthy controls demonstrate intact cortisol downregulation, while TMD patients show sustained activation. Conversely, social-evaluative stress elicits stronger cortisol responses in poor-sleeping healthy controls, possibly due to heightened threat sensitivity after impaired sleep, whereas TMD patients exhibit blunted responses, potentially reflecting HPA exhaustion or chronic stress habituation. Future research with larger samples and objective, longitudinal sleep measures is needed to replicate these patterns and clarify mechanisms linking sleep and HPA regulation in TMD.

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SLEEP HEALTH AMONG MEDICAL STUDENTS IN ABAKALIKI NIGERIA: A DESCRIPTIVE STUDY

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Introduction: Sleep health focuses on those measurable characteristics of sleep that are most clearly associated with physical, mental, and neurobehavioral well-being, and not necessarily the absence of sleep disorder. Sleep health is characterised by subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours. Adequate and restful sleep is particularly crucial for medical students, who face unique challenges due to the demanding nature of their academic and clinical responsibilities. There is limited data on sleep health among medical students in Nigeria. This research study investigated the pattern of sleep health among medical students in Abakaliki Nigeria.

Materials and methods: This cross-sectional observational study was undertaken among the medical students of 2 public institutions in Abakaliki Nigeria from 16th to 23rd June 2023. The data collection was done using SATED Questionnaire.

Results: Out of the 288 medical students (males- 53.1%, females- 46.9%), good sleep health was recorded in 6.6%. The mean SATED sleep score was 4.9 ± 1.7 (male- 4.9 ± 1.8 , female- 4.9 ± 1.6) (p -value = 1) and it was significantly lower among the final-year students. Age difference, sex difference and presence of chronic headache did not significantly affect the SATED sleep score. The mean sleep duration was 6.1 ± 1.5 hours (male- 6.1 ± 1.6 , female- 6.0 ± 1.4). Sleep duration (54.5%) had the best rating while sleep efficiency (44%) had the lowest rating among the assessed sleep domains.

Conclusions: Sleep health as measured with the SATED sleep health score is poor among medical students in Abakaliki Nigeria. It is significantly poorer among final-year medical students.

In view of the attendant consequences of poor sleep health, interventions like education about sleep hygiene, the formation of support groups, the use of cognitive behavioural therapy (CBT), and the provision of resources to manage anxiety could help improve sleep health among medical students and ensure that they are well-rested and ready to learn and practice medicine.

Acknowledgments: We acknowledge the staff of the Medical Records Department of AEFUTHA for the help in data collection

SLEEP HEALTH AMONG PATIENTS ATTENDING ADULT NEUROLOGY CLINIC IN ABAKALIKI NIGERIA

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Introduction: Sleep health indicates how well an individual or population sleeps. Good sleep health is characterized by subjective satisfaction, sustained alertness during waking hours, appropriate timing, high efficiency, and adequate duration. Poor sleep health is associated with many short-term and long-term health consequences. There are limited data on the pattern of sleep health in Nigeria. Against this backdrop, we embarked on this study to determine the Pattern of Sleep Health among patients attending the Adult Neurology clinic in a Federal Teaching Hospital, in Abakaliki, Nigeria.

Materials and methods: This was a cross-sectional observational hospital-based study undertaken from July to September 2022 at the Adult Neurology clinic of the Alex Ekwueme Federal University Teaching Hospital Abakaliki, Nigeria.

Results: Out of the 267 (Male- 146) patients recruited for the study, 19% had good sleep health with SATED scores of 8 to 10 while 81% had poor sleep health. The absence of alcohol abuse, cigarette smoking, and neurological diagnosis were statistically associated with poor sleep health with no sex and age predilection. The mean sleep duration was 7.47 ± 1.50 hours (male= 7.63 hours, female= 7.28 hours, 18- 64years= 7.43 hours, ≥ 65 years =7.88 hours). **Timing** of sleep (mean= 0.97) was the least rated while sleep **satisfaction** (mean= 1.54) was the best-rated sleep dimension.

Conclusions: Sleep health is poor among patients attending the adult Neurology clinic at Abakaliki Nigeria and it is associated with smoking, absence of alcohol abuse, and neurological diagnosis. Self-reported Sleep duration may not be a sensitive measure of sleep health and should always be used in combination with other sleep health dimension measures as contained in the SATED questionnaire. Sleep health should be assessed routinely at the outpatient clinics with the SATED questionnaire and appropriate treatment should be instituted promptly to forestall the adverse consequences of poor sleep health.

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Sleep Health in Type 2 Diabetes: The Role of Sleep Variability in Glycemic Control

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Introduction: Sleep health is now recognized to be at a level playing field as other lifestyle behaviors in managing people with diabetes. Sleep health consists of multiple dimensions (e.g. duration, timing, regularity/ variability, efficiency) which may contribute differently to glycemic control in persons with type 2 diabetes (T2D). This study aimed to comprehensively evaluate the associations between sleep health dimensions and glycemic control in T2D.

Materials and methods: Seventy-four persons with T2D participated in this study. They were recruited in a study exploring sleep in T2D with and without diabetic retinopathy (DR), NCT 04547439. Sleep duration, sleep efficiency, sleep midpoint and sleep variability (standard deviation, SD, of sleep duration) were obtained from 14-day actigraphy recordings. Sleep satisfaction and daytime sleepiness (Epworth Sleepiness Scale, ESS) were obtained from questionnaires. Multidimension sleep health (MSH) score was created from a sum of sleep scores in each dimension (range 0-6, with higher score reflecting better sleep). Obstructive sleep apnea was assessed using an overnight home monitor (WatchPAT300). Hemoglobin A1C (A1C) and high sensitivity C-reactive protein (hs-CRP) were obtained. Correlation and multiple regression analyses were performed to establish an independent association between sleep measures and A1C.

Results: Mean (SD) age was 54.0 (6.0) years, body mass index of 34.3 (7.0) kg/m², diabetes duration of 13.4 (8.4) years, 58.0% of the participants were female, and 68.9% had DR. Their median (IQR) A1C was 7.6 (6.6, 8.8)%, 58.1% were taking insulin and the mean (SD) number of non-insulin antihyperglycemic medications was 1.85 (0.8). For objectively measured sleep dimensions, mean (SD) sleep duration was 6.2 (1.0) h with 75% of participants sleeping <7h, median sleep efficiency was 82.1 (77.1, 86.6)% with 68.9% of the participants had sleep efficiency <85%, mean sleep midpoint was 03:18 (01:22) AM, SD of sleep duration was 69.2 (56.6, 89.3) minutes with 62.2% having values ≥60 minutes. Mean ESS was 8.2 (5.2) with 24.3% of participants reporting excessive daytime sleepiness, and 71.6% reporting that their sleep quality was “very good” or “fairly good”. The mean MSH score was 3.41 (1.13). Median apnea hypopnea index (AHI) was 14.8 (6.6, 25.0). Bivariate analyses suggested that SD of sleep duration ($p<0.05$), AHI and insulin use ($p<0.1$), hs-CRP/ sleep efficiency/ DR status (all $p<0.2$) might be related to A1C. Other sleep dimensions and MSH score were not related to A1C. Stepwise regression analysis adjusting for insulin use, hs-CRP and DR status revealed that SD of sleep duration (natural-log transformed), but not sleep efficiency or AHI, was independently associated with A1C (natural-log transformed), $B=0.148$, $p=0.016$.

Conclusions: Participants with T2D in this study exhibited poor sleep in multiple dimensions. However, among them, irregular day-to-day sleep duration appeared to be a significant predictor of glycemic control. Interventions to enhance sleep regularity could potentially be beneficial in improving glucose control in persons with T2D.

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Sleep Health of Preschool Children in Bangladesh

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Introduction: Sleep affects a range of physical and neurodevelopmental outcomes, including executive function, growth, and obesity risk, which are public health priorities in low- and middle-income countries (LMICs). However, most data on children's sleep health come from high-income countries, and their recommendations may not apply to LMICs. Despite the importance of childhood sleep and emerging evidence of cross-cultural variation in early childhood sleep, little is known about children's sleep health in Bangladesh, a lower middle-income country in South Asia experiencing rapid urbanization and growing socioeconomic inequality.

Materials and methods: We collected sleep health data from 433 preschoolers in Dhaka, Bangladesh, using the Brief Infant Sleep Questionnaire Short Form (BISQ-R-SF) to assess children's sleep patterns and parental perceptions and behaviors. Additionally, we conducted qualitative research through two

focus group discussions (6 participants each) and seven in-depth interviews to explore maternal knowledge and attitudes toward children's sleep needs, co-sleeping, and potential sleep health interventions.

Results: Children aged 3–4 years slept an average of 10.3 hours per day (SD 1.5 h), with 40% sleeping less than the recommended duration (10–13 hours). Only 17.5% of children meet WHO's recommendation for maximum screen use (1h/day); mothers reported an average of 3.2 h (SD 1.9) of daily screen use for their preschoolers. Night-waking was common, only 30% of children slept through the night, while 66% woke 1–2 times at night, and 10% woke 3 or more times. Children went to bed on average at 10:30 p.m. (SD 1.2 h), about two hours later than the Western norm of 8:30 p.m. Screen time was positively associated with later bedtimes (p for trend < 0.001). Children of more educated mothers also had later bedtime and longer daytime naps. Co-sleeping was nearly universal. During in-depth interviews and FGDs, mothers expressed strong reluctance to allow children to sleep alone before age seven. Some linked their child's night-waking to their own sleep disturbances and daytime fatigue. Most mothers were unaware of recommended sleep durations, and the concept of a bedtime routine was unfamiliar. Although sleep interventions were described as “foreign”, mothers actively sought advice on best practices.

Conclusions: Preschool children in Bangladesh sleep less than recommended and frequently wake at night. Higher screen time is linked to poorer sleep outcomes. These findings, along with limited parental knowledge about healthy sleep practices, highlight the need for culturally adapted sleep promotion interventions in Bangladesh.

Sleep Health Profile In Early Infancy Is Associated With Emerging Executive Function Development

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Introduction: Infant sleep health is increasingly recognized as a key component of brain maturation and executive function (EF) development in early childhood. Data from low-resource settings remain scarce, where environmental and cultural factors may uniquely shape sleep patterns.

Materials and methods: Data were collected from 200 mother-infant dyads in a prospective cohort study in Gugulethu, Cape Town, South Africa. Infant sleep was assessed using the Brief Infant Sleep Questionnaire at 2–5, 6–10, 12–15, 16–19, and 20–24 months. At 24 months of age, executive function was assessed using the Spin the Pot (STP) task for both inhibitory control and working memory. Nonparametric K-means clustering identified sleep profiles of bedtime, night and day sleep duration and night-waking frequency. Multiple linear regression models were used to examine associations between sleep clusters at each time point and EF outcomes. Models were adjusted for maternal education, anxiety, depression, family income, and age at EF assessment.

Results: Four sleep profiles emerged: (1) Optimal (25.4%) with early bedtime, long night and total sleep, and few night-wakings; (2) Good (26.1%) with later bedtime, long day and total sleep, and frequent night-wakings; (3) Poor (26.3%) with shorter total sleep and longer day sleep; and (4) Poorest (28.3%) with latest bedtime and shortest total sleep. A dose-response relationship between sleep profiles during 2–5 months of age and STP scores (P for trend = 0.01) was observed. The poorest sleepers scored 2.1 points lower (95% CI: -3.6, -0.63) than optimal sleepers in the STP task. Sleep clusters at later ages were not associated with STP scores.

Conclusions: Sleep health in early infancy may critically influence EF development, particularly working memory and inhibitory control. Findings emphasize the need for culturally tailored interventions to promote healthy sleep habits in infancy.

SLEEP-HOPE: Evaluating Sleep Quality and Quantity in Menopausal Patients living with Hypothyroidism Using Hormonal, Pharmacological, and Complementary Therapies in Canada

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Introduction: Sleep disturbances are common in menopausal and hypothyroid patients, significantly impairing quality of life. While hormonal replacement therapies, pharmacological interventions, and complementary and alternative medicine (CAM) approaches are available, their comparative effectiveness in improving sleep quality in real-world Canadian settings remains underexplored. This study aims to evaluate improvements in subjective sleep quality, measured by the Sleep Quality Scale (SQS), in menopausal and hypothyroid patients undergoing various therapeutic interventions. Secondary outcomes include changes in quality-of-life metrics assessed using the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Thyroid-Specific Patient-Reported Outcome Measure (ThyPRO), and Short Form-8 Health Survey (SF-8).

Materials and methods: The SLEEP-HOPE study is an observational, longitudinal study conducted across three private endocrinology practices in Montreal, Canada. Female patients with menopause and hypothyroidism reporting unsatisfactory sleep were recruited. Participants completed standardized questionnaires, including PSQI, ESS, ThyPRO, and SF-8, at baseline and three-month follow-ups. Treatment modalities included hormonal therapies (e.g., thyroid hormone replacement, menopausal hormone therapy), pharmacological interventions (e.g., hypnotics, antidepressants), and CAM therapies (e.g., melatonin, ashwagandha, yoga). Additional data on comorbidities, medication adherence, and lifestyle factors were collected.

Results: Descriptive statistics will summarize participant characteristics and treatment distributions. Paired t-tests and ANOVA will compare pre- and post-intervention scores, while multivariate regression analyses will explore associations between treatments and outcomes, adjusting for confounders such as age and BMI.

Conclusions: This study aims to provide valuable insights into the effectiveness of hormonal, pharmacological, and CAM therapies in addressing sleep disturbances among menopausal patients with hypothyroidism. Findings are expected to show moderate benefits of hormonal therapies while emphasizing the unmet need for optimizing sleep quality. These results will support the development of evidence-based, holistic management strategies to improve sleep and overall quality of life in this patient population.

Sleep Hygiene Awareness and Behavior Among Young Adults in Urban India Background

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Introduction: With India's growing youth population and rising prevalence of insomnia and sleep-related complaints, understanding the level of sleep hygiene awareness and behaviour is essential for early interventions and public health strategies.

Objectives: To assess the awareness and practices related to sleep hygiene among urban Indian young adults aged 18–23.

Materials and methods: Survey conducted on Sleep Hygiene Awareness & Practices. Received 1076 responses from students in the age group of 18-23 yr. (54% of respondents are male & 46% are female).

Results:

- Sleep Hygiene is average/ poor for 92% of the respondents – in line with global data of 70-95% non-ideal sleep hygiene practices
- Only 20% of individuals with poor sleep hygiene are seeking help – in line with global data, but very sub-optimal from overall health & wellness perspective
- 38% feel sleepy during the day & 30% have noticed memory/ concentration issues - Clear correlation between daytime sleep and memory/ concentration loss.
- 66% of the respondents mentioned “strongly agree” & 28% mentioned “agree” to the question, “Do you think sleep quality affects your performance?” – but people seeking help is minimal

Conclusions: The study highlights a critical gap in sleep hygiene awareness among urban Indian youth, exacerbated by lifestyle choices, academic pressures, and digital overuse. This behavioural and knowledge disconnect calls for targeted public health interventions – including curriculum-based sleep education, social media awareness campaigns, and digital sleep health tools tailored for youth.

References: Mastin DF, Bryson J, Corwyn R. Assessment of sleep hygiene using the Sleep Hygiene Index (SHI). *J Behav Med.* 2006;29(3):223-7

Acknowledgments: Arete Hospitals, Hyderabad, India, <https://www.aretehospitals.com>

Sleep in Context: How Activities During Waking Hours Shape Sleep in First-Year University Students

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Introduction: Sleep is shaped by a combination of internal processes that regulate sleep and wake, and external influences that modulate these systems. Our waking hours are filled with activities that affect our sleep in different ways, including those that directly influence our bed and wake times. In the present study, we used time-use diaries to capture the timing of a wide variety of daily activities in combination with sleep metrics from the Oura ring to examine how the structure and content of daily activities are associated with sleep in a sample of first-year undergraduate university students.

Materials and methods: 608 incoming first-year university students completed daily time-use diaries for up to three weeks using our custom-made app, Z4IP (8,356 days in total). Activities were reported in 15-minute intervals for the full 24 hours. 11 categories were used to capture different aspects of student life, including major university activities (Lessons, Self-study, Co-curricular Activities), leisure (Social, Digital Leisure, Exercise), and other essential daily activities (Sleep, Meals, Self-care, Transport, Other). Latent class analysis (LCA) was used to identify the underlying patterns of activity in students' daily lives. In addition, objective measures of bedtime, wake time, sleep duration and wake period duration were collected using the Oura ring.

Results: LCA revealed eight categories with distinct daily activity patterns: AM Lessons, PM Lessons, Self-study, Evening Co-curricular Activity (CCA), Evening Social, Day Social, Late Digital Leisure and Other.

Average wake times ranged from 07:31 to 11:01, with AM Lessons being the earliest and Late Digital Leisure the latest. Wake times were approximately 08:30-09:00 for the other categories. Average bedtimes ranged from 00:43 to 02:59. Late Digital Leisure days had the latest bedtime, followed by Evening Social and Evening CCA days at 02:50 and 01:42 respectively. Categories with morning or evening activities showed the longest wake period durations. The AM Lessons, Evening CCA and Evening Social categories all had wake periods of over 17 hours, whereas days with less structure, Self-study and Late Digital Leisure days, had wake period durations under 16 hours.

Engagement in digital leisure regularly preceded sleep in all but two categories (Evening CCA and Evening Social), suggesting it was a common pre-sleep activity when there were no other competing evening activities.

Conclusions: In the present study, LCA effectively identified characteristic patterns of time-use data to produce eight interpretable day categories from 8,356 days. Morning lessons, evening CCA activities and socialising significantly affected wake and bedtimes, compromising students' sleep duration. While extended evening digital leisure activity was associated with much later sleep timing, shorter periods of digital leisure activity were also observed prior to sleep on days with both earlier and later bedtimes.

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Sleep Irregularity, Anxiety and Depressive Symptoms in Young Adults with Delayed Sleep Wake Phase Disorder and Insomnia

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Introduction: In the general population, irregular sleep-wake patterns are associated with poor mental health outcomes. However, there is a lack of research on the relationship between sleep irregularity and mental health in young adults with unmanaged sleep disorders. Sleep irregularity likely mediates the relationship between sleep disorders and daytime functioning and may increase the risk of negative mental health outcomes. This study aimed to: (i) explore the association between unmanaged sleep disorders, sleep irregularity, and mental health outcomes; and (ii) determine whether sleep irregularity explains effect heterogeneity in the association between sleep disorders and mental health.

Materials and methods: The sleep-wake timings of 60 young adults (60% female, mean±SD age=25.1±4.6y) were recorded through sleep-wake diaries for up to three weeks. Validated questionnaires (e.g., Insomnia Severity Index, Epworth Sleepiness Scale), structured clinical interviews and in-laboratory polysomnography (PSG) were used to determine diagnoses. Sleep irregularity was measured using the Sleep Regularity Index (SRI). The General Anxiety Disorder (GAD-7), and Patient Health Questionnaire (PHQ-9) were used to assess anxiety and depression symptom severity, respectively. Bootstrapped regressions were used to determine the associations between SRI and mental health symptoms, with an interaction term of sleep disorder*SRI included to explore effect heterogeneity in the relationship between sleep disorders and mental health symptoms.

Results: 78% of participants had unmanaged Insomnia or Delayed Sleep Wake Phase Disorder (DSWPD) (43% Insomnia and 35% DSWPD) while 22% did not meet diagnostic criteria for a sleep disorder ('healthy sleepers'). The SRI was lower, reflecting greater irregularity, in young adults with unmanaged DSWPD (Median SRI(IQR) = 75.3(66.0-79.2); B = -8.96, 95% CI [-16.03, -2.55], $p=0.08$), than in healthy sleepers (79.4(76.0-85.0), 95% CI [76.46, 84.86]), while SRI scores were not significantly different for those with unmanaged insomnia (78.2(69.8-82.3); B = -2.59, 95% CI [-7.42, 2.16], $p=0.29$). Having either DSWPD or insomnia was independently associated with an increase in depressive symptoms (B = 2.48, 95% CI [1.22, 3.59], $p<0.01$), but not anxiety symptoms (B = 0.37, 95% CI [-1.20, 1.75], $p=0.62$). Preliminary moderation analyses were conducted given prior evidence that SRI is associated with mental health. SRI did not modify the association between sleep disorders and depressive symptoms (Insomnia: B = -0.01, 95% CI [-0.32, 0.23], $p=0.89$; DSWPD: B = -0.09, 95% CI [-0.38, 0.11], $p=0.35$) or anxiety symptoms (Insomnia: B = -0.03, 95% CI [-0.40, 0.45], $p=0.93$; DSWPD: B = -0.04, 95% CI [-0.43, 0.42], $p=0.89$).

Conclusions: Young adults with DSWPD had less regular sleep than healthy sleepers. This likely reflects the known sleep patterns of those with DSWPD, where they need to wake earlier to meet early morning commitments despite delayed bed and wake times when their schedule permits. Sleep irregularity did not modify the association between sleep disorders and mental health symptoms. Sleep disorder symptom severity or the type of sleep disorder may have a greater influence on mental health than sleep irregularity. Future research examining the relationship between sleep irregularity and long-term health outcomes is needed.

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Sleep latency and sleep duration association with depression symptoms among US adolescents and young adults: A NHANES 2005 – 2018 analysis

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Introduction: Sleep and mental health are deeply intertwined and impose a substantial public health and economic burden globally. Neurobiological mechanisms may include disruptions in circadian rhythms, sleep architecture, and neurophysiological markers such as reduced sleep spindle activity. Numerous studies indicate that both insufficient and excessive sleep are associated with depression, suggesting a complex bidirectional relationship. More specifically, sleep problems can precede, exacerbate, or result from depressive episodes, with short sleep duration being linked to increased loneliness, anxiety, and affective disorders. In this study, we aimed to provide a measurable effect size for the association of sleep duration and sleep latency with depression. We assessed depression symptoms and sleep among US adolescents and young adults using 14 years of NHANES pooled cross-sectional data.

Materials and methods: We conducted a pooled cross-sectional analysis using data from the U.S. National Health and Nutrition Examination Survey (NHANES), cycles 2005–2018. Participants aged 18–25 years were included. Primary outcomes were self-reported sleep duration (minutes/night) and sleep latency (minutes to fall asleep). Depressive symptoms were assessed via the Patient Health Questionnaire-9 (PHQ-9) and categorized as none, mild, moderate, or severe. ANCOVA with Tukey post hoc tests controlling for cycle compared group means. A multivariable linear regression model was then adjusted for gender, age, race/ethnicity, BMI, and snoring complaints or other comorbidities. NHANES sampling weights were incorporated to ensure national representativeness.

Results: The sample included 6,506 participants for sleep duration and 2,064 participants for sleep latency. Mean sleep duration was 438.9 ± 93.3 minutes, and mean sleep latency was 23.3 ± 19.0 minutes. A statistically significant difference was observed between depression groups in mean sleep duration ($F=14.8$, $p < 0.0001$) and sleep latency ($F=25.4$, $p < 0.0001$) with a dose-dependent response. Sleep duration decreased with any depression severity (mild -16.6 min, $p < 0.0001$; moderate -18.6 , $p < 0.001$; severe -21.0 , $p=0.053$ compared to no depression). Sleep latency increased in a dose-dependent manner with depression severity (mild 6.7 min, $p < 0.001$; moderate 11.6 min, $p < 0.001$; severe 15.2 min, $p < 0.001$). In a fully adjusted model, depression remained independently associated with shorter sleep duration ($\beta=-12.8$, 95% CI= $-23.6 - -1.9$, $p=0.02$) and longer sleep latency ($\beta=8.4$, 95% CI= $4.8-12.0$, $p < 0.0001$).

Conclusions: In this nationally representative sample of US adolescents and young adults, depression was associated with ~16-21 minutes shorter sleep duration and with a ~6-15 minutes longer sleep latency. In other words, depressive symptoms were associated with shorter subjective sleep duration and increased difficulties in sleep initiation, both consistent with insomnia symptoms. Our findings highlight the intricate relationship between sleep and mental health, underscoring the importance of early sleep-focused interventions among adolescents and young adults to mitigate the burden of mental health in this population. Further trials exploring the temporal relationship between sleep and mental health are required to elucidate the results of this exploratory analysis.

Sleep Myths and Student Health: Exploring the Link Between Misbeliefs, Sleep Hygiene, and Sleep Quality in Indian Youth

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Introduction: Sleep deficiency has become an alarmingly common phenomenon among college students with negative consequences on their physical, cognitive, and emotional well-being as well as academic performance. Specifically, the prevalence of sleep-related myths and the influence of these myths on their sleep quality and sleep practices remains unknown in Indian college students. The study explored associations between sleep-related beliefs and their self-reported sleep hygiene and quality of sleep.

Materials and methods: The cross-sectional study comprised of 200 college students (83% females) between the ages of 18 to 25 years (mean 22.5 years). Sleep beliefs were assessed in six different domains using 20 statements identified by the experts as sleep myths. A higher score indicated more sleep myths. Sleep Hygiene Index was used to assess the practice of sleep hygiene behaviors, with a higher score representing poorer sleep hygiene. Sleep quality was examined using the Pittsburgh Sleep Quality Index. Data was analysed using frequencies, percentages and Linear correlation.

Results: In all 38% of the participants either agree or strongly agree with the sleep myths. The PSQI of 83 % of participants is poor, more than 60% have just fair sleep hygiene, 28% have poor sleep hygiene. None of the participants showed excellent sleep hygiene. Correlation analysis suggests that sleep beliefs are positively associated with poor sleep quality ($r= .516$; $p < .01$) and poor sleep hygiene ($r= .433$; $p < .01$). The beliefs, hygiene and quality of sleep remained the same across the demographics indicating the poorer sleep practices amongst all participants despite their educational, cultural or socio-economic backgrounds.

Conclusions: This study highlights a critical concern regarding the prevalence of sleep-related myths and their significant association with poor sleep hygiene and sleep quality among Indian college students. A substantial proportion of participants endorsed inaccurate beliefs about sleep, which were strongly correlated with suboptimal sleep practices and poor sleep outcomes. Alarmingly, none of the respondents reported excellent sleep hygiene, and the vast majority exhibited poor sleep quality. The

findings may be useful in developing sleep health campaigns to promote sleep health of college students by correcting myths and maladaptive sleep health practices.

Keywords: India, Sleep health campaigns, Sleep hygiene behaviors, Sleep practices, Sleep Quality, Students Health, Indian Youth

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Sleep N' Quit: an EMA Study on Daily Sleep and Smoking among Lower Socioeconomic Smokers Who Want to Quit Smoking in the U.S.

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Introduction: Cigarette smoking is the leading preventable cause of morbidity and mortality in the United States, and is highly concentrated among individuals with lower socioeconomic status (SES). Previous studies have shown that lower SES is associated with higher rates of poor sleep, and poor sleep is associated with lower likelihood of smoking cessation. However, the temporal associations between daily sleep and smoking remain poorly understood. Therefore, the current study aimed to assess the feasibility and compliance of a real-time data capture approach of sleep and smoking among lower SES smokers who are attempting to quit.

Materials and methods: Participants were lower SES smokers who sought treatment at the 11 state-funded tobacco quit centers across New Jersey. Eligibility criteria included: 1) household income <200% of the federal poverty line, 2) a score ≥ 4 on the Rapid Estimate of Adult Literacy in Medicine-Short Form, 3) willingness to quit smoking 14 days after the baseline visit, 4) ≥ 18 years of age, 5) an expired CO level ≥ 7 ppm, 6) currently smoking ≥ 5 cigarettes per day, 7) no overnight shiftwork, and 8) not currently using potentially sedating medications. This study was conducted 100% remotely. Study participation lasted 6 weeks (2-week pre-quit and 4-week post-quit) and included 4 virtual visits. Participants were provided with a study phone, Actiwatch and Bluetooth breathalyzer with detailed instructions regarding the use of the phone, Actiwatch, and EMA procedures via mail. Participants completed questionnaires at the baseline visit, including assessment of sleep, other tobacco use, past/current medical history. Subjects wore an Actiwatch and used the study app and Bluetooth breathalyzer to record daily sleep and smoking-related behaviors for the entire 6-week study period. At the end of the study, participants returned the Actiwatch and study phone via mail.

Results: Since April 2024, 28 participants have completed the six-week EMA study. Participants were 70% White, 30% Black, and 64% female, with a mean age of 51.3 years. EMA compliance averaged 80% during Pre-Quit and 77% during Post-Quit. Biochemically confirmed abstinence rates were 30% on the quit date and 19% at the end of the study virtual visits. Participants' daily smoking abstinence rates were 22.6% (131/580 days) during Pre-Quit and 32.9% (279/847 days) during Post-Quit ($p < .001$). Most participants (23 out of 28) wore the Actiwatch on more than 90% of study days. Self-reported EMA sleep data showed a mean sleep onset latency of 45 minutes, waking up an average of 1.6 times per night, with an average of 1 hour of wake-time during the night, and spending 3 hours and 15 minutes in bed awake on average.

Conclusions: Collecting real-time data via devices over 6 weeks was feasible and acceptable among individuals with lower SES who want to quit smoking. The role of sleep health and circadian rhythms has been understudied in smoking cessation interventions. This is the first known study to elucidate associations between daily sleep dysregulation and smoking cessation using mHealth technology. Findings from this project will inform the development of future tailored sleep interventions in smoking cessation programs for this underserved population.

Sleep, physical activity and mental health among French business leaders: a cross-sectional study

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Introduction: Recent studies revealed that more than half of French business leaders are at risk of burnout, they sacrifice sleep, physical activity and often work over 60 hours weekly. Poor sleep and lack of exercise contribute to major health issues in general population. To date, no study explored the variations in health status among business leaders across different types and sizes of companies. This study aims to assess health among French business leaders, focusing on sleep quality, physical activity, anxiety, and stress levels across their different organizational contexts. We hypothesized that hierarchical positions and level of responsibility was associated with severity of health issues

Materials and methods: 361 business managers (158 women and 203 men) comprising 37.4% of Large Enterprises and Intermediate-Sized Enterprises and 62.6% of Very Small Enterprises and Small and Medium-sized Enterprises, agreed to complete questionnaires including: Pittsburg Sleep Quality Index, Perceived Stress Scale, Global Anxiety Disorder and International Physical Activity Questionnaire. RStudio software was utilized for descriptive statistics and analyses.

Results: Results revealed that 67.3% of them have poor sleep, 47.8% are highly stressed, and 22.5% have very low levels of physical activity. Women exhibit worse mental health and top leaders of small enterprise experience more stress, practice less physical activity and have poorer sleep

Conclusions: Our findings reveal the critical need for immediate action to support leaders and managers health. The intrinsic distinctive characteristics of a leader's lifestyle might require the creation of specific programs to enable them to engage long term in healthier self-care practices that take into consideration sex and organizational context.

Sleep, PTSD, and Eating Disorders: A Longitudinal Study on Sleep and Mental Health in a Community Sample Following Collective Trauma

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Introduction: Sleep disturbances are a common and persistent consequence of trauma exposure, but their role as a pre-existing vulnerability factor for post-traumatic stress disorder (PTSD) and eating disorders (EDs) remains almost underexplored. Sleep is increasingly recognized as a critical component of mental health, influencing emotional regulation, physiological stress responses, and susceptibility to psychopathology. Night eating syndrome (NES), characterized by excessive food intake during the evening and nighttime hours, has been associated with both trauma and poor sleep quality. This longitudinal study examined how poor sleep quality prior to a collective trauma event predicts later PTSD symptoms and disordered eating patterns in a community sample.

Objectives and Hypotheses:

We hypothesized that: (1) poor sleep quality at baseline, T1 (August 2023) would predict greater PTSD symptoms at T2 (five months after the October 7th); (2) PTSD risk at T2 would predict increased severity of NES and other ED symptoms at T3 (a year after the October 7th); and (3) PTSD symptoms would mediate the relationship between sleep quality and later eating-related psychopathology.

Materials and methods: A community sample of 240 Israeli adults (Mean age = 41.37, 58% female) participated in a three-wave longitudinal study. Participants completed validated self-report questionnaires online at three time points. Measures included: Pittsburgh Sleep Quality Index (PSQI), (at T1), the PTSD risk (PCL-5) (at T2), the Night Eating Questionnaire (NEQ), and the SCOFF questionnaire for general ED symptoms (at T3). Sociodemographic data, including age, gender, education, marital and employment status, were also collected. Structural equation modeling with

bootstrapped confidence intervals was used to test the hypothesized mediation model, controlling for demographic variables. Group comparisons were conducted based on a PSQI cutoff score (>5).

Results: Preliminary analyses showed all variables were positively and significantly correlated. Poor sleep quality at T1 predicted higher PTSD symptoms at T2 ($\beta = .429$, $p < .001$). PTSD symptoms at T2 significantly predicted NEQ scores ($\beta = .461$, $p < .001$) and SCOFF scores ($\beta = .390$, $p < .001$) at T3. Mediation analyses indicated that PTSD symptoms significantly mediated the relationship between sleep quality and both NES (indirect $\beta = .197$) and ED symptoms (indirect $\beta = .167$). A direct effect was observed between sleep disturbances and NES ($\beta = .219$, $p < .01$), but not with general EDs. Clinically, participants with poor sleep quality at T1 (PSQI > 5) had significantly higher PTSD, NEQ, and SCOFF scores at follow-ups ($p < .001$).

Conclusions:

The present study provides important insights into the relationship between sleep quality or sleep disturbances, PTSD risk, and various types of EDs within a community sample. By utilizing a three-wave design, this study uniquely captured how pre-existing sleep difficulties contribute to psychological distress following trauma exposure. The findings emphasize that poor sleep quality is not merely a consequence of trauma but may act as an independent risk factor, heightening vulnerability to PTSD symptoms and subsequent disordered eating patterns. In the context of collective trauma, such as the recent and ongoing war in Israel, identifying at-risk populations and modifiable risk factors is crucial for preventive interventions.

Sleep Quality among University Students in Lebanon during War Conflicts: A Cross-Sectional Study

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Introduction: Sleep is a vital component for cognitive function, emotional well-being, and overall health, yet it is frequently disrupted by external stressors, such as war and conflict. University students, particularly those in conflict zones, face increased risks of poor sleep quality due to academic pressure, psychological stress, and trauma exposure. This study aims to assess the prevalence of poor sleep quality, sleep latency, and sleep efficiency among university students in Lebanon during the 2023-2024 war conflicts, and the direct and indirect effects of war exposure.

Materials and methods: A cross-sectional study was conducted on 631 university students in Lebanon using the Pittsburgh Sleep Quality Index (PSQI) to evaluate sleep quality. Sociodemographic characteristics and the type of war exposure (direct or indirect) were also assessed. Inferential statistical tests were performed to identify correlations between sleep quality and sociodemographic factors, as well as sleep quality and war exposure. The Prevalence Rate Ratio (PRR) was calculated to identify risk and protective factors for poor sleep quality in each socio demographic group. A binary regression model was applied to predict the most significant risk factors for compromised sleep quality.

Results: 73.5% of Lebanese university students had poor sleep quality (PSQI > 5), with a mean Global PSQI score of $8.20 (\pm 3.95)$. Students with direct war exposure had the highest mean score of 10.57 ($p < 0.001$), compared to 8.04 for those with indirect exposure. The average sleep latency PSQI score was 1.46 ± 1.04 , and the average sleep efficiency PSQI score was 1.00 ± 1.00 . Compared to no exposure, indirect exposure resulted in a 22% higher prevalence (PRR=1.22) of poor sleep, while direct exposure showed a 60% higher prevalence (PRR=1.60). The binary exposure showed that female gender increased the odds of poor sleep by 2.71 ($p=0.035$), and direct war exposure increased the odds by 19.76 times ($p = 0.001$).

Conclusions: This study highlights the profound impact of war exposure on sleep quality among Lebanese university students, with direct exposure having the greatest risk. Poor sleep quality in war-affected zones can lead to severe disruptions in academic performance, cognitive function, and overall mental and physical health. The findings underscore the need for targeted interventions, including mental health support and stress management programs, to limit sleep disturbances in conflict-affected populations. Further research is warranted to explore effective coping mechanisms and long-term sleep health in similar contexts.

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Sleep quality and hypertension: correlation between Pittsburgh Sleep Quality Index (PSQI) scores and the prevalence of hypertension and blood pressure reduction patterns

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Introduction: This study investigated the association between sleep quality and hypertension, evaluating the correlation of Pittsburgh Sleep Quality Index (PSQI) scores with hypertension prevalence and blood pressure dipping patterns.

Materials and methods: From anonymized subjective and objective sleep and blood pressure data collected via commercial wearable health devices from over 150,000 volunteers, we screened and included 17,462 participants with complete blood pressure data, among whom 5,490 had PSQI scores. Participants were stratified into "high sleep quality" (PSQI ≤ 5) and "low sleep quality" (PSQI ≥ 6) groups. Chi-square tests were used to compare hypertension prevalence between the two groups. Further analysis was conducted on 926 hypertensive patients, categorized into "dipper" and "non-dipper/reverse-dipper" groups, with chi-square tests performed to assess sleep quality differences.

Results: Among 17,462 participants, 3,882 (22.2%) had hypertension. In the 5,490 participants with PSQI scores, the hypertension prevalence was higher in the "low sleep quality" group (17.9%) compared to the "high sleep quality" group (13.9%), indicating that poor sleep quality was associated with an increased risk of hypertension (99.9% CI, * $p = 0.0008617$). However, among the 926 hypertensive patients, no statistically significant difference in subjective sleep quality was observed between dippers and non-dippers/reverse-dippers.

Conclusions: Higher PSQI scores (worse sleep quality) were associated with an elevated risk of hypertension. However, subjective sleep quality did not significantly differ between dippers and non-dippers/reverse-dippers, suggesting that abnormal blood pressure circadian rhythms may not directly contribute to perceived sleep disturbances. Further research incorporating objective sleep monitoring is warranted.

Sleep, shift work disorder and risk for depression in South African ambulance emergency care personnel

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Introduction: Ambulance emergency care personnel (ECP) have long working hours, a rotating shift schedule and a high workload. They are also at risk of developing sleep and mental health issues, such as shift work disorder and depression, due to the stressful nature of the job. In a country with exceptionally high violent crime and motor vehicle associated injuries and fatalities, such as South Africa, ECP are exposed to a high workload while being under-resourced and understaffed; and the related trauma may further enhance sleep and mental health issues. Thus, this study investigated self-reported subjective sleep, risk for depression and shift work disorder in South African ECP.

Materials and methods: Ambulance ECP working for a private medical and emergency care provider were recruited around Gauteng, South Africa. The two typical shift structures in South Africa (2Day2Night4Off and Long-Short) were investigated. Demographics, BMI, years of rotating shift experience and self-rated overall health were collected. Participants completed questionnaires which investigated sleep quality (Pittsburgh Sleep Quality Index (PSQI)), depression symptoms (Patient Health Questionnaire-2 (PHQ-2)) and risk for shiftwork disorder (SWD) (Shift Work Disorder Questionnaire (SWDQ)).

Results: A total of 65 ambulance ECP (58.5% male, 33.6 ± 8.4 years, $BMI = 29.4 \pm 6.7$ kg/m²) participated in the study. The mean ($\pm$ SD) years' experience of rotating shifts was $8.7 (\pm 6.8)$ years. The mean ($\pm$ SD) PHQ-2 score was $1.5 (\pm 1.4)$ and 21% ($n=14$) of the participants were at risk of higher depressive symptoms (PHQ-2 ≥ 3). The participants had poor sleep quality with the mean global PSQI score at $7.8 (\pm 3.7)$ and 70.8% ($n=46$) of the sample being poor sleepers (PSQI > 5). ECP with poor sleep quality had higher depressive symptoms ($p = 0.002$). There was a significant difference between shift type and PSQI components for sleep latency ($p = 0.005$) and sleep disturbances ($p = 0.037$), with the long-short shift having more sleep disturbances and a longer sleep latency than 2day2night4off shift. No significant differences in PHQ-2, PSQI and SWD were found between shift types. A high risk for SWD occurred in

40% (n=24) of the participants and was associated with poor sleep quality ($p<0.001$) and higher depressive symptoms ($p=0.015$). Female participants had a higher PSQI score compared to males (8.9 ± 3.0 vs 7.1 ± 3.9 , $p=0.019$). When adjusting for age and shift type (β estimate =1.92, SE= 0.89; $p=0.036$) women had higher odds to be classified as poor sleepers (92.6% vs 55.3%, $p=0.001$) and at high risk for SWD compared to men (OR= 3.69, 95% Wald CI 1.09-12.49).

Conclusions: South African ambulance emergency care personnel have a high risk for shift work disorder and poor sleep quality. Poor sleep quality was associated with higher depressive symptoms and women reported worse sleep compared to men. We found no difference according to shift type. Interventions are warranted to improve sleep and mental health of emergency care personnel, especially for women.

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Sleep Stage Classification over Continuous Positive Airway Pressure Signals with Multi-Period Convolutional Neural Network

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Introduction: Continuous Positive Airway Pressure (CPAP) therapy is the standard treatment for obstructive sleep apnea (OSA), yet its potential for passive sleep monitoring remains underexplored. Polysomnography (PSG), the clinical gold standard for sleep staging, is resource-intensive and impractical for routine home use. To address this gap, we developed a deep learning-based framework that classifies sleep stages using only CPAP signals.

Materials and methods: We propose the **Multi-Period Convolutional Neural Network (MP-CNN)**, a novel architecture specifically designed to extract temporal features from CPAP-derived respiratory signals. Unlike conventional CNNs that rely on fixed receptive fields, MP-CNN incorporates multiple period-specific convolutional kernels ($p=3$, $p=9$, and $p=21$) to simultaneously capture short- and long-term respiratory dynamics. The model processes 630-second input windows with subject-normalized input features, including **CPAP flow (Cflow)**, **positive airway pressure (PAP)**, and **instantaneous respiratory rate (IRR)**. We augment features by reducing redundancy while preserving temporal information. Specifically, every 25 samples are downsampled to 1 Hz, and four statistical descriptors (mean, standard deviation, maximum, minimum) are computed within each window to capture local dynamics. This multi-period design allows MP-CNN to more effectively uncover the intrinsic relationships between CPAP signals and sleep stages, which may be overlooked by standard CNN architectures. The model was evaluated on split-night PSG sleep studies, where CPAP titration began midway through the recording. Data from 32 subjects with moderate to severe OSA were included, with ground truth sleep stages annotated by trained technicians according to AASM guidelines. A 3-fold cross-validation protocol was applied to ensure robust evaluation.

Results: Our proposed MP-CNN achieved a **macro F1-score of 0.685** and a **Cohen's Kappa of 0.523** in three-stage classification, with **per-stage sensitivity/specificity of 0.693/0.908 (Wake)**, **0.520/0.930 (REM)**, and **0.818/0.669 (NREM)**. These results demonstrate competitive or superior performance compared to existing approaches that rely on more intrusive signals. Feature ablation studies further revealed that downsampled statistical features were essential for improving model performance, particularly in REM detection. In addition, the model showed a strong correlation with ground truth sleep metrics, such as **total sleep time (Pearson's $r = 0.85$)**. We also assessed demographic effects by stratifying subjects by gender, BMI, and age. No statistically significant differences in performance were observed across subgroups, although females and younger subjects exhibited slightly higher agreement in some cases. Overall, the model generalized well across demographic factors, indicating that demographic variability was not a primary source of cross-dataset performance differences.

Conclusions: Our results demonstrate the feasibility of leveraging CPAP-derived respiratory signals for unobtrusive sleep stage classification. The MP-CNN architecture enables accurate sleep staging without the need for additional sensors, offering a scalable and cost-effective solution for home-based sleep monitoring. Future work will focus on extending the framework to include deep sleep detection and adaptive integration with automatic positive airway pressure (APAP) systems.

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Sleep Temporal Entropy: A Novel Sleep Fragmentation Biomarker Predicting Cardiometabolic Disease and Mortality Risk

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Introduction: Sleep fragmentation involves frequent arousals and irregular sleep stage transitions, which impair physiological recovery and contribute to increased cardiometabolic and mortality risk. Conventional fragmentation metrics such as Wake After Sleep Onset (WASO), Sleep Efficiency (SE), and Arousal Index (Arl) rely on arbitrary thresholds and fail to capture the temporal complexity of sleep transitions. Advanced EEG-derived indices offer deeper insights but are less practical for long-term monitoring and have rarely been evaluated against serious outcomes. To address these limitations, we developed a novel metric—Sleep Temporal Entropy (STE) which quantifies variability in the duration derived from the hypnogram. This study aimed to evaluate STE's ability to predict adverse health outcomes, compare its performance with traditional and existing metrics, and examine its relationship with mortality and cardiometabolic disorders.

Materials and methods: We analyzed data from the Shanghai Sleep Health Study Cohort (SSHSC, n=3,219, clinic-based) and the Sleep Heart Health Study (SHHS, n=4,862, community-based). STE was calculated by applying Shannon entropy to the temporal distribution of each sleep stage (Wake, N1, N2, N3, REM), yielding both whole night and stage-specific. In both cohorts, five machine learning models including Extreme Gradient Boosting (XGBoost) were trained to predict cardiometabolic conditions and mortality. SHapley Additive exPlanations (SHAP) were used to assess the relative importance of each feature. In SHHS, survival analysis was conducted using Cox proportional hazards regression models. STE values were categorized into quintiles, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated across unadjusted and adjusted models. Proportional hazards assumptions were tested, and restricted cubic splines were used to evaluate non-linearity.

Results: In both cohorts, STE—especially REM and N3-stage STE—ranked consistently among the most important predictors in SHAP analysis, surpassing conventional fragmentation metrics. In SSHSC, XGBoost achieved the highest predictive performance (AUC = 0.84, accuracy = 0.81), with STE contributing more than WASO or ArI in predicting hypertension, diabetes, and hyperlipidemia. In SHHS, machine learning models confirmed STE's relevance in predicting all-cause and cardiovascular mortality. Cox regression revealed a U-shaped association between STE and mortality risk. Compared to the reference quintile (Q3), participants in the lowest quintile of REM STE had a significantly elevated risk of all-cause mortality (HR = 1.58, 95% CI: 1.16–2.15) and cardiovascular mortality (HR = 2.83, 95% CI: 1.66–4.80). Similarly, participants in the highest REM STE quintile also showed increased CVD mortality risk (HR = 2.13, 95% CI: 1.14–3.96). Overall STE showed similar U-shaped patterns, whereas Wake STE exhibited a linear positive association with both outcomes.

Conclusions: STE provides a more comprehensive quantification of sleep fragmentation and irregularity than traditional metrics, offering a multidimensional assessment of sleep quality. Our findings demonstrate that STE is a robust predictor of cardiometabolic disorders and mortality, as evidenced by its performance in both machine learning models and Cox regression analyses. Notably, the U-shaped risk association for STE suggests an optimal range of STE for better health.

Sleep Timing and Cardiovascular Events: A Systematic Review & Meta-Analysis

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Introduction: Cardiovascular disease risk is associated with multiple aspects of sleep health. There is a large body of evidence linking short and long sleep durations as well as sleep disorders like obstructive sleep apnea and insomnia with the occurrence of cardiovascular events. However, the risk of cardiovascular events with circadian factors such as sleep timing is less well studied. We performed a systematic review to determine the effect of bedtime or sleep onset timing on the risk of cardiovascular events (acute coronary events and stroke) and mortality.

Materials and methods: We performed a systematic search of the MEDLINE, Embase, Scopus, and Cochrane Central Register of Controlled Trials (CENTRAL) databases. Two authors independently screened the titles/abstracts and the full texts to identify studies that observed the risk of cardiovascular events and mortality based on bedtime or sleep onset timing. The risk of bias among the included studies was adjudged using the ROBINS-E tool. Meta-analysis was performed using a random effects model to estimate the pooled hazard ratios of cardiovascular mortality with early and late sleep timings. The review protocol was prospectively registered in PROSPERO.

Results: A total of seven studies were included. The exposure was measured either as bedtime using a questionnaire (five studies) or as sleep onset timing using actigraphy over one week (two studies). The outcomes included cardiovascular mortality (three studies), cardiovascular events (three studies), coronary events (two studies), and stroke (one study). All studies had some concerns of risk of bias. All studies adjusted for confounders, including age, sex, smoking status, socioeconomic status, and various clinical risk factors. Among three studies comprising of 95,764 subjects, meta-analyses revealed increased risk of cardiovascular mortality among both early sleepers (bedtime/sleep onset before 10 or 11 PM; HR = 1.23, 95% confidence intervals: 1.07 – 1.42, $I^2 = 0\%$) and late sleepers (bedtime/sleep onset after 12 AM; HR = 1.37, 95% CI: 1.12 – 1.68, $I^2 = 25.3\%$) compared to those with intermediate sleep timings. Meta-analyses could not be performed to assess the risk of cardiovascular events due to the variable definitions of the outcome. All three studies found an increased risk of cardiovascular events with early sleep timing (before 9 or 10 PM), whereas two out of three studies found an increased risk of cardiovascular events with late sleep timing (after 12 AM) compared to intermediate sleep timings. One out of two studies found that late sleep timing increased the risk of acute coronary events. The sole study that reported on stroke found an increased risk with both early (at/before 9 PM) and late (after 12 AM) bedtime.

Conclusions: We found that both early and delayed bedtime/sleep onset timings can increase the risk for cardiovascular events and mortality compared with intermediate sleep timings. Public health interventions to improve sleep health should incorporate measures to optimize both sleep duration and timing.

Sleep timing, sleep duration and serum metabolites in healthy adults

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Introduction: Short and long sleep duration as well as poor sleep quality have been linked to higher prevalence of metabolic disorders. However, it is still unclear how diverse sleep variables relate to

different metabolic pathways. This study examines how different features of sleep health relate to serum metabolites.

Materials and methods: The study used data from 197 healthy individuals aged 20-79 (Females n=103) from the IronAge study performed at Karolinska Institutet in Sweden. Sleep variables were assessed with the Karolinska Sleep Questionnaire, where the following variables were computed: sleep duration, sleep debt, midpoint, social jetlag (i.e., the discrepancy between midpoint on free and workdays), napping frequency and sleep quality. Morning fasting blood samples were collected and ^1H NMR spectroscopy was utilized for metabolomic analysis. The metabolites were categorized according to their major metabolic pathways: amino acid, lipid, carbohydrate, energy and gut microbiota. Linear regressions were performed to examine the relationship between each sleep variable and metabolite.

Results: Sleep duration, midpoint of sleep on free days, social jetlag and chronotype associated with eight metabolites at a significance level of $p < 0.01$. Notably, midpoint associated with most metabolites spanning multiple pathways. A later midpoint was associated with higher levels of metabolites in the lipid pathway, and lower levels in the amino acid and energy pathway.

Conclusions: These observations indicate that sleep timing features, *midpoint* and *social jetlag*, have a stronger relationship with morning metabolism than other sleep health dimensions. Following replication in larger samples, these complex relationships may hold potential for health promotion.

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Sleep-Wake Classification Using Heart Rate and HRV Derived From Short PPG Signals

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Introduction: Accurate classification of sleep-wake states is essential not only for diagnosing sleep disorders but also for developing vigilance detection and alerting systems in high-risk environments, such as drowsy driving or critical occupational settings. While polysomnography (PSG) remains the gold standard for sleep staging, its high cost and complex measurement requirements limit its practical application in daily life. Therefore, there is growing interest in non-invasive simplified approaches based on physiological signals. This study proposes a method for classifying sleep and wake states every 30 seconds using only heart rate (HR) and heart rate variability (HRV) features derived from photoplethysmography (PPG), exploring the feasibility of implementing this approach using a single-sensor PPG system.

Materials and methods: This study utilized overnight PPG data from 1,680 subjects in the Multi-Ethnic Study of Atherosclerosis (MESA) dataset provided by the National Sleep Research Resource (NSRR). Each subject's PPG signal was segmented into 30-second epochs. Signal preprocessing, peak detection, and RR interval extraction were then performed for each epoch to compute HR and five HRV features (SDNN, RMSSD, pNN50, SD1, and SD2). Considering the dominance of parasympathetic activity during sleep, parasympathetically mediated features (RMSSD, pNN50, SD1) were emphasized, along with SDNN, representing overall autonomic activity, and SD2 indicating long-term variability. The dataset was divided into training and test set in a 7:3 ratio, stratified by subject, and undersampling was applied to address class imbalance. A Random Forest classifier was selected due to its computational efficiency. Optimal hyperparameters were identified through grid search, and the classifier was trained separately for four classification scenarios: binary (Wake/Sleep), three-class (Wake/NREM/REM), four-class (Wake/LS/DS/REM), and five-class (Wake/N1/N2/N3/REM).

Results: For Wake-Sleep classification, the model achieved an accuracy of 69.5%, with precision, recall, and F1-score of 74%, 60%, and 66%, respectively, for the wake class. These results indicate that reliable sleep-wake classification can be achieved even when using a limited set of physiological features. However, classification performance decreased as the number of sleep stages increased, achieving accuracies of 47.3%, 40.1%, and 32.8% for the 3-class, 4-class, and 5-class classifications, respectively. These results indicate that using only HR and HRV-derived features may not provide adequate discriminatory power for detailed sleep staging.

Conclusions: This study demonstrates the feasibility of classifying sleep-wake states using short PPG segments at a 30-second resolution, based solely on HR and HRV features. The independent processing performed at every 30 seconds highlights the potential for real-time implementation in embedded systems, such as wearable or portable monitoring devices. Furthermore, the proposed method could be extended to applications requiring continuous short-term monitoring of vigilance and fatigue.

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Social bedtime procrastination is associated with need to belong and results in shorter sleep and poorer next-day mood

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Introduction: Late-night social activities often compete with time for sleep. Socializing plays a key role in buffering stress and promoting feelings of enjoyment and belonging. However, social interactions can contribute to bedtime procrastination, defined as going to bed later than intended when there is no external need to do so. In this study, we investigated drivers and consequences of face-to-face social bedtime procrastination in residential college students. We hypothesized that instances of social bedtime procrastination would be associated with shorter sleep and poorer next-day wellbeing, and predicted by greater need to belong and extraversion.

Materials and methods: University students in a single residential college ($n=104$, 59 women) wore actigraphy watches and Bluetooth proximity beacons during the same 2-week period to track their nocturnal sleep and physical proximity to one another. Daily diaries recorded instances of social bedtime procrastination and the friend(s) involved in delaying bedtime, as well as next-day mood and daytime sleepiness. The Need to Belong Scale assessed individual differences in the desire for acceptance and belonging, and the Big Five Inventory was used to assess extraversion (score range=1-5 for both instruments). Mixed models were used to test associations of social bedtime procrastination with daily sleep behavior (onset, offset, duration), negative morning mood, positive affect, and daytime sleepiness. Diary-reported social interactions were analyzed to construct the social bedtime procrastination network. Exponential random graph models were used to test associations of psychological traits with membership and tie strength in the network.

Results: On nights when students engaged in face-to-face social bedtime procrastination, their sleep duration was more than an hour shorter compared to nights when they did not go to bed later than intended. ($\beta=-1.21$ h, 95% CI=-1.48 to -0.95 h, $P<0.001$). These nights were associated with a next-day increase in negative morning mood ($P=0.008$), decrease in positive affect ($P=0.004$), and higher odds of daytime sleepiness ($P=0.001$). Students' bedtimes were strongly correlated with the timing of their last objectively measured proximity event with the person who delayed their bedtime ($r=0.83$, $P<0.001$). The odds of a social bedtime procrastination event were nearly 2-fold higher for a 1-point increase in need to belong score (adjusted OR=1.88, 95% CI=1.49 to 2.36), and 1.3-fold higher for a 1-point increase in extraversion score (adjusted OR=1.30, 95% CI=1.06 to 1.57).

Conclusions: Social bedtime procrastination may be an important factor contributing to late bedtimes and short sleep among students living in residential colleges. Students who seek social opportunities to satisfy their drive to socialize or need to belong are more likely to engage in face-to-face social bedtime procrastination. These insights could inform interventions aimed at promoting healthier sleep habits within social contexts.

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Socio-economic disparities in sleep duration and latency among U.S adolescents: 14 years pooled cross-sectional analysis of NHANES data

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Introduction: Sleep is crucial to optimal health and quality of life. Nevertheless, recent data shows this fundamental right is not equitably distributed across racial and ethnic groups. To address the crucial gap in the association of youth's sleep with social, economic, and racial/ethnic variables, our study assesses 14 years of nationally representative sleep duration and latency data from the U.S. National Health and Nutrition Examination Survey (NHANES).

Materials and methods: We analysed pooled cross-sectional data from NHANES cycles 2005–2018, including participants aged 16–18 years. Self-reported sleep loss (<7 hours) and short sleep latency (<10 minutes) were the primary dependent variables. Race, ethnicity, income, education, and household reference marital status were the main independent variables. Both univariable and multivariable logistic regression models were used, adjusting for gender, age, physical activity, BMI, and other health comorbidities.

Results: We included 3,766 participants in the sleep loss, and 1,346 participants in the sleep latency analysis. Sleep loss was positively associated with the Black non-Hispanic ethnicity group (OR 1.8, 95% CI: 1.4-2.3, $p<0.001$) and at least some high-school education (OR 1.7, 95% CI: 1.1-2.6, $p<0.01$), while negatively associated with being married (OR 0.6, 95% CI: 0.5-0.9, $p<0.01$). After adjusting for covariates, independent associations with sleep loss persisted for Black non-Hispanic (aOR 2.0, 95% CI: 1.3-3.0, $p<0.001$) and Hispanic ethnicities (aOR 1.7, 95% CI: 1.1-2.8, $p<0.01$); at least some high school (aOR 1.9, 95% CI: 1.1-3.3, $p<0.05$) and at least some college (aOR 2.4, 95% CI: 1.3-4.5, $p<0.01$).

Short sleep latency was associated with the Black non-Hispanic (OR 2.1, 95% CI: 1.4-3.2, $p<0.0001$) and the Hispanic (OR 1.6, 95% CI: 1.3-2.0, $p<0.0001$) ethnicities. These associations remained statistically significant after adjustment: Black non-Hispanic (aOR 2.8, 95% CI: 1.6-4.9, $p<0.01$) and Hispanic (aOR 3.3, 95% CI: 1.9-5.8, $p<0.001$).

Conclusions: Black non-Hispanic and Hispanic adolescents reported significantly shorter sleep durations and shorter sleep latency compared to their White non-Hispanic peers, even after adjustment for socio-demographic variables, suggesting a high prevalence of sleep deprivation in this population. Notably, marriage was protective against sleep loss, while higher parental education was associated with greater sleep loss, possibly due to earlier wake times, less bedtime supervision, or greater academic demands. Unmeasured factors likely contributing to these disparities include cultural sleep practices and environmental exposures such as noise and light pollution. Additionally, psychosocial stressors such as perceived discrimination, neighborhood safety, limited social support, and anxiety may mediate sleep loss among U.S. minorities. The findings underscore the need for greater ethnic diversity in sleep research to better address sleep health disparities and elucidate their contribution to increased morbidity and mortality among these vulnerable populations.

Structural Factors Impeding or Facilitating Freshmen Sleep Habits

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Introduction: Starting college is a time of transition that can be stressful. Developing healthy sleep habits in this period of relative autonomy is important for physical and mental wellbeing. We evaluated freshmen sleep, activity and wellbeing through different phases of the academic calendar using a wearable (Oura Ring) and a proprietary app (Z4IP). A comprehensive understanding of the structural factors that impede or facilitate freshmen sleep as they adapt to college life can inform programs to optimize student life and wellbeing.

Materials and methods: 638 freshmen underwent multi-factor evaluation across a 20-week semester using a combination of objective sleep measurements (Oura Ring), daily subjective reports of sleep and well-being (Z4IP), and periodic time-use diaries (Z4IP). We explored how sleep patterns were affected by the academic calendar, early morning classes, and staying on- versus off-campus.

Results: During instructional weeks, freshmen woke 49.8min earlier on weekdays compared to weekends ($t_{629}=24.14$, $p<0.0001$), especially when there were early morning classes. However, delaying

waketimes after the midterm break ($\beta=5.81$, $p<.0001$), often past the first class, resulted in increased sleep ($\beta=5.56$, $p<.0001$). In contrast, bedtimes were stably late across the semester, with minimal weekday-weekend differences (15.2min). Despite reduced needs for commuting, freshmen staying on-campus obtained less sleep than those staying off-campus ($t_{629}=-6.36$, $p<.0001$), even after accounting for naps ($t_{629}=-5.26$, $p<.0001$), due mainly to later bedtimes ($t_{629}=6.62$, $p<.0001$). Four hours before going to bed, on-campus students spent 60min on social and co-curricular activities, and compositional data analyses indicated that those spending more time on these activities slept later. Additional digital leisure activities showed similar effects for off-campus students.

Conclusions: Freshmen's sleep evolved across the semester as they adapted to college life. By the second half of the semester, more sleep was obtained by waking up later, often past early morning classes. Residential status also affected their sleep habits, and the type of activities that delayed when they went to bed. The mix of predicted and unpredicted findings underscores the utility of our minimally obtrusive, multi-factor, longitudinal behavioural and physiological phenotyping approach.

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Structured Breathing Exercises as a Treatment for Insomnia, Anxiety, and Depression in Young Individuals: A Randomized Controlled Trial

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Introduction: Insomnia is a prevalent and often debilitating condition among young individuals with anxiety and depression. Sleep disturbances, including difficulty initiating and maintaining sleep, are associated with emotional dysregulation, cognitive impairments, and an increased risk of chronic mental health conditions. Evidence suggests that structured breathing exercises (SBE) may enhance sleep quality by modulating autonomic nervous system activity, reducing hyperarousal, and promoting relaxation.

This study aims to evaluate the efficacy of SBE in improving sleep quality and reducing symptoms of insomnia, anxiety, and depression in young individuals aged 16–24 years.

Materials and methods: Methods

A randomized controlled trial (RCT) is currently in preparation and will be conducted during the summer and autumn of 2025. The study will recruit 100 participants from a mental health support program, who will be randomized into an SBE intervention group or a control group. The intervention consists of a four-week program including guided breathing techniques such as diaphragmatic breathing, box breathing, and Tummo breathing. Exercises will be practiced daily via an app, with weekly group sessions. Sleep outcomes will be assessed using the Insomnia Severity Index (ISI), and mental health measures will include the Hospital Anxiety and Depression Scale (HADS) and the General Health Questionnaire (GHQ-28).

Results: Expected Results

SBE is hypothesized to improve sleep quality by increasing parasympathetic activation, lowering cortisol levels, and reducing nocturnal hyperarousal. Controlled breathing techniques may enhance sleep onset, decrease nighttime awakenings, and improve overall sleep efficiency. If effective, this intervention could serve as a non-pharmacological, accessible approach for managing insomnia in young individuals with mental health concerns.

Conclusions: This study, set to begin in mid-2025 and findings could inform clinical practice by integrating breathwork as a complementary strategy for treating sleep disturbances in youth with anxiety and depression.

Subjective Sleep Parameters Associated with Anxiety and Depression in Mexican Young Adults: A Cross-Sectional Study

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Introduction: A growing body of evidence supports a robust association between sleep disturbances and an elevated risk of mood disorders. However, the specific contribution of individual sleep parameters to the manifestation of mood-related symptoms, particularly within non-clinical populations, remains insufficiently explored. This study aimed to investigate the associations between subjective sleep parameters and self-reported symptoms of anxiety and depression in a cohort of young Mexican adults.

Materials and methods: A cross-sectional survey was conducted among a non-probabilistic sample of 198 participants aged 18 to 25 years, residing in Mexico City. The assessment protocol included self-reported measures of sleep duration, sleep latency, frequency of nocturnal awakenings, and daytime sleepiness, the latter rated on a Likert-type scale. Additionally, participants completed the validated Spanish versions of the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDII). Multiple linear regression analyses were performed to evaluate the predictive value of sleep-related variables on anxiety and depression scores. Assumptions of homoscedasticity and absence of multicollinearity were verified prior to analysis. The study was approved by the Institutional Research and Ethics Committee (CEI/379/2024).

Results: The sample consisted of 49 males and 149 females, with a mean age of 19.7 years (SD = 1.5). The average reported sleep duration was 445.3 minutes per night (SD = 70.5), with a mean sleep efficiency of 89.9% (SD = 6.5) and an average sleep latency of 22.3 minutes (SD = 22.2). Excessive daytime sleepiness was reported by 18% of participants. Multiple linear regression analyses indicated that both excessive daytime sleepiness ($\beta = -0.255$, $p < 0.01$) and the number of nocturnal awakenings ($\beta = 0.219$, $p < 0.01$) were significant predictors of anxiety symptoms. These variables also significantly predicted depressive symptoms, although the association with nocturnal awakenings was weaker (daytime sleepiness: $\beta = -0.263$, $p < 0.01$; nocturnal awakenings: $\beta = 0.179$, $p = 0.014$). Other sleep parameters did not demonstrate statistically significant associations with mood symptoms.

Conclusions: Impairments in sleep maintenance and elevated levels of daytime sleepiness are significantly associated with mood symptoms in young adults, even when total sleep duration and sleep efficiency fall within normative ranges. These findings emphasize the clinical importance of identifying and addressing specific sleep disturbances, which may play a critical role in the development or exacerbation of affective symptoms in this population.

Subjective sleep quality in psoriatic patients and its association with symptoms severity

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Introduction: Psoriasis is a prevalent dermatological condition frequently associated with sleep disturbances. Evidence suggests a bidirectional relationship between sleep impairment and psoriatic symptoms, creating a vicious cycle that significantly impacts quality of life. This study investigated the subjective quality of sleep among patients diagnosed with psoriasis with mild symptom severity. The main aim was to determine the relationship between self-reported sleep quality and the perceived severity of psoriasis symptoms.

Materials and methods: Psoriatic patients were recruited from Dermatology Units based on the following criteria: 18–65 years, mild symptom severity (PASI < 10; DLQI < 5), no systemic treatment (topical only), absence of comorbid medical conditions (including psychiatric and sleep disorder diagnoses), no history of drug or alcohol abuse, limited caffeine (no more than 150 mg/day) and alcohol (no more than 250 mL/day) consumption. Control participants were recruited via social media and advertisement following the same inclusion criteria except for the presence of psoriatic disease. Participants filled out the Pittsburgh Sleep Quality Index (PSQI), addressing habitual sleep quality

across seven subscales (i.e., subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorders, sleep medication use, daytime dysfunctions due to sleepiness), with higher scores indicating poor sleep quality. Participants were also required to complete a 10-item Numeric Rating Scale for 7 consecutive days to report psoriasis-related levels of itch and pain at bedtime and upon awakening. Additionally, participants completed a set of questionnaires exploring anxiety (Beck Anxiety Inventory; BAI) and depression symptoms (Beck Depression Inventory; BDI), habitual sleepiness (Epworth Sleepiness Scale; ESS), and Quality of Life (SF-36 questionnaire).

Results: Nineteen patients (12M, 7F; age = 37.89 ± 12.93) and 53 controls (14M, 39F; age = 28.33 ± 13.29) were recruited.

No between-groups differences emerged in PSQI scores nor in BAI, BDI, ESS, and SF-36 scores.

Patients' PSQI total scores exhibited a positive correlation with the level of itch and pain referred at bedtime (itch: $p=.608$; pain: $p=.006$; pain: $p=.613$; $p=.005$) and risetime (itch: $p=.568$; pain: $p=.110$; pain: $p=.594$; $p=.007$).

As for PSQI subscales, level of itch and pain, both at bedtime and risetime, positively correlated with subjective sleep quality (bedtime: itch: $p=.019$; pain: $p=.023$; risetime: itch: $p=.040$; pain: $p=.021$), sleep latency (bedtime: itch: $p=.048$; pain: $p=.050$; risetime: itch: $p=.049$; pain: $p=.014$) and daytime dysfunction (bedtime: itch: $p=.046$; pain: $p=.044$; risetime: itch: $p=.015$; pain: $p=.016$).

Moreover, patients' PSQI total score correlated with the SF-36 subscale of Physical functioning ($p=.024$), Fatigue ($p=.014$), and emotional well-being ($p=.012$), and with BAI scores ($p=.019$).

Conclusions: This study explored subjective sleep quality in psoriatic patients, focusing on the level of itch and pain intensity as key indicators of self-reported disease burden. Our findings revealed that poorer subjective sleep quality was positively correlated with perceived psoriasis symptoms. This result highlights the relevance of addressing sleep quality in psoriatic patients, even when symptom severity is low. Optimizing sleep emerges as a key factor in overall patient well-being and potentially contributes to a more effective and comprehensive management of the disease.

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Summertime bedroom overheating in un-airconditioned UK urban apartments during Heat Alert periods: thermal comfort and sleep outcomes

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Introduction: The increasing frequency of heatwaves associated with global warming has implications for urban sleep quality in temperate regions. Growing epidemiological evidence has linked higher night-time air temperatures to indices of subjective sleep disturbance. Less research attention, however, has focussed on the mediating impact of bedroom overheating on both subjective and objective sleep outcomes during periods of untypically hot weather. The ongoing UK Home Heat Health project monitored the bedroom climate and sleep outcomes in un-airconditioned London apartments during the summers of 2023 and 2024.

Materials and methods: Following recruitment and screening, the sleep of 123 healthy adults (mean age = 35; 82 female) living in separate un-airconditioned London apartments was continuously monitored using actigraphy (CamnTech Motionwatch 8; epochs=30s) and a phone app consensus sleep diary (which included daily ratings of bedroom thermal comfort and heat-related sleep disturbance). Participant bedrooms were fitted with HOBO MX1101 sensors recording temperature at half hourly intervals. Using a quasi-experimental design, outcomes from 5-7 days of continuous 'typical' temperatures (Baseline: BL) and the first night of periods covered by UK Met Office 'Heat Health Alert' warnings (Hot Nights: HN) were compared in repeated measures general linear models.

Results: Night-time (22.00-07.00) bedroom temperatures rose significantly during Heat Alert nights (mean/range BL = 22.4°C / 17.5 - 26.4°C ; HN = 25.5°C / 22.0 - 29.3°C , $p<0.001$) with the average number of 30min periods exceeding 26°C , the CIBSE TM59 threshold for bedroom overheating, increasing from (mean/SD) 0.5 per night/0.1 at BL to 6.5 per night/8.0 on HN ($p<0.001$). Relative to BL,

participant ratings of bedroom thermal discomfort ($p < 0.001$) and sleep disturbance attributed to bedroom temperature ($p < 0.001$) both increased significantly on HN. Actigraphy showed modest but significant reductions in Total Sleep Time (mean/SD BL = 389.4/53.3; HN 379.0/62.2, $p = 0.04$) and Time in Bed (mean/SD BL = 492.4/53.2; HN 478.1/75.1, $p = 0.04$). Average rise times were 21 minutes earlier following HN ($p < 0.001$).

Conclusions: In these un-airconditioned apartments typical of London housing stock, bedroom overheating and subjective bedroom thermal discomfort was common on hot nights. However, while ratings of sleep disturbance attributed to bedroom temperature also increased significantly, most sleep outcomes (sleep latency, wake after sleep onset, sleep efficiency, sleep fragmentation, mobility during sleep) showed no significant BL-HN change. All the Heat Alerts captured here received the lowest health risk classification of 'yellow'. For these lower range hot spells, the immediate impact of bedroom overheating appears to be reflected more in experience (subjective ratings) and behaviour (e.g. rise times) than sleep architecture. Monitoring for higher risk Heat Alerts, and longer term low-risk alerts is ongoing in the Home Heat Health project.

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Summertime bedroom temperatures in un-airconditioned UK urban apartments: factors influencing subjective and objective sleep outcomes

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Introduction: The increasing frequency of heatwaves associated with global warming has implications for urban sleep quality, with epidemiological evidence showing clear links between higher night-time air temperatures and subjective sleep disturbance (e.g. Obradovich et al, 2017; Khosravi et al, 2025). In understanding factors mediating these subjective reports, however, less research has focussed on the influence of bedroom temperatures or on individual differences in sleep reactivity. We examined actigraphic total sleep time (TST) and subjective sleep experiences in relation to bedroom temperatures and scores on the Ford Insomnia Response to Stress Test (FIRST) during periods of untypically hot London weather.

Materials and methods: The UK Home Heat Health project monitored bedroom climate and sleep outcomes during the summers (June-September) of 2023 and 2024. Following recruitment and psychometric profiling 123 healthy adults (mean age = 35; 82 female) living in separate un-airconditioned London apartments were continuously monitored using actigraphy (CamnTech Motionwatch 8) and a phone app Consensus Sleep Diary with additional 10-point ratings of bedroom thermal comfort and degree of heat-related sleep disturbance. Bedroom temperatures were monitored half-hourly using HOBO MX1101 sensors. Outcomes from 5-7 days of continuous 'typical' temperatures (Baseline: BL) and the first night of periods covered by UK Met Office 'Heat Health Alert' warnings (Hot Nights: HN) were first compared in general linear models. For ratings of thermal comfort, heat-related sleep disturbance, feeling 'rested' in the morning, and actigraphic total sleep time (TST), change scores (BL minus HN) were then computed and entered as dependent variables in 4 separate linear regression models with maximum bedroom temp (°C), age (years), gender (M/F) and FIRST scores as independent variables (IVs) in each.

Results: Night-time (22.00-07.00) bedroom temperatures rose significantly during HN (mean/range BL = 22.4°C /17.5-26.4°C; HN = 25.5°C/22.0-29.3°C, $p < 0.001$) with 46% of bedrooms exceeding the CIBSE TM59 threshold (26°C) signifying overheating. HN thermal comfort ($p < 0.001$), feelings of being 'rested' ($p < 0.001$) and actigraphic TST ($p < 0.05$) significantly decreasing, while ratings of heat-related sleep disturbance significantly increased ($p < 0.001$). In the regression models entering all IVs, only (increasing) maximum bedroom temperatures significantly predicted these negative changes in thermal comfort (standardized beta = - 0.2; $p = 0.037$), heat-related sleep disturbance (standardized beta = - 0.2; $p = 0.03$) and feeling 'rested' in the morning (standardized beta = - 0.23; $p = .012$). For actigraphic TST all IVs in the model were non-significant.

Conclusions: In these un-airconditioned apartments typical of London housing stock bedroom overheating was common on hot nights. However, while the magnitude of change indicating thermal discomfort, heat-related sleep disturbance, and morning feelings of being 'unrested' increased with bedroom temperature, the magnitude of objectively measured changes in TST did not. All outcomes were independent of sleep reactivity (FIRST) scores. For less severe hot spells in temperate climates, the linear impact of rising bedroom temperatures is reflected more in subjective experience than in sleep architecture. This has implications for inferences drawn from subjective reports, and will be examined further in the ongoing Home Heat Health project.

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Targeting Sleep to Improve Risky Driving: Results from a Randomized Controlled Trial in Young Drivers

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Introduction: Young adults are over-represented in sleepiness related road crashes. Given the critical role that sleep plays in risky driving in young people, addressing sleep loss through targeted interventions should be a priority. To date, no randomized controlled trials have assessed the effects of increased sleep on on-road driving risk. Addressing this gap, the current study examined the effectiveness of a community-based sleep extension and education intervention on 1) increasing objective sleep duration and reducing sleep restriction episodes, and 2) reducing on-road risky driving in sleepy young drivers.

Materials and methods: This pragmatic, parallel-group randomized controlled trial involved young Australian drivers who reported habitual sleep of <7 hours per night and <6 hours on at least two nights per week, with no diagnosed sleep disorders or overnight shift work. Participants were randomized to either a sleep extension and education intervention or a placebo control condition receiving nutrition information. Outcomes were assessed using wrist actigraphy and in-vehicle accelerometers during three, two-week naturalistic assessment periods: Baseline (weeks 1–2), Intervention Maintenance (weeks 6–7), and 6-Month Follow-Up (weeks 33–34). The intervention group received brief sleep health education and an individualized sleep extension plan, implemented over a 3-week period following Baseline assessment. Primary outcomes were changes from baseline in objective sleep duration, frequency of sleep restriction, and risky driving behaviours (harsh starts, stops, and rapid turns). Secondary outcomes included diary reported sleep duration, subjective sleep disturbance, and sleep related daytime impairment. Analyses were conducted on an intention-to-treat basis using mixed-effect linear models.

Results: Of 951 participants screened for eligibility, 115 were randomized, and 99 completed the study (*Mean* = 20.62, *SD* = 1.90, 73% female). Significant intervention effects were observed in objective risky driving (reduction in proportion of harsh starts/stops (β = -0.14, 95% CI: -0.27, -0.02, p = 0.024), and rapid turning (β = -0.07, 95% CI: -0.14, -0.005, p = 0.036) for participants in the sleep extension condition relative to the placebo condition during the intervention maintenance phase, but not during follow-up. Participants in the sleep intervention group reported a significant reduction in subjective sleep-related daytime impairment during the intervention maintenance phase (β = -5.64, 95% CI: -9.14, -2.14, p = 0.002). However, this effect was not sustained at follow-up. No significant intervention effects were observed in objective or subjective sleep duration or frequency of sleep restriction episodes between groups at maintenance, or follow-up assessment.

Conclusions: A behavioural sleep extension and education intervention led to short-term improvements in objective risky driving indicators and reductions in daytime impairment among young adult drivers, despite no significant change in objective sleep duration. Although effect sizes were modest, g-force events are strong predictors of crash risk and suggest a potentially meaningful

population-level impact. Our findings highlight the promise of sleep-focused interventions in road safety strategies, while underscoring the need for ongoing support to sustain behavioural change.

Temporal Dynamics of Sleep, Depression, and Fatigue During Pregnancy: A Multilevel Vector Autoregression Analysis

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Introduction: Pregnant women often experience complex and evolving physical and psychological symptoms including sleep disturbance, depression, and fatigue. Few studies have used person-centered longitudinal models that capture dynamic, reciprocal relationships among multiple symptoms. To address this gap, this study aimed to examine the temporal and between-subject associations of those symptoms across different trimesters.

Materials and methods: A prospective cohort design was used. Pregnant women (N=228) were followed up during the first, second, third trimester, and 6-month postpartum. At each time point, participants completed a sleep diary for seven consecutive days. Sleep parameters were calculated using the 7-day averages. According to previous literature on the operationalization of multidimensional sleep health, a composite score was calculated based on five indicators: early chronotype (defined as a 7-day average sleep mid-point < the median 3:26 AM), sufficient sleep duration (7-8 hours per night), absence of insomnia (Insomnia Severity Index ≤ 7), no loud snoring (one item from the STOP-Bang), and low daytime sleepiness (Epworth Sleepiness Scale < 10). One point was assigned for meeting each criterion, with a total score ranging from 0 to 5. Fatigue was assessed using a single item from the sleep diary (rated 0-10), and the 7-day mean was used. Depressive symptom was measured using the Edinburgh Postnatal Depression Scale. We used a multilevel vector autoregressive (MLVAR) model to examine temporal and between-person association and uncover potential feedback loops among the symptoms across time. The model was estimated using the mlVAR package (R v4.4.2), with participants as the grouping variable.

Results: Participants mean age was 31.7 years (SD 3.8, range 21-48). The temporal effects revealed several significant associations. Fatigue at the previous time point significantly predicted worse sleep health at the subsequent time point ($\beta = -0.142$, $p = 0.002$). Depressive symptom significantly predicted better sleep health ($\beta = 0.113$, $p = 0.024$) and lower fatigue ($\beta = -0.080$, $p = 0.027$) at the following time point. Both depressive symptom ($\beta = -0.122$, $p = 0.003$) and sleep health ($\beta = -0.092$, $p = 0.029$) demonstrated a significant negative autoregressive effect, indicating an inverse temporal association within depression or sleep across adjacent time points. All other temporal and autoregressive paths not reported were statistically non-significant. The between-subject results further revealed that individuals with higher fatigue reported higher depression (partial $r = 0.210$, $p = 0.001$) and poorer sleep health (partial $r = -0.316$, $p < 0.001$), and those with higher depression also reported lower sleep health (partial $r = -0.338$, $p < 0.001$).

Conclusions: Fatigue emerged as a robust predictor of subsequent declines in sleep health, highlighting its relevance as a potential intervention target. Negative autoregressive patterns indicated temporal instability in both sleep and depression. Temporal analyses showed that higher depressive symptoms predicted better subsequent sleep, whereas between-subject results indicated that greater depression was associated with poorer overall sleep health. These cross-level inconsistencies suggest that temporal effects may capture short-term, dynamics, while between-subject effects reflect stable individual differences—highlighting the need for intensive longitudinal designs to disentangle these processes.

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Temporal profile of distal skin temperature change at sleep onset across multiple nights in adolescents and older adults

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Introduction: At sleep onset, there is a decrease in core body temperature and an increase in distal skin temperature (DST). However, most studies have focus on single night lab measurements in adults. There is a need for naturalistic studies over different age groups to understand the night-to-night variability of this physiological herald of sleep. We sought to determine temporal kinetics of peri-sleep DST increase using a wearable sleep tracker and the consistency of these measurements across multiple nights in adolescents and older adults.

Materials and methods: DST was measured using Oura rings (Gen 2 and 3) equipped with NTC thermistors sensitive to 0.01°C temperature changes. N2 sleep onset was determined via EEG (SOMNOtouch and Dreem band) over 8 to 10 nights and up to 5 naps for adolescents. DST measurement and analysis focused on the time between the Time Attempting To Sleep (TATS) and N2 sleep onset. A novel semi-automatic algorithm was developed to identify the rise in DST, calculating both the temperature delta and rate of increase. Mixed-effects models were employed to explore relationships between temperature rise characteristics and N2 sleep onset timing and temperature. All models were controlled for age and sex.

Results: Analyses included 42 adolescents (224 nights and 73 naps) and 45 older adults (197 nights), 52% of participants were female across both studies and mean age was 16.4±0.9 and 75.0±3.3 years respectively. Average temperatures at the start of the rise were 30.8±2.6 °C (adolescents, 30.0±1.9 for naps) and 33.6±1.2 °C (older adults) reaching 35.4±0.3 °C (35.2±0.9 °C for naps) and 35.6±0.8 °C at the end of the rise while N2 sleep onset temperatures were 35.2±0.6 °C (34.2±0.5 °C for naps) and 35.4±0.9 °C. The rates of change were 0.16±0.06 °C/min (0.29±0.08 for naps) and 0.10±0.06 °C/min, in adolescents and older adults. Weak associations were found between the timing of the rise in temperature and N2 sleep onset latency (adolescents nights: $\beta = 0.26$, $p < .001$; adolescents naps: $\beta = 0.29$, $p = 0.005$; adults: $\beta = 0.31$, $p < .001$). Stronger associations were found between the final DST of the rise and N2 sleep onset DST (adolescents nights: $\beta = 0.57$, $p < .001$; adolescents naps: $\beta = 0.71$, $p < .001$; adults: $\beta = 0.73$, $p < .001$). DST at the end of the rise is affected by bedtime. Interestingly, with later bedtimes, DST reached at end of the sleep onset ramp in DST was higher for adolescents ($\beta = 0.18$, $p = 0.005$) but lower for older women ($\beta = -0.25$, $p = 0.023$). This suggests an age x timing interaction of the temperature rise that needs to be further studied.

Conclusions: The Oura ring can detect a rise in DST around N2 sleep onset across populations. Even accounting for intra-individual variability of the starting DST, this rise consistently concludes proximate to (but not at) DST at N2 sleep onset, suggesting there is a DST threshold indicative of sleep initiation that is modulated by age differences in circadian timing.

The Association between Sleep Duration, Insomnia, Daytime Sleepiness, Health, Quality of Life, and Sociodemographic Factors in General Populations Across Africa, Asia, Europe, and the Caribbean: Findings from the Burden of Obstructive Lung Disease (BOLD) Study

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Introduction: Sleep duration and quality are crucial determinants of health. Yet, few studies have examined their associations with cardiometabolic diseases and sociodemographic factors across diverse global settings using standardized tools. This study investigates how sleep duration, insomnia, and daytime sleepiness relate to health outcomes and social determinants across 18 sites in 15 countries.

Materials and methods: We analyzed data from 5,929 participants aged ≥50 years in the BOLD (<https://www.imperial.ac.uk/nhli/bold/>) follow-up study (2019–2021). Standardized questionnaires assessed sleep duration, insomnia (≥3 nights/week), daytime sleepiness (≥3 days/week), socioeconomic

status, and doctor-diagnosed cardiometabolic diseases. Associations were explored using mixed-effects logistic regression models adjusted for age, sex, BMI, smoking, and study site.

Results: Average sleep duration was 7.1 hours (SD: 1.4). Sleep duration was inversely associated with education and wealth, but unemployment was linked to longer sleep. Short sleep (<6 hours) was more prevalent in high-income countries (e.g., Norway, Iceland), while long sleep (>8 hours) was common in lower-income settings (e.g., Malawi, Jamaica). Higher-latitude countries in Northern Europe had shorter sleep durations and a higher proportion of short sleepers, and lower-latitude tropical regions had the longest sleep durations and fewer short sleepers. Western locations reporting longer sleep durations and fewer short sleepers and eastern longitudes with higher proportions of short sleepers.

Both short and long sleepers more often self-estimated their health as poor compared to normal sleepers. Short sleep alone did not show a statistically significant association with cardiometabolic diseases. Insomnia alone was significantly associated with an increased risk of hypertension (OR = 1.26), heart disease (OR = 1.33), and stroke (OR = 1.65). Among those with short sleep and insomnia the risk increased for heart disease (OR = 2.36) and diabetes (OR = 2.05). Daytime sleepiness is an independent predictor of cardiometabolic disease; hypertension (OR = 1.34), heart disease (OR = 1.48), diabetes (OR = 1.94) and stroke (OR = 1.49). Short sleepers with daytime sleepiness exhibited even greater risks, particularly for heart disease (OR = 1.95) and diabetes (OR = 3.30). Those with only long sleep had increased risk for stroke (OR = 1.92), but when long sleep was combined with daytime sleepiness, the stroke risk increased (OR = 2.38). Long sleepers with insomnia had increased risk for hypertension (OR = 2.75).

Conclusions: Our findings emphasize the role of poverty, education, and geography in shaping global sleep disparities. Sleep duration alone is an incomplete marker of health risk. Instead, sleep health should be evaluated multidimensionally—considering insomnia, daytime sleepiness and socioeconomic in context with sleep duration. Interventions targeting sleep quality and daytime functioning may be more effective in mitigating cardiometabolic risks than focusing on sleep duration alone.

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The association between weekend catch-up sleep and the reduction of obesity and overweight risk in adolescents with insufficient weekday sleep

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Introduction: Some researches have emphasized the need to explore the relationship between sleep habits, particularly weekend catch-up sleep (CUS), and overweight/obesity outcomes in adolescents. However, the protective effect of compensatory sleep on weight remains controversial. This study investigates the association between weekend CUS and overweight/obesity in Korean adolescents, focusing on weekday sleep sufficiency.

Materials and methods: A nationwide cross-sectional study was conducted among 12,434 high school students in South Korea. Sleep patterns including total sleep duration and weekend CUS were assessed using self-reported questionnaires. Body mass index (BMI) was calculated and categorized into overweight/obese and normal weight groups based on age- and sex-adjusted Z-scores. Logistic and linear regression models were used to assess the associations between sleep variables and overweight/obesity.

Results: Students with 3 or more h of CUS had lower odds of being overweight/obesity (odds ratio = 0.67, 95% confidence interval: 0.57–0.80) compared to those with non-CUS. This protective effect remained significant in the subgroup with perceived insufficient weekday sleep. Furthermore, students with 3 or more h of CUS had significantly lower BMI z-scores ($\beta = -0.18, p < 0.001$), an association that was also observed in those with perceived insufficient sleep ($\beta = -0.16, p = 0.003$). The analysis showed a dose-dependent pattern, with greater weekend CUS being associated with a stepwise reduction in BMI z-scores.

Conclusions: Weekend CUS may serve as an important compensatory mechanism for adolescents to reduce the risk of being overweight or obese. However, no additional benefits of CUS were observed in adolescents with sufficient sleep quality.

The Association of Sleep Duration and Quality with Obesity-related Cancers: Results from the Health Examinees Study

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Introduction: Sleep has emerged as a modifiable risk factor for metabolic dysfunction and cancer. However, prospective evidence linking sleep duration and quality to cancer risk remains inconclusive. This study aims to investigate the associations of self-reported sleep duration and quality with obesity-related cancer risk in a large-scale Korean population.

Materials and methods: This prospective cohort study utilized data from the Health Examinees-Gem (HEXA-G) cohort, comprising 67,910 adults aged ≥ 40 years who were recruited between 2004 and 2013. Sleep quality were self-reported at baseline and assessed based on multiple dimensions, including sleep duration (6–<8 hours), bedtime (20:00–24:00), difficulty initiating or maintaining sleep (not at all), sleep disturbance due to worries (not at all), nonrestorative sleep (not at all), daytime fatigue (not at all), habitual snoring (<3 times per week) and snoring with breathing interruptions (no) as reference. Each response was summarized into a composite sleep quality score (score range 0–14) and categorized into quartiles. This study adopted obesity-related cancers, defined by the International Agency for Research on Cancer. Cancer cases were identified through national cancer registration data from the Korea Central Cancer Registry of the Korea National Cancer Center. Cox proportional hazards models were applied to assess hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations of sleep quality with risk of obesity-related cancer, with follow-up from baseline to first cancer diagnosis, death, loss to follow-up, or end of study.

Results: Among the individual components of the composite sleep quality score, significant associations of frequent daytime fatigue (HR: 1.53, 95% CI: 1.18–1.99, $p=0.003$), habitual snoring (HR: 1.24, 95% CI: 1.03–1.50, $P=0.025$), and snoring with breathing interruptions (HR: 1.40, 95% CI: 1.08–1.82, $p=0.011$) with obesity-related cancer risk were demonstrated in females. Sleep duration, bedtime, difficulties in initiating or maintaining sleep, sleep disturbances due to worries, and nonrestorative sleep were not significantly associated with obesity-related cancer risk. Furthermore, females in the highest quartile of the composite sleep quality score had increased risk of obesity-related cancer (HR: 1.17, 95% CI: 1.02–1.35); however, the effect size of this association was smaller compared to the associations observed for specific symptoms, including frequent daytime fatigue, habitual snoring, and snoring with breathing interruptions. In males, combined sleep quality without sleep duration was significantly associated with higher obesity-related cancer risk (HR: 1.47, 95% CI: 1.09–1.97, $p=0.010$), even in the absence of significant associations with individual sleep quality components.

Conclusions: In this large-scale prospective cohort study, higher composite sleep scores combining sleep duration with sleep quality were associated with elevated risk in females, and poor sleep quality without considering sleep duration was associated with elevated risk in males. These findings underscore the importance of multidimensional sleep quality assessment as a modifiable behavioral factor in the prevention of obesity-related cancer.

The association of sleep quality with post-surgery functional status and quality of life in patients with spinal degenerative diseases: A prospective study

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Introduction: Sleep plays an important role in individual well-being. Sleep quality of patients with spinal degenerative diseases (SDD) can be severely impaired. Few studies have explored whether sleep quality was associated with post-surgery recovery. This study aimed to examine the association between sleep quality with post-surgery functional status and quality of life among people with SDD.

Materials and methods: This prospective cohort study included 185 patients recruited between August 2022 and June 2023 from the spine center of a tertiary hospital in Shanghai, China. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Functional status was measured by the Oswestry Disability Index or Neck Disability Index, while quality of life was assessed using the EuroQoL 5-Dimension 5-Level questionnaire. Potential confounders, e.g., depression and pain, were measured using validated instruments. Data was collected before the surgery and one-month post-surgery. Change in sleep quality before and after the surgery was calculated and used for the analyses. Minimal clinically important difference (MCID) for sleep quality was calculated as 0.5 times the standard deviation. Participants were classified into “Clinically improved”, “Clinically worsened”, or “No significant change.” Multivariate analysis of covariance (MANCOVA) was conducted to examine the association between sleep quality with the combined functional status and quality of life. Effect size was calculated using partial η^2 .

Results: Participants mean age was 46.8 years (SD=12.2), and 59.5% were males. The mean BMI was 24.4 kg/m² (SD=3.5). Lumbar surgery was performed in 67.0% of cases (N=124), while 33.0% underwent neck surgery (N=61). Based on MANCOVA, in addition to age, surgery site, changes in depression ($p=0.001$, partial $\eta^2=0.07$) and pain ($p=0.003$, partial $\eta^2=0.06$), change in sleep quality ($p=0.006$, partial $\eta^2=0.06$) was a significant predictor of the outcomes. The effect size was moderate. Additionally, the MCID for PSQI was 2.03. When sleep quality change was classified into “Clinically improved” ($\Delta\text{PSQI} \leq -2.03$, N=45, 24.3%), “Clinically worsened” ($\Delta\text{PSQI} \geq 2.03$, N=43, 23.2%), and “No significant change” ($-2.03 < \Delta\text{PSQI} < 2.03$, N=97, 52.4%), the association remained statistically significant ($p=0.004$, partial $\eta^2=0.040$).

Conclusions: In addition to traditional factors (e.g., age, surgery site, pain, depression), sleep quality was a significant predictor of post-surgery functional status and quality of life among patients with SDD. Change in sleep quality from pre- to post-surgery was not only statistically significant, but also clinically meaningful. Incorporating sleep assessment and management into peri-operative care may facilitate post-surgery recovery.

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The Cost of Compromised Sleep: Links Between Sleep Health Dimensions and Daytime Sleepiness and Fatigue in healthy adults

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Introduction: Sleep health dimensions include sleep duration, efficiency, timing, quality and regularity and have been studied both, individually and collectively, for their associations with various health outcomes. These dimensions can be reflected in metrics that can be assessed through self-report, behavioural measures like actigraphy, and physiological data. These metrics are easily interpretable and hold strong validity, making them useful to study both clinical and general population. Sleepiness, mental and physical fatigue, however distinct, are interrelated dimensions that can impact daytime activities. These symptoms are associated with different health outcomes and can occur not only in individuals with sleep disorders, but also in healthy individuals when sleep health dimensions are disrupted. This study aims to determine which actigraphy and questionnaire-based metrics best capture these daytime functioning aspects, in particular sleepiness assessed by the Epworth Sleepiness Scale (ESS), mental and physical fatigue assessed by the Multidimensional Fatigue Inventory (MFI).

Materials and methods: We analysed data from 143 healthy working-age adults (median age: 34 years; IQR: [23–49]; 53.15% female) who wore an actigraphy device (ActTrust or ActLumus, Condor Instrument™) for an average of 27 consecutive days (above 3700 days of actigraphy). Objective metrics included: transition probability from rest to activity during the main sleep bout (kRA), lowest five hours of activity (L5), highest ten hours of activity (M10), intradaily variability (IV), and interdaily stability (IS), derived using pyActigraphy Python package. MSFsc (“sleep chronotype”) was derived from the Munich Chronotype Questionnaire, while perceived sleep quality and duration were extracted from the Pittsburgh Sleep Quality Index (PSQI). General linear models adjusted for age and sex were used to evaluate associations between sleep metrics, fatigue and daytime symptoms were conducted using GraphPad Prism v.10.3.0 with significance set at $p < 0.05$.

Results: In the Poisson regression model predicting sleepiness ($R^2=0.31$), higher kRA ($\beta=1.98$, $p=0.011$), higher L5 ($\beta=0.001$, $p=0.011$), and lower IS ($\beta=-0.424$, $p=0.037$) were significantly associated with greater ESS scores. PF also showed a significant positive association ($\beta=0.037$, $p<0.001$). In the MF model ($R^2=0.24$), significant predictors included lower kRA ($\beta=-1.66$, $p=0.025$), younger age ($\beta=-0.006$, $p=0.016$), higher PF ($\beta=0.024$, $p=0.015$), and poorer perceived sleep quality ($\beta=0.132$, $p=0.031$). Regarding the PF model ($R^2=0.32$), higher ESS scores ($\beta=0.028$, $p=0.002$), higher mental fatigue ($\beta=0.021$, $p=0.024$) and lower IV ($\beta=-1.03$, $p=0.009$), were significant predictors. Male sex ($\beta=-0.140$, $p=0.031$) was also associated with greater PF. Additionally, lower perceived sleep quality was associated with greater PF ($\beta=0.134$, $p=0.018$).

Conclusions: Our findings reveal a divergence in how different aspects of sleep health relate to daytime symptoms in healthy adults. Sleepiness was more strongly associated with objective indicators of irregular and fragmented activity rhythms, not subjective sleep complaints, mirroring patterns observed in sleep apnea patients. In contrast, mental and physical fatigue were more closely linked to perceived poor sleep quality and general tiredness. These findings highlight the importance of distinguishing between sleepiness and fatigue when evaluating sleep health, as they may reflect different underlying mechanisms and intervention targets.

The Cross-cultural Application of the Peds B-SATED Model for Assessing Pediatric Sleep Health

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Introduction: Pediatric sleep health has a profound impact on children's physical growth, cognitive development, emotional regulation, and overall well-being. This study is grounded in the Peds B-SATED model developed by Meltzer et al. It systematically outlines six core dimensions of pediatric sleep health, including sleep satisfaction, alertness, timing, efficiency, duration, and related behaviors. Drawing on the socio-ecological systems theory, the paper further explores the multi-level interactive influences of family, school, culture, and the physical environment on children's sleep.

Materials and methods: Existing sleep assessment models have predominantly been developed within Western cultural contexts, which may limit their applicability to the distinct sleep patterns and sociocultural environments of Chinese children. To bridge this gap, this study outlines several key research directions: the integration of subjective and objective assessment methods (e.g., sleep diaries, the CSHQ, and wearable devices) to construct a pediatric sleep health evaluation framework tailored to China's socio-ecological context; the exploration of artificial intelligence applications in real-time monitoring and personalized interventions; and the advancement of the clinical and public health utility of the Peds B-SATED model through cross-cultural validation and interdisciplinary collaboration. These initiatives aim to generate contextually relevant, evidence-based strategies to support the promotion of pediatric sleep health in China.

Results: This study systematically reviews over 20 commonly used subjective and objective sleep assessment tools across both domestic and international contexts, including sleep diaries, the Children's Sleep Habits Questionnaire (CSHQ), actigraphy, and polysomnography (PSG). Subjective instruments, such as ISAS, TSAS, and ASHS, are user-friendly and accessible but are susceptible to bias from proxy reporting. In contrast, objective measures like PSG and wearable technologies offer high accuracy but are limited in scalability due to their cost and technical complexity. The study further explores emerging applications of artificial intelligence (AI) in pediatric sleep assessment, highlighting real-time monitoring systems and deep learning algorithms based on multimodal data sources—such as

actigraphy, environmental sensors, and sleep diaries—as well as the potential of wearable devices for enabling personalized interventions. In addition, the research identifies key challenges in the cross-cultural adaptation of the Peds B-SATED model. For example, prevalent practices in China, such as routine daytime napping and delayed bedtimes associated with academic demands, necessitate culturally sensitive modifications to the model. Accordingly, the inclusion of 'nap quality' as a component of sleep satisfaction is proposed as a contextually relevant optimization strategy.

Conclusions: The Peds B-SATED model, characterized by its systematic structure and developmental sensitivity, is redefining clinical approaches to pediatric sleep health. To enhance its applicability in the Chinese context, future research should prioritize multicenter validation, the development of culturally responsive assessment instruments, and the integration of artificial intelligence (AI) technologies into clinical practice. Moreover, incorporating stratified intervention strategies—such as adjusting school start times and enhancing synchronization of family routines—holds promise for advancing the comprehensiveness and precision of pediatric sleep health assessment in real-world settings.

The effectiveness of acupressure on sleep quality in cancer patients: A systematic review and meta-analysis of randomized controlled trials

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Introduction: Poor sleep quality is prevalent among cancer patients and significantly impacts their physical and psychological well-being and quality of life. Studies increasingly support the effectiveness of acupressure for improving sleep quality. However, it remains unclear whether the effect of acupressure on sleep quality can be generalized across various cancer conditions. The population-level and intervention-level characteristics of acupressure that are associated with sleep quality are also unclear. Hence, this meta-analysis aims to examine the effectiveness of acupressure on sleep quality in cancer patients and to identify the population-level and intervention-level characteristics associated with the intervention outcome of sleep quality.

Materials and methods: PubMed, EMBASE, APA PsycInfo, Web of Science, CINAHL, Cochrane Library, China National Knowledge Infrastructure, and WanFang were searched for eligible randomized controlled trials (RCTs) from inception to April 2024. Two reviewers independently conducted the searches, screened the retrieved studies, and extracted data from the eligible studies. Methodological quality was assessed using the Cochrane Risk of Bias Tool for Randomized Trials 2.0. A random-effects model was used for the meta-analysis. Subgroup analyses were conducted to examine the effects of cancer type, cancer treatment type, acupressure type, stimulation materials, acupressure provider, and control condition using Review Manager Software 5.4. Meta-regression analyses including sample sizes, number of acupoints, number of acupressure sessions, duration of each acupressure session, and overall duration of acupressure intervention were performed using R version 4.3.2. Both the subgroup analyses and the meta-regression aimed to investigate potential heterogeneity and identify characteristics that may be associated with more favorable acupressure outcomes.

Results: A total of 22 RCTs involving 2,113 participants from 8 regions were included in this meta-analysis. Compared with sham acupressure, usual care, patient education, and no intervention control groups, acupressure exhibited a significant beneficial effect on sleep quality in cancer patients at post-intervention (Standardized Mean Difference [SMD] = -1.38, 95% CI [-1.81, -0.95], $p < 0.001$, $I^2 = 94\%$) and at 4-week follow-up (SMD = -0.33, 95% CI [-0.56, -0.10], $p = 0.004$, $I^2 = 13\%$). Acupressure also showed statistically significant improvements in sleep efficiency (SMD = 0.77, 95% CI [0.27, 1.26], $p = 0.002$, $I^2 = 78\%$) and total sleep time (SMD = 0.68, 95% CI [0.15, 1.22], $p = 0.010$, $I^2 = 81\%$) at post-intervention. None of the characteristics significantly affected the overall effect size on sleep quality.

Conclusions: Acupressure appears to be a promising intervention for enhancing sleep quality among cancer patients. Future studies should focus on elucidating the long-term effects of acupressure on sleep quality, identifying the specific characteristics of acupressure that yield better intervention outcomes, and determining which types of cancer patients can benefit from this intervention.

The Effect of Continuous Positive Airway Pressure (CPAP) on Lower Urinary Tract Symptoms (LUTS) in Obstructive Sleep Apnea (OSA) patients with depression

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Introduction: There is a bidirectional connection between depression and LUTS⁽¹⁾. Moreover, OSA can contribute to LUTS⁽²⁾.

This study aimed to assess the immediate effect of CPAP on LUTS in patients with depression and OSA in Hong Kong.

Materials and methods: Patients referred for sleep studies were recruited from 15/02/2025 to 30/05/2025. The Patient Health Questionnaire-9 (PHQ-9) is a valid tool to evaluate depression and depression was defined as PHQ-9 score ≥ 4 ⁽³⁾.

In addition, the International Prostate Symptom Score (IPSS) has been validated to evaluate LUTS in female and male patients our locality⁽⁴⁾, and IPSS was assessed before and after one night of CPAP.

Results: A total of 94 patients were recruited, and among them 49 patients were depressive as defined by PHQ-9 score ≥ 4 (52.1%). There was no difference in age, body mass index, neck circumference or apnea-hypopnea index ($p>0.05$). Patients with depression presented with a higher IPSS than the control group ($p<0.05$). Additionally, there was a better response in LUTS among patients with depression.

Conclusions: This pilot study showed that the use of CPAP after one night significantly improves LUTS in obstructive patients with depression and sleep apnea.

CPAP may play a role in LUTS patients with depression and sleep apnea. However, due to sample size, a larger study with longer follow is required to reach any solid conclusion.

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The effect of sleep hygiene education combined with Schroth exercises on sleep quality among adolescents with idiopathic scoliosis: A randomized controlled trial

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Introduction: Adolescent Idiopathic Scoliosis (AIS) is the most prevalent type of scoliosis affecting adolescents 10 to 18 years of age. Around 43% of individuals with AIS report poor sleep quality that negatively affect their quality of life. Schroth exercises are widely used among people with AIS, they consist of sensorimotor, postural and breathing exercises aimed to adjust normal postural alignment, static/dynamic postural control, and spinal stability. Although sleep hygiene education (SHE) is the most common used sleep management technique, no previous study explored the combined effects of performing Schroth exercises with SHE on sleep quality among individuals with AIS. Therefore, the aim of this study was to explore the combined effect of SHE with Schroth exercises on sleep quality, quality of life, and Cobb angle among individuals with AIS using a randomized control study design.

Materials and methods: Using a single-blinded randomized controlled design, 30 participants were randomly assigned using block randomization into two groups: Group A (SHE and Schroth) ($n=15$, mean age= 14.00 ± 2.24), and group B (Schroth alone) ($n=15$, mean age= 14.27 ± 2.76). Participants in both groups performed Schroth exercises twice a week for 12 weeks supervised by a certified Schroth physical therapist. Group A received SHE and were contacted once a week to monitor compliance to the SHE program. All participants completed the following assessments at baseline and post intervention: Pittsburgh Sleep Quality Index (PSQI) to assess global sleep quality, Sleep Hygiene Index (SHI) to assess sleep related behaviors, Scoliosis Research Society-22 revised (SRS-22r) to assess quality of life, and radiographic Cobb angle measurement to assess degree of spinal curvature. Ethical approval was received from the Institutional Review Board of the Royal Medical Services (472024//1).

Results: There was a significant difference in PSQI scores between the two groups post intervention, in which group A had lower scores compared to group B ($t = -4.039$, $p = 0.001$), SHI was also significantly different between the two groups post intervention, in which group A had lower scores compared to group B ($t = -3.393$, $p = 0.003$). Although both groups had lower Cobb angle degrees and higher scores in the SRS-22r post intervention, the change was not significantly different between the two groups.

Conclusions: This study demonstrates that a 12 week SHE program combined with Schroth exercises can significantly improve sleep quality and sleep hygiene among individuals with AIS. Findings from this study emphasizes the need to address poor sleep quality among individuals with AIS, in which the use

of SHE combined with Schroth exercises provides a non-pharmacological management approach to these issues among this population. Large scale future studies are needed to confirm these findings.

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The effects of physical activity timing and adherence to physical activity guidelines on sleep in children with Attention-deficit/hyperactivity disorder

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Introduction: Regular physical activity (PA) has been shown to benefit sleep. However, the effects of PA timing and adherence to the WHO's recommended 60-minute moderate-to-vigorous physical activity (MVPA) guideline on sleep remain unclear, especially for children with Attention-deficit/hyperactivity disorder (ADHD) who often experience sleep problems. This study examined whether the timing of MVPA influenced objectively measured sleep, including sleep latency (SL), sleep efficiency (SE), total sleep time (TST), and wake after sleep onset (WASO), among children with ADHD.

Materials and methods: This cross-sectional study involved 253 children clinically diagnosed with ADHD (Mage=8.60 ± 1.31 years, 81% boys). MVPA timing was categorized as more than 8 hours before bedtime, 3–8 hours before bedtime, and less than 3 hours before bedtime. Meeting the MVPA guideline was defined as engaging in at least 60 minutes of MVPA daily. PA and sleep were recorded using an ActiGraph GT9X accelerometer for 7 consecutive days. A multivariate analysis of covariance (MANCOVA) controlling for age, sex, IQ, BMI, comorbidity, medication, and ADHD subtypes was carried out to compare the group differences in physical activity levels, timing of MVPA, and sleep parameters. Hierarchical regression models were used to examine the association of sleep parameters (i.e., SL, SE, TST, and WASO) with the timing of MVPA.

Results: Among the participants, 174 children (68.8%) met the WHO daily guideline of 60 minutes of MVPA, and, across all monitoring days, 77.94% of days met the MVPA guideline. These children had better sleep outcomes than those who did not meet the guideline, with shorter sleep latency ($F=50.98$, $\eta^2=.173$), higher sleep efficiency ($F=24.04$, $\eta^2=.090$), and less WASO ($F=17.54$, $\eta^2=.067$). Regarding PA timing, meeting the MVPA guideline and MVPA time more than 8 hours before bedtime were associated with reduced SL ($\beta=-.265$, $p=.001$), improved SE ($\beta=.268$, $p=.002$) and reduced WASO ($\beta=-.263$, $p=.002$). Conversely, MVPA time less than 3 hours before bedtime was associated with decreased SE ($\beta=-.211$, $p=.002$) and increased WASO ($\beta=.231$, $p<.001$).

Conclusions: The current study provides evidence that children with ADHD who have achieved the MVPA guideline have better sleep quality than those who have not. Attainment of the MVPA guideline and MVPA at 8 h before bedtime are associated with improved sleep. MVPA close to bedtime is related to decreased sleep efficiency and increased WASO. Future research should consider implementing PA intervention to determine the best timing of exercise for improving sleep in this clinical group.

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The Effects of Sleep Extension on Emotion Regulation Among Chronically Sleep-Restricted Young Adults: The Moderating Role of Intervention Adherence

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Introduction: Chronic sleep restriction in emerging adults is associated with altered emotion regulation (ER) including reactivity and regulatory capacity (Tomaso et al., 2021). One-week sleep extension (SE) interventions could improve affective states (e.g., increased positive emotions), but fail to alter conscious ER strategies (Parsons & Young, 2022). However, neuroimaging evidence suggests extended interventions may induce neuroplasticity: a 9-day SE protocol reduced amygdala activity and enhanced prefrontal-amygdala connectivity during rest, implicating implicit ER mechanisms (Motomura et al., 2017). Thus, the impact of over-one-week SE intervention on ER is worth further investigation, particularly for young adults, whose cognitive development is still ongoing (Benitez & Gunstad, 2012). Besides, a study found that higher adherence to a 5-week SE protocol correlates with greater sleep gains and emotional benefits (Dyk et al., 2017). This suggests that level of adherence may have a moderating effect on the impact of SE on emotions. However, there is still a gap in how adherence moderates the SE-ER relationship.

Therefore, this study aims to examine (a) how a two-week at-home SE protocol affects the ER capability of chronically sleep-restricted young adults, and (b) the extent to which adherence moderates the SE-ER relationship. It is hypothesised that: (1) the SE intervention will improve ER, and (2) greater adherence will amplify the efficacy of SE on ER.

Materials and methods: 110 participants (aged 18–29) with habitual sleep ≤ 7 hours/night) will be randomized into the SE group (n=55) and the sleep hygiene (SH) control group (n=55), after a 1-week baseline and 1-week SH education. By participating in an intervention interview, the SE group will receive a 2-week SE intervention (target: +60 mins/night). While the SH group will receive SH education only.

ER will be assessed through the Ecological Momentary Assessment (EMA): At least 3×/day prompts via PRO-Diary. The assessments involve:

1. Affective states: affective states on The Positive and Negative Affect Schedule, PANAS;
2. ER strategy use: 6 strategies (distraction, reappraisal, suppression, acceptance, avoidance, rumination) rated on 5-point Likert scales.

Adherence will be comprehensively measured based on the EMA/sleep diary completion rates, and the proportion of extended sleep, which is operationalized as $[(\text{intervention sleep duration} - \text{baseline duration})/60] \times 100\%$. Multilevel models will test whether adherence moderates the SE-ER relationship by examining the significance and directionality of the Group $\times$ Adherence interaction term.

Results: It is anticipated that the SE group will show greater improvement in adaptive strategy use (reappraisal and distraction). For the moderating role of adherence, high-adherence SE participants will exhibit more sustained emotional stability and larger ER gains than low-adherence peers.

Conclusions: This study could demonstrate the SE-ER relationship among sleep-restricted young adults. The benefits of intervention may be facilitated by personalized adherence support. The findings could inform future sleep education programs to target/find ways to increase protocol and goal adherence to facilitate behaviour change.

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The experience of poor sleep of living with HIV in Indonesia: Toward an Intervention Development

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Introduction: Poor sleep quality is a health problem primarily experienced by people living with HIV (PLHIV). The impact of poor sleep quality not only affects the HIV disease itself but also extends to many areas of life.

Objective: This study aimed to explore the experience of poor sleep quality in people living with HIV/AIDS (PLWHA) in Indonesia.

Materials and methods: The research method used was qualitative using semi-structured in-depth interviews with 12 PLHIV from a national peer support group. Approximately 60 minutes of interviews

were run through Zoom and recorded. The data was analyzed descriptively and interpretatively for 3 clusters of PLHIV that differ in the severity of sleep problems. These three clusters have been determined using an initial analysis based on Insomnia Severity Index (ISI) scores. Further data analysis was based on a hermeneutic form of PLHIV narratives

Results: three themes were developed: 1) I have a lot of things in my mind that prevent me from sleeping; 2) I would rather switch to TLD (Tenofovir Lamivudine Dolutegravir) so that I can have my sleep back; 3) When I can't sleep, I end up scrolling through my phone.

Conclusions: HIV-positive status and any HIV medication taken may affect PLHIV's sleeping pattern. However, there are many potentials to improve the sleep health of Indonesian PLHIV.

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The function and mechanism study of lncRNA LOC105**5 and its gene polymorphism on sleep fragmentation in OSA patients**

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Introduction: Obstructive sleep apnea (OSA) is characterized by sleep fragmentation and disrupted sleep-wake architecture, though its underlying mechanisms remain poorly understood. Our previous large-scale genome-wide association study (GWAS) initially identified a significant association between the single nucleotide polymorphism (SNP) rs75****65 (G>A) and increased wake bouts in OSA patients. This SNP is located within the intron of gene lncRNA LOC105****5 whose function is unknown. How lncRNA LOC105****5 regulates sleep-wake and how rs75****65 affects the sleep-wake cycle in OSA patients via lncRNA LOC105****5 are not known.

Materials and methods: Materials: The GWAS analysis included 5208 patients with OSA diagnosed by standardized polysomnography (PSG) and 753 controls (AHI<5 beats/hour) selected from the Shanghai Sleep Health Study (SSHS) cohort, which provided genotypic and PSG-confirmed OSA phenotypes. Methods: QPCR, FISH, Western blot, RNA affinity chromatography, RIP, RNA Scope and other molecular technologies; AAV infection technology and CRISPR/Cas9 gene-editing technology; protein mass spectrometry, RNA sequencing and other multi-omics technologies; mouse brain stereotactic injection, EEG/EMG polysomnography monitoring technology, open field test (OFT), object recognition test (ORT) and patch clamp technique.

Results: lncRNA LOC105****5 exhibited high expression level in human central nervous system and base substitution of rs75****65, which was significantly associated with sleep fragmentation in our GWAS on OSA, markedly reduced its expression in cells. In mice, lncRNA LOC105****5 overexpression in nucleus accumbens (NAc) significantly reduced sleep-wake transitions and prolonged bout duration of each cycle. Further, integrated multi-omics approaches revealed a conserved GPCR as the downstream target of lncRNA LOC105****5. Neuronal conditional knockout of this GPCR recapitulated the LOC105****5 overexpression phenotype by reducing sleep-wake fragmentation. Moreover, mechanistic studies revealed that lncRNA-GPCR axis functions by affecting the neuronal excitability of NAc neurons.

Conclusions: Our study demonstrates that lncRNA LOC105****5 reduces sleep fragmentation in mice by affecting the excitability of NAc neurons, mediated through downregulation of a target GPCR. Additionally, the SNP rs75****65 may contribute to impaired sleep quality in OSA patients by suppressing the lncRNA LOC105****5 expression. These findings advance the physiological understanding of sleep regulation and highlight potential therapeutic targets for treating sleep fragmentation in OSA.

The impact of ambient temperature on sleep duration: findings from GRAPHS cohort

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Introduction: Higher environmental temperatures have been associated with poorer sleep outcomes. However, the impact of temperature on objective sleep metrics has been difficult to isolate due to the widespread use of temperature-modifying technologies such as heating and cooling systems. This study investigates the association between personal ambient temperature and actigraphic sleep duration in a pre-existing Ghana Randomized Air Pollution and Health Study (GRAPHS) cohort of post-partum women in the Kintampo North Municipality and Kintampo South District of Ghana, where such technologies are limited. Kintampo lies at a latitude of 8.1 degrees north of the equator and has a tropical climate with relatively stable temperatures year-round and distinct wet and dry seasons, rather than large seasonal variations in temperature or light duration. We hypothesize that higher personal ambient temperature is associated with decreased actigraphic sleep duration.

Materials and methods: The GRAPHS study enrolled pregnant women from 2013 to 2016. At 4- and 8-years post-partum, participants wore RTI MicroPEM V3.2 monitors over a 48-hour period, capturing personal ambient temperature, relative humidity, and fine particulate matter (PM_{2.5}) concentrations. Simultaneously, participants wore MicroMotionlogger actigraphy devices which recorded multi-night measures of sleep including total sleep time (TST), time in bed (TIB), wake after sleep onset (WASO), sleep efficiency, and number of nighttime awakenings. Sleep intervals were visually identified and scored using the Cole-Kripke algorithm. Linear regression models adjusting for age, BMI, and household size were used to assess associations between personal ambient temperature and sleep outcomes.

Results: A total of 115 participants, with a mean age of 34.5 ± 7.2 years and BMI of 24.0 ± 4.1 kg/m², contributed an average of 3.1 ± 2.0 nights of actigraphy data. The mean personal ambient temperature was 35.6 ± 2.0 °C and ranged between 28.6 – 42.9 °C. Average TST was 6.1 ± 1.2 hours, TIB was 7.6 ± 1.3 hours, WASO was 74.7 ± 36.9 minutes, sleep efficiency was $80.4 \pm 7.9\%$, and participants experienced an average of 19.1 ± 6.9 nighttime awakenings. Adjusted linear regression models showed that each 1 °C increase in ambient temperature was associated with reductions of TST by 12.2 ± 3.3 minutes ($p=0.007$) and TIB by 11.6 ± 3.5 minutes ($p=0.005$). No significant associations were identified between average ambient temperature and sleep efficiency, WASO, or number of nighttime awakenings.

Conclusions: In a tropical, rural Ghanaian setting with limited access to temperature-modifying technologies, higher personal ambient temperatures were significantly associated with reductions in objective total sleep time, time in bed, and sleep onset latency. These findings confirm our hypothesis and underscore that even modest heat elevations can materially erode sleep time. This effect may reflect the disruption of thermoregulatory processes essential to initiating and maintaining sleep. Given that shorter sleep duration has been linked to increased cardiovascular and metabolic health risks, our findings highlight the importance of addressing global warming as a public health priority. As global temperatures rise, interventions to improve thermal environments may be critical to safeguard sleep health and mitigate associated health disparities.

The impact of comorbid insomnia and sleep apnea (COMISA) on work ability: Results from population-based panel data in Korea

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Introduction: Comorbid insomnia and sleep apnea (COMISA), represents a unique clinical phenotype associated with greater functional impairment than either condition alone. Despite growing interest,

the impact of COMISA on occupational functioning, particularly work ability (WA), remains understudied. This study aimed to evaluate the effects of COMISA on WA in the Korean working population using longitudinal panel data.

Materials and methods: Data were obtained from the Korean Work, Sleep, and Health Study, a population-based panel survey conducted between July 2022 and September 2024, including 10,086 wage-earning participants aged 19–70 years. COMISA was defined as the concurrent presence of high-risk sleep apnea (identified via the Berlin Questionnaire) and nocturnal insomnia symptoms (assessed using the Insomnia Severity Index). WA was assessed using the validated Korean version of the Work Ability Index (WAI). WA scores below 28 points were classified as “poor.” Generalized estimating equation models were used to assess associations between sleep disorder groups and WA, adjusting for age, gender, and occupation. Subgroup analyses were conducted by sex, age, occupational group, and shift work status.

Results: Participants with COMISA had markedly lower WA than those without sleep disorders. In fully adjusted models, the odds ratio (OR) for poor WA in the COMISA group was 5.742 (95% confidence interval [CI]: 4.715–6.993) compared to the normal group. The mean WAI score in the COMISA group was 4.377 points lower (95% CI: –4.593 to –4.161) than in the normal group. Individuals with insomnia and low-risk sleep apnea showed increased odds of poor WA (OR = 4.461; 95% CI: 3.598–5.531), although the association was weaker than that observed for COMISA. In contrast, isolated high-risk sleep apnea without insomnia demonstrated a limited association with reduced WA (OR = 1.145; 95% CI: 0.784–1.673). Significant associations between COMISA and poor WA were observed across all subgroups defined by sex, age, occupation, and shift work status, with stronger associations among men, white-collar workers, daytime workers, and individuals under 60 years of age.

Conclusions: COMISA is strongly associated with decreased WA among Korean workers, with certain populations demonstrating heightened vulnerability. These findings underscore the need for targeted workplace strategies and clinical interventions, such as routine screening, flexible work schedules for treatment and integrated treatment approaches that address both insomnia and sleep apnea.

Addressing COMISA may help mitigate productivity loss and promote workforce sustainability.

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The Impact of Problematic Smartphone Use on Sleep Duration and Quality

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Introduction: This systematic review and meta-analysis seek to comprehensively elucidate the impact of problematic smartphone use (PSU) on both sleep duration and sleep quality. This study aims to address existing research gaps, as prior studies have predominantly focused on either duration or quality in isolation.

Materials and methods: In accordance with PRISMA 2020 guidelines, a comprehensive search of 10 electronic databases, including PubMed and Embase, was conducted from their inception through August 20, 2024. Studies providing quantitative data on the effects of PSU on sleep duration and sleep quality were subjected to meta-analysis using Review Manager 5.4, while studies without specific effect sizes underwent descriptive analysis.

Results: A total of 28 studies published between 2015 and 2024 were included, involving 46,603 participants aged 13 to 41 years from countries such as Australia, Germany, China, Brazil, and Malaysia. The r/ρ subgroups were chosen to present the findings. The meta-analysis showed that PSU was slightly but significantly negatively associated with long sleep duration (SMD = -0.13, $p < 0.00001$, $I^2 = 23\%$), while no significant association was found with short sleep duration ($p > 0.05$). In contrast, PSU was moderately positively associated with poor sleep quality (SMD = 0.22, $p < 0.00001$, $I^2 = 42\%$) and significantly negatively associated with good sleep quality (SMD = -0.19, $p < 0.00001$, $I^2 = 50\%$).

Conclusions: This review underscores the adverse effects of problematic smartphone use, particularly its negative impact on sleep quality. While the effect on sleep duration appears small or non-significant, PSU can exacerbate other health issues such as depression, anxiety, cognitive impairment, and poor academic performance. These findings highlight the need for strategies aimed at mitigating PSU to promote healthier sleep patterns and overall well-being.

The impact of shift work and clinical paramedic scenarios on paramedics' sleepiness, fatigue and perceived workload: A novel simulation-based study

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Introduction: Most paramedics work on a rotating shift schedule involving a combination of day and night shifts. Despite the known impact of shift work on sleep loss, and resultant performance and physiological impairments, few studies have examined the impact of rotating shift work on paramedics. The current study uses a simulated work rotation to explore the impact of rotating shift work and clinical work on paramedics' sleepiness, fatigue and perceived workload.

Materials and methods: In pairs, Australian paramedics complete a two 12-hour day shift, two 12-hour night shift simulated work rotation. Participants have an 8-hour sleep opportunity prior to the first day shift and between each subsequent shift. All sleep opportunities during the rotation occur in the Monash Sleep and Circadian Medicine Laboratory and are monitored with polysomnography. Simulated paramedic shifts take place in the Monash Paramedic Simulation Centre, where participants engage in four high-fidelity immersive paramedic clinical scenarios throughout each shift. Before and after each paramedic scenario, participants complete subjective assessments that monitor sleepiness (Karolinska Sleepiness Scale, KSS) and fatigue (Samn-Perelli fatigue Scale, SPS). After each scenario they also complete a multidimensional measure of perceived workload (NASA Task Load Index, NASA-TLX). Between scenarios, participants complete two cognitive and decision-making batteries per shift. Data was analysed via linear mixed models to compare within and between shift changes for participants.

Results: A total of 16 participants (69% female, mean age = 33.7 ± 8.0 years) have completed the simulated shift work rotation. Mean KSS scores increased between the first day shift (3.75) and the first (4.2, $p < 0.1$) and second night shifts (4.75, $p < 0.05$). Mean KSS scores also increased as the shifts progressed, increasing from 3.36 for the first clinical scenario of the shift to 4.32 ($p < 0.001$) for the third scenario and 4.94 ($p < 0.001$) for the last scenario. SPS values followed a similar trend to the KSS, with mean SPS values increasing from the first day shift to the last night shift (3.04 to 3.75, $p < 0.001$) and from the first scenario of the shift (2.66) to the third (3.34, $p < 0.001$) and fourth scenarios (3.95, $p < 0.001$). When NASA-TLX scores were deconstructed by subdimension, participants reported an increase in perceived physical demands between shifts, from 6.31 on the first day shift to 8.36 ($p < 0.01$), 8.34 ($p < 0.01$) and 8.29 ($p < 0.05$) on day shift two, night one and night two, respectively. Despite the increase in sleepiness, fatigue and physical demand, participants reported no change between or within shifts in any other subdimension or mean overall workload on the NASA-TLX.

Conclusions: This study is the first of its kind to examine the impact of a multi-day simulated shift work rotation on paramedics. Preliminary findings demonstrate that while participants experienced increased sleepiness, fatigue and physical demands throughout the rotation, their perception of overall workload did not significantly change. These findings provide valuable insight into the compensatory mechanisms present in populations regularly engaging in shift work and performing clinical work.

The Impact of Sleep Deprivation on Mental and Physical Functioning Among Medical Students: A Mixed-Methods Study

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Introduction: Current research indicates that sleep deprivation induces significant neurocognitive impairments in healthy adults, including impaired synaptic plasticity, reduced brain volume, disrupted memory consolidation, and decreased alertness. Medical students typically experience shorter sleep duration and irregular sleep pattern, due to high-intensity academic tasks and clinical workload. This study aimed to assess the impact of sleep deprivation on mental and physical functioning as well as the daily life, among the medical students.

Materials and methods: This sequential explanatory mixed-methods study received ethical approval from the Ethics Committee of GPHCM (No. YE2022-266). All participants provided written informed consent prior to the enrolment. Phase 1 was a quantitative survey of medical students aged 18-26

years, interning in Guangzhou with self-reported average sleep duration ≤ 7 hours/night over the past week. Participants completed the Profile of Mood States (POMS), Epworth Sleepiness Scale (ESS), and Psychomotor Vigilance Task (PVT) to assess their emotional states, daytime sleepiness, and cognitive performance (reaction time, vigilance, and sustained attention). Based on the pilot study indicating cognitive impairment (defined as >10 PVT lapses) in 10% of participants, a sample size of 35 was expected. Phase 2 was a semi-structured qualitative interview, recruiting participants from the Phase 1, aiming at supplementing the quantitative findings. Data were analysed using statistics, thematic analysis, and triangulation validation between the quantitative and qualitative results.

Results: Quantitative analyses showed a significant negative correlation between sleep duration and PVT lapses ($p < 0.05$), indicating vigilance declined with reduced sleep duration. While sleep duration correlated negatively with PVT response speed, this relationship was not statistically significant ($p > 0.05$). Sex, body mass index, menstrual period, medical school and caffeinated beverages consumed did not significantly affected the PVT performance, POMS scores, or ESS scores ($p > 0.05$ for all).

Qualitative data revealed that all interviewees subjectively perceived sleep deprivation as negatively affecting their next-day work and study performance, including cognitive deficits, emotional instability, and uncomfortable physical symptoms. Common manifestations included reduced attention and psychomotor slowing (consistent with PVT results), alongside with impaired short-term memory, fatigue, and headaches, which was beyond the quantitative findings. Subgroup-analysis suggested that participants with mild sleep deprivation (6–6.5 hours/night) experienced appetite suppression and chest tightness, whereas severe deprivation (4–5 hours/night) had complaints about severe fatigue, excessive daytime sleepiness, memory impairment, and hyperarousal.

Conclusions: Even short-term sleep deprivation impairs brain functioning, causes discomfort and disrupts daily life in medical students. These findings underscore the urgent need to develop targeted healthcare interventions for medical students to mitigate these adverse effects, which may include sleep hygiene education, workload adjustments, and psychological support services.

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The impact of urban transportation noise and bedroom temperatures on sleep quality during summertime

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Introduction: Heatwaves pose increasing risks to sleep health (Chevance et al., 2024), particularly in un-airconditioned apartments where high nighttime temperatures impair rest and thermal comfort. Equally, transportation noise, especially from road traffic, has been linked to sleep fragmentation and reduced sleep quality (Smith et al., 2022), yet its role in moderating heat-related sleep disturbances is not clear. This study integrated Department for Environment, Food and Rural Affairs strategic noise-map data (DEFRA, 2022) with continuous bedroom temperature logs and daily sleep-quality ratings, to understand whether road and rail noise independently predict the change in sleep quality experienced during UK summertime.

Materials and methods: The UK Home Heat Health project monitored bedroom climate and sleep in 123 healthy adults (mean age 35 years, 82 female) residing in un-airconditioned London apartments during June–September 2023–2024 (Lomas et al., 2024). Participants wore CamnTech actigraphs and completed a Consensus Sleep Diary with 10-point ratings of sleep quality, thermal comfort and heat-related sleep disturbance each day. Bedroom temperature was logged every 30 minutes via temperature sensors.

External night-time noise (11 pm–7 am) for road and rail sources was extracted from DEFRA strategic noise maps (35 dB cutoff), categorised in 5 dB bands (reference < 35 dB). Noise levels are modelled on a 10-metre grid at a receptor height of 4m above ground. Each participant apartment was assigned a

road noise level and rail noise level matching the exact location to the noise maps.

Analysis:

A multiple linear regression modelled change in sleep quality scores (baseline – hot spell night) as a function of maximum bedroom temperature, road- and rail-noise, controlling for age and sex. A total of 119 participants with complete data and noise mapping were included in the analysis.

Results: A multiple regression was conducted to predict the change in sleep-quality score (baseline minus hot-spell night) from maximum bedroom temperature, road-noise bands, rail-noise bands, age group, and sex. The overall model approached significance, $F(14, 104) = 1.75$, $p = .057$, and accounted for 19.0 % of the variance in sleep-quality change ($R^2 = .190$; adjusted $R^2 = .081$).

Examination of individual predictors showed that higher maximum bedroom temperature was associated with greater change in sleep quality, ($p = .042$). Among noise predictors, only the 65–70 dB road noise band significantly predicted change in sleep quality versus < 35 dB, ($p = .005$). No other road- or rail-noise bands, age, or sex reached significance ($p > .05$).

Conclusions: Although the model was only marginally significant, results indicate at possible interactive effects of overnight heat and traffic noise on sleep quality. These preliminary findings, based on noise-map estimates rather than direct measurements, highlight the importance of further research to clarify how thermal and acoustic stressors jointly influence sleep health in the context of urban apartments. Future studies should integrate primary noise monitoring, ventilation behaviour logs, and indoor climate data to explore these dynamics in depth.

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The Influence of Sleep Position and Pillow Height on Sleep Quality in Patients

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Introduction: Sleep quality is an essential determinant of overall health, with sleep position and pillow height serving crucial functions in ensuring adequate spinal alignment and comfort during sleep. Inadequate alignment resulting from improper pillow height or less than ideal sleep positions may lead to musculoskeletal discomfort, disturbances in sleep patterns, and the aggravation of conditions such as sleep apnea and gastroesophageal reflux disease. The objective of this research is to assess the interactive influences of sleep position and pillow height on the quality of sleep among patients, emphasizing aspects such as physiological alignment, comfort, and subjective sleep experiences.

Materials and methods: A cross-sectional analysis was conducted involving adult participants who were assessed under various pillow heights and sleep positions. Objective measures included cervical spine alignment, head-neck pressure distribution, and muscle activity, while subjective comfort and sleep quality were evaluated using validated questionnaires. Participants experienced different pillow types and heights in both supine and side-lying positions.

Results: The experiment involved participants lying in a supine position and supine position for a duration of 10 minutes under same pillow conditions. Data analysis was performed using one-way repeated measures analysis of variance (ANOVA), with a significance threshold established at $p < 0.05$. Optimal pillow height was found to maintain the natural curvature of the cervical spine, reduce muscle activity in the neck, and improve pressure distribution, thus enhancing comfort and reducing morning stiffness. Research indicates that side and back sleeping positions, when accompanied by suitable pillow support, enhance spinal alignment and alleviate symptoms associated with sleep apnea and discomfort, in contrast to stomach sleeping or the use of inappropriate pillow heights. Hybrid pillows that incorporate supportive cores and possess sufficient fluffiness have been found to provide the greatest levels of subjective comfort and promote optimal cervical alignment.

Conclusions: The position in which one sleeps, as well as the height of the pillow used, are critical factors influencing sleep quality among patients. It is advisable to select pillow height based on individual preferences for sleep position in order to enhance spinal alignment, reduce discomfort, and facilitate restorative sleep. These results highlight the significance of ergonomic factors in sleep settings as a means to improve patient outcomes.

Acknowledgments: Keywords: Sleep, pillow heights, Sleep quality, Sleep position. Thanks supported by Kaohsiung Armed Forces General Hospital and series sleep study project.

The life style, sleep time and sleep duration of the people in different social stratus during previous four decades in Taiwan

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Introduction: Nearly half of adults report poor sleep quality, though most do not meet diagnostic criteria for insomnia. The concept of “poor sleep” has been introduced to describe insufficiently restorative sleep or reduced satisfaction in the absence of a clinical disorder ([Leger et al.](#)). Risk factors include unmodifiable characteristics such as age and sex, as well as modifiable contributors like lifestyle and sleep habits.

We hypothesize that demographic and lifestyle factors influence self-reported sleep quality. This study aims (1) to summarize sleep epidemiology with respect to quality, duration, and time, and (2) to examine associations between sleep quality and demographic and lifestyle factors, including age, sex, social stratum, sleep time and duration, and habitual inactivity.

Materials and methods: The Taiwan Social Change Survey (TSCS) can be accessed on the Survey Research Database organized by the Institute of Sociology and the Center for Survey Research of the Academia Sinica in Taiwan ([Taiwan Social Change Survey](#)). It provides cross-sectional and panel study data that reveals Taiwan's economic, social, and cultural changes from 1984 till today.

Eight features were included in the analysis: year of survey, gender, age, social stratum, habitual inactivity, sleep time, sleep duration and sleep quality. The surveys spanned 1984–2022 and involved participants aged 19–97 (mean 44.3) years. Social stratum was classified into six levels, from core cities to less-developed towns. Habitual inactivity was categorized into four levels: often, sometimes, rarely, and never. Sleep time was grouped into four categories: (1) 18:00–22:00 (earlier–early), (2) 22:00–24:00 (later–early), (3) 00:00–02:00 (earlier–late), and (4) 02:00–05:00 (later–late). Sleep quality was defined by frequency of sleep loss (never, rarely, sometimes, often). After data cleaning, 30,902 records remained for analysis. Chi-square tests and ordinal logistic regression were applied to identify risk factors.

Results: Overall, $9.2 \pm 3\%$ of participants reported often experiencing poor sleep quality. Social stratum was excluded after chi-square test ($p > 0.10$). Female gender emerged as the strongest predictor (odds ratio [OR] = 1.39, $p = 0.031$), followed by habitual inactivity (OR = 0.91, $p = 0.045$). Later sleep time (OR = 1.19, $p = 0.36$) and shorter sleep duration (OR = 0.90, $p = 0.60$) showed nonsignificant associations, with fluctuating p-values among different years. Epidemiology demonstrates that earlier sleep time exhibits longer sleep duration. Age was not a significant factor; although prevalence of poor sleep was higher in individuals aged ≥ 70 years (7.8%), prior literature suggests this is more attributable to inactivity, limited social engagement, and comorbid conditions rather than aging itself ([Ohayon et al.](#)).

Conclusions:

1. Females are more likely to experience poor sleep.
2. Habitual inactivity is associated with poor sleep.
3. Good sleep quality may still be achievable with late sleep time or short sleep duration, awaiting further validation.

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The lived experience of sleep disorders: patient perspectives and priorities

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Introduction: Sleep disorders have a significant impact on quality of life for millions of people, but the perspectives and priorities of people with lived experience of sleep disorders are not well understood. Understanding the impact of sleep disorders from the perspectives of people with lived experience is important for clinical care and research. This research project explores the impact of sleep disorders on quality of life, capturing the voices of people with lived experience of sleep disorders. Better understanding the lived experience is essential to ensure patient perspectives can help inform advocacy, education, research, policy and practice.

Materials and methods: In this qualitative research project, members of a lived experience advisory group were invited to answer four questions regarding their sleep disorder and treatment journey. This research includes the stories of 11 people with a broad range of sleep disorders (6 females and 5 males, aged between 27-72 years). Thematic analysis was used to look for patterns and themes in the data.

Results: Three different themes were identified in the data. Firstly, the personal impact of sleep disorders, including impacts on physical and mental health, relationships and productivity. Secondly, health system impacts including the long journey to treatment, which was often self-initiated and with many different health professionals. Thirdly, societal impacts including the low priority of sleep, public unawareness and sleep disorders are often overlooked. These themes all interact to make it difficult for people with sleep disorders to seek help and navigate complex treatment pathways.

Conclusions: This project provides valuable insight to understand the lived experience and impact of sleep disorders on quality of life. These impacts make it more difficult for people to navigate the challenges and barriers associated with diagnosis and treatment of sleep disorders. By investigating the personal impacts of sleep disorders, we can inform public health and advocacy messaging to create messages that are meaningful to people with sleep disorders. We can also improve education of health professionals by incorporating patient voices and perspectives into training programmes. Lived experience can also help inform research into treatment options and pathways, to ensure treatments are affordable, accessible and easy to navigate. This work highlights the importance of working with people with lived experience for advocacy, and collaboration and co-design in academic research.

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The longitudinal mediating role of sleep in the bidirectional relationship between depression and functional disability among older adults: A systematic review and conceptual framework

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Introduction: The increasing prevalence of depression and functional disability in older adults highlights the need for targeted interventions. Sleep, as a potentially modifiable factor, holds promise in addressing these challenges. Given that sleep health provides clues for understanding the potential causes that could mitigate the negative effects of depression and functional disability, a better understanding of the relationship between sleep, depression, and functional disability is crucial for crafting effective preventive strategies and personalized interventions for older adults.

Materials and methods: This review and conceptual framework aimed to examine the pairwise bidirectional associations between sleep, depression, and functional disability and identify the longitudinal mediating role of sleep in the bidirectional relationship between depression and functional disability in older adults. The academic databases PsycArticles, PubMed, MEDLINE, Science Citation Index, Social Sciences Citation Index, ProQuest Dissertations and Theses Global, Cochrane, and Scopus were searched for research published in English between January 2000 and June 2024. Systematic review and cohort study designs were eligible. All included studies were assessed for quality using the Critical Appraisal Skill Programme checklist (CASP 2024). A narrative synthesis approach will be applied to integrate the findings, including an analysis of variability in terms of setting, population, exposure/ intervention, and outcomes.

Results: 397,289 citations were identified, and 82 studies meeting the inclusion criteria were included. Cohort studies and reviews provide evidence that there is a dynamic reciprocal correlation between sleep, depression, and functional disability in the older population. The research identifies reciprocal

causal pathways—depression exacerbates functional disability through unhealthy sleep, while functional disability worsens depression via unhealthy sleep—highlighting a vicious cycle that accelerates health decline in aging populations. Sleep longitudinally mediates the bidirectional relationship between depression and functional disability in older adults, acting both as a result and a driver in this dynamic interplay. The proposed framework prioritizes sleep health as a modifiable target for breaking the depression-functional disability cycle, offering actionable strategies to mitigate adverse outcomes in older adults.

Conclusions: This review and conceptual framework highlight that sleep health can provide crucial insights for mitigating the adverse effects experienced by older adults due to depression and functional disability. For healthcare professionals and policymakers, it provides evidence about prioritizing sleep health as an accessible step to foster a healthy lifestyle.

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The overlooked trio: sleep duration, sampling time and physical exercise alter levels of olink-assessed blood biomarkers of cardiovascular risk

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Introduction: Biomarker profiling from biofluids such as blood are widely measured in clinical research, using for example Olink proteomics panels. One such research focus area is cardiovascular disease (CVD), for which chronic sleep restriction (SR) is a risk factor. However, it remains unclear whether blood levels of commonly measured CVD biomarkers are sensitive to acute dynamic factors such as SR, physical exercise (PEX), and time of day.

Materials and methods: 16 normal-weight, healthy men participated in a crossover design in which they underwent three highly standardized in-lab nights of sleep restriction (SR, 4.25 h/night) and normal sleep (NS, 8.5 h/night) in randomized order. Blood samples were collected in the morning, evening, and immediately before and repeatedly after 30 min of high-intensity exercise, with 88 cardiovascular disease protein biomarkers quantified using Olink technology and selected validation by ELISA.

Results: Significant time-of-day-dependent changes in several CVD biomarkers were identified. Whereas several proteins were exercise-induced across sleep conditions (such as the canonical exerkines IL-6 and BDNF), exercise-induced proteomic dynamics differed in response to recurrent SR, compared with following NS. Moreover, SR compared with NS resulted in a biomarker profile previously associated with increased prospective risk of several CVDs across large-scale cohorts (such as higher circulating levels of IL-27 and LGALS9).

Conclusions: Our findings highlight how dynamic physiology can modulate CVD biomarker levels. These results also underscore the need to consider sleep duration as a key determinant of cardiovascular health—an emphasis reflected in recent American Heart Association guidelines. Further studies in women, older individuals, and patients with prior CVD, and across different chronotypes and dietary schedules are warranted.

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The Relationship between Digital Emotion Regulation and Bedtime Procrastination

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Introduction: Bedtime procrastination (BP) is defined as going to bed later than intended without having external reasons for doing so. BP has been shown to function as an emotional regulation strategy for many individuals. This study explores bedtime procrastination based on James Gross's Process Model of Emotion Regulation, proposing that the phenomenon represents a nuanced, often maladaptive, strategy to manage pre-sleep emotional states. We hypothesize that individuals engage in bedtime procrastination by implicitly or explicitly employing various regulation strategies: situation selection/modification, attentional deployment, and cognitive change. This framework allows for a deeper understanding of the underlying psychological mechanisms driving the delay of sleep.

Materials and methods: A total of 22 young adults with high levels of BP (scores of 33 or higher) participated in the study. Bedtime procrastination, Process Model of Emotion Regulation Questionnaire (PMERQ) and a 7-day sleep diary were assessed using self-report questionnaires. The PMERQ is a 45-item instrument assessing ten emotion regulation strategies across Gross's five-stage process model, with each strategy categorized as engagement- or disengagement-focused. To examine the relationship between BP and Gross's process model of emotion regulation, a nonparametric Spearman correlation analysis was conducted.

Results: Participants (mean age 21.95 ± 2.1 , 86.4% female) were mostly university students (77.3%). Participants showed a mean sleep onset latency of 11.1 minutes ($SD=7.11$), total sleep time of 397.8 minutes ($SD=52.6$), bedtime procrastination of 86.6 minutes ($SD=41.7$), and spent an average of 93.5 minutes ($SD=39.2$) using their phones within the 3 hours before bedtime. Correlation analyses were conducted to examine the associations between BP and items from the PMERQ. BP was positively correlated with the situation selection subscale of the PMERQ ($r = .457, p < .05$) and was particularly associated with the disengagement strategy within the situation selection domain ($r = .449, p < .01$). BP also showed a significant positive correlation with PMERQ item 26 ("negotiating to resolve conflict") ($r = .443, p < .01$).

Conclusions: BP was significantly associated with both engagement and disengagement items of situation modification, as well as with the situation selection subscale. Intentionally postponing bedtime could be interpreted as a strategy to exert control over the environment to reduce emotional burden or stabilize emotions. According to Gross's process model of emotion regulation, BP may particularly reflect early-stage regulation strategies such as situation selection and situation modification. This conceptualization highlights bedtime procrastination not merely as a failure of self-regulation, but also a complex interplay of emotional regulation attempts.

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The role of physical activity in modulating weekday and weekend sleep duration among patients with newly diagnosed type 2 diabetes

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Introduction: Sleep duration is a modifiable health factor closely linked to both physical and metabolic well-being. Its integration into chronic disease management has received increasing attention. However, the interplay between physical activity (PA), sedentary behavior, and sleep duration remains underexplored, particularly in individuals with newly diagnosed type 2 diabetes mellitus (T2DM).

Materials and methods: The current study investigated patterns of PA, sedentary behavior, and self-reported sleep duration on weekdays and weekends in patients with newly diagnosed T2DM. Participants were categorized into low, moderate, and high PA groups based on the International Physical Activity Questionnaire. Clinical, behavioral, and demographic data were collected and analyzed. Group comparisons and generalized linear models were used to examine the potential role of PA in modulating weekday and weekend sleep durations.

Results: A total of 340 participants (mean age 43.4 ± 10.2 years) were recruited from the endocrinology clinic of The Affiliated Hospital of Hangzhou Normal University. All patients were enrolled at the time of diagnosis and had not yet initiated hypoglycemic therapy. At baseline, the mean fasting plasma glucose was 9.19 ± 4.06 mmol/L, mean HbA1c was $8.51 \pm 2.60\%$, and the mean 2-hour postprandial glucose was 14.82 ± 7.86 mmol/L. Regarding sleep health, the average weekday sleep duration was 6.73 ± 0.81 hours, while weekend sleep duration averaged 7.39 ± 1.08 hours. Based on total weekly MET-minutes, 21.2% of participants were classified as having low PA, 49.7% as moderate PA, and 29.1% as high PA. To explore associations, our simple group comparisons revealed that participants in the high PA group had significantly longer sleep durations on both weekdays and weekends compared to those in the low PA group ($p < 0.01$). Furthermore, linear regression analysis showed that higher total PA ($B = 0.00003$, $p < 0.001$) and vigorous PA ($B = 0.000013$, $p < 0.001$) were independently associated with longer weekday sleep duration. In contrast, higher fasting plasma glucose was significantly associated with shorter weekday sleep ($B = -0.066$, $p = 0.011$). Notably, these associations were not observed when weekend sleep duration was used as the dependent variable.

Conclusions: In patients with newly diagnosed T2DM, insufficient physical activity is linked to reduced weekday sleep duration. These findings highlight the importance of incorporating sleep management and promoting physical activity into early lifestyle interventions for diabetes care.

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The Role of Sleep Health in Glycemic Regulation Among Non-Diabetic Pregnant Women

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Introduction: Sleep plays a critical role in glucose metabolism during pregnancy, yet most prior research has focused on non-pregnant adults. Recent studies link sleep disturbances to increased risk of gestational diabetes, poor cardiometabolic health, and other complications, but often examine isolated aspects such as sleep quality or timing. Sleep health is a multidimensional construct, including quality, duration, efficiency, timing, and regularity, offers a more comprehensive understanding of sleep's impact on metabolic outcomes. This approach remains underexplored in pregnant populations,

particularly African American pregnant women (AAPW), who experience both sleep disparities and glycemic dysregulation. This study investigates between-person and within-person associations between sleep health and glycemic outcomes in non-diabetic AAPW.

Materials and methods: Data from 55 non-diabetic AAPW enrolled in the BETTER lifestyle counseling study (NCT05234125) were analyzed. Sleep health was assessed using the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, and 7-day Fitbit-derived measures for sleep duration, efficiency, timing (sleep midpoint), and regularity (standard deviation of sleep midpoint). Glycemic outcomes were assessed through 7-day continuous glucose monitoring (mean glucose, SD, mean amplitude of glycemic excursions (MAGE), and coefficient of variation (%CV). Between-person associations were examined using multivariable regression, while within-person temporal associations were tested using mixed-effects models with day-level sleep and glucose data. All models were adjusted for maternal age, gestational age, BMI, average daily steps, and education.

Results: The analytic sample included 55 non-diabetic AAPW (mean age= 29.6 ± 5.5 years; gestational age= 17.7 ± 2.7 weeks; BMI= 33.2 ± 5.1 kg/m²). Among between-person associations, poorer sleep quality was significantly associated with greater glycemic variability. Specifically, higher PSQI scores were linked to higher glucose SD ($\beta = 0.42$, $p = 0.011$), %CV ($\beta = 0.44$, $p = 0.005$), and MAGE ($\beta = 1.10$, $p = 0.003$). For temporal (within-person) associations, daily sleep dimensions were lagged by one day to predict next-day glucose outcomes. Analyses included 51 participants with ≥ 3 days of matched sleep and CGM data; 4 were excluded due to insufficient data. In these models, higher sleep efficiency was associated with higher mean glucose the following day ($\beta = 0.22$, $p = 0.029$). This finding may reflect complex or bidirectional interactions between sleep and glucose metabolism during pregnancy on daily level. Notably, the sample exhibited high average sleep efficiency (mean= $88.8\% \pm 3.4$) with low within-person variability, which may limit the ability to detect typical temporal associations. No other sleep health dimensions were significantly associated with glycemic outcomes in either between-person or within-person models. Other Continuous Glucose Monitoring Metrics (e.g., Time-in-Range, Time-Below-Range and Time-Above-Range) were not significantly predicted by any of the sleep dimensions.

Conclusions: These findings highlight the importance of sleep health in glycemic regulation during pregnancy. Poorer sleep quality was associated with greater glycemic variability between individuals. Unexpectedly, higher daily sleep efficiency predicted higher next-day glucose levels within individuals. This may be influenced by the overall high sleep efficiency and low night-to-night variation observed in the sample. Together, these results suggest that both stable sleep patterns and night-to-night variations may influence glucose regulation in non-diabetic AAPW. Further research is needed to clarify these relationships.

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Time-Frequency Representation Learning Based on PPG Signals for Sleep Staging

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Introduction: Sleep health is closely related to a range of chronic diseases, which has led to increased public awareness and the rapid development of consumer-grade sleep monitoring devices. At present, most wearable devices leverage photoplethysmography (PPG) signals in combination with accelerometer data to analyze sleep stages. However, existing PPG-based sleep staging methods suffer from two main limitations: a heavy reliance on manual feature engineering and the necessity of large-scale electrocardiogram data for pre-training. These limitations hinder the model's generalization ability and its practical applicability.

Materials and methods: This study introduces a U-shaped sleep staging framework based on PPG signals, which combines time-frequency domain transformation with sequential feature extraction to enhance the time-frequency representation capability of PPG signals. The model integrates convolutional neural networks with a symmetric connection mechanism, enabling effective local feature extraction while enhancing time series modeling capabilities, thus improving classification accuracy.

To preprocess the PPG signals, an 8th-order Chebyshev Type II filter was applied with a cutoff frequency of 8 Hz. This filtering step removed high-frequency noise while preserving low-frequency information, such as heart rate and blood flow, which are relevant to sleep stage classification. Subsequently, the filtered signals were downsampled to 32 Hz, a frequency selected to retain key physiological characteristics such as heart rate variability and respiration-related frequencies, while also reducing data volume.

The experimental data were collected from the Interdisciplinary Sleep Medicine Center at Charité – Universitätsmedizin Berlin, including fingertip pulse oximeter PPG signals from 42 healthy participants (average age 37.5 ± 14.5 years). The dataset comprises 120 sleep recordings, with each participant contributing data from at least two nights. The study systematically assessed the impact of input sequence length on model performance and employed various cross-validation strategies, including random 10-fold cross-validation, leave-subjects-out, and leave-one-night-out, to evaluate the model's stability and generalization performance across different data splits.

Results: The model demonstrated optimal performance in classifying the four sleep stages—Wake, Light sleep, Deep sleep, and REM sleep—with an F1-score of 0.76 ± 0.03 and a Kappa coefficient of 0.69 ± 0.02 . Mann-Whitney U tests revealed no significant differences between the various cross-validation strategies ($p > 0.05$), indicating good stability of the model. As the number of input epochs increased (1, 8, 32, 64, 128, 256), the Kappa values for 10-fold cross-validation were 0.57, 0.61, 0.62, 0.62, 0.65, and 0.68, respectively.

Conclusions: The time-frequency representation learning method based on PPG signals proposed in this study effectively distinguishes between the four sleep stages, with model performance improving as the input segment length increases. This suggests that the model can effectively capture long-term dependencies in PPG data. The results highlight the potential of using PPG signals for sleep stage recognition, offering a low-cost, non-invasive, and intelligent solution for home sleep monitoring.

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Timing Matters: Differential Associations of Pre-Bedtime vs. In-Bed Objective Phone Use with Sleep among University Students

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Introduction: Despite recommendations to the contrary, smartphones have increasingly become integral to many people's bedtime routines. An array of recent studies reported negative sleep outcomes due to nighttime phone usage, however, most of these studies relied on self-report measures. It is not clear how these outcomes are reflected in objective sleep and phone usage records. The present study used high-resolution smartphone sensing, ecological momentary assessments, and wearable sleep tracking to follow a cohort of university students under free-living conditions over a semester-long monitoring period.

Materials and methods: First-year undergraduates ($N = 233$) reported daily timings of getting into bed and intention to sleep via ecological momentary assessment, corroborated by objective data measured by a sleep tracking wearable (Oura ring 3). To objectively measure participants' phone usage, an app installed on participants' Android phones continuously and anonymously recorded their phone use sessions through touchscreen interactions (taps) along with the timestamp and the most active app for each tap within the sessions. Nightly phone usage patterns were characterized in the three separate time windows: before bedtime (3-hours prior to getting into bed), in-bed prior to intention to sleep, in-bed after intention to sleep. A total of $>13,000$ nights with paired diary, wearable, and phone use data were recorded. Linear mixed models were used to examine within- and between-subjects associations between phone usage in different time windows and sleep outcomes.

Results: During the 3 hours before getting into bed, participants used their phone for $70.08 (\pm 25.67)$ minutes. While in bed but before intention to sleep (14.97 ± 15.85 minutes), participants used their phones for $8.61 (\pm 11.30)$ minutes. The average interval between intention to sleep and sleep onset was $23.28 (\pm 8.97)$ minutes, during which participants used their phones for $8.51 (\pm 6.46)$ minutes. Counter to our hypothesis, higher phone usage (by 1 min) before getting into bed was associated with

same-night earlier sleep onset (0.25 mins, $p < 0.001$) and increased total sleep time (0.22 mins, $p < 0.001$). Higher pre-bedtime phone use was also associated with increased wakefulness after sleep onset (0.01 mins, $p = 0.04$). In contrast, 1-min increase in in-bed phone usage (both before and after intention to sleep) was associated with same-night later sleep onset (before intention to sleep: 0.37 mins, $p < 0.001$; after intention to sleep: 0.52 mins, $p < 0.001$), later wake-up time (before intention to sleep: 0.39 mins, $p < 0.001$; after intention to sleep: 0.59 mins, $p < 0.001$), but no change in TST. In-bed usage was also related to increased sleep onset latency and reduced sleep efficiency ($ps \leq 0.03$).

Conclusions: Undergraduates continued to spend a significant amount of time using their phone while in bed, even after the first attempt to fall asleep. Strikingly, higher pre-bedtime phone use was associated earlier sleep onset and longer sleep duration, while higher in-bed phone use was associated with worse sleep outcome. This highlights the potential importance of distinguishing between different periods of nighttime phone usage when examining their associations with sleep outcomes.

Title: Relationship between initial pressure setting and continuous positive pressure therapy compliance

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Introduction: Various factors are known to affect continuous positive airway pressure (CPAP) therapy compliance. However, there is no consensus on its risk factors regarding compliance, since every study shows different results. Furthermore, there are no prior studies regarding initial CPAP pressure setting and CPAP compliance. This study focuses on initial pressure setting and clinical characteristics of patients using CPAP to investigate factors affecting CPAP adherence.

Materials and methods: We retrospectively reviewed the medical records of patients diagnosed with OSA and treated with CPAP at the Haeundae-Paik Hospital, between November 2019 and July 2023. Patients' demographics, BMI (body mass index), past medical history, CT 90 (percentage of time spent with SaO₂ below 90% of the total recording), AHI (apnea-hypopnea index), percentage of days used for at least 4 hours were gathered. The patients were divided into 2 subgroups. One group started CPAP with wide pressure range (4~15 cmH₂O) and changed to narrow range afterward. The other group was treated with narrow pressure range (commonly 8~11 cmH₂O) from start to end. Patients' clinical factors were compared. Using logistic regression analysis, factors associated with CPAP compliance were investigated.

Results: During the study period, 157 patients were treated with CPAP after diagnosed as OSA. After exclusion, 142 patients were included for data analysis (mean age 52.126, male : female 116 : 26). There were 45 (31.7%) patients in the wide to narrow range group, 97 (68.3%) patients in the narrow group. CPAP Adherence rates were 48.8% in the wide to narrow group, 77.3% in the narrow group respectively. Chi square test result showed $p=0.001$. Logistic regression showed that BMI, age, CT 90 had strong correlation with adherence rate.

Conclusions: Patients undergone treatment with narrow range initial pressure significantly showed higher rate of passing adherence test, compared with patients started with wide range. Also, BMI, age, CT 90 were associated with poor adherence rate of CPAP.

Title: Short-Term Effects of Daily Stress on Sleep and Physiological Markers: Resilience as a Moderator

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Introduction: This study aimed to investigate the short-term effects of daytime stress on sleep quality and physiological indicators (salivary chromogranin A [CgA] and blood pressure) in full-time working adult males. Additionally, we examined the relationships between cumulative stress and psychological health indicators (perceived stress and sleep quality), and explored the role of individual resilience in moderating these associations.

Materials and methods: Twenty-four full-time employed adult males (mean age = 37.2, SD = 6.96) participated in a 15-day study. Participants recorded their daily stress levels (5-point scale; lower scores indicate greater stress) and sleep evaluations, including satisfaction with sleep onset and perceived depth of sleep (both on 5-point scales, with lower scores reflecting poor sleep). On days perceived as highly stressful and minimally stressful, salivary CgA samples were collected at bedtime, upon awakening, and 45 minutes post-awakening. Blood pressure was measured at bedtime and upon awakening. On the final day of the study, participants completed the Perceived Stress Scale (PSS) and Pittsburgh Sleep Quality Index (PSQI) to assess the previous two weeks. The Brief Resilience Scale (BRS) was also administered to evaluate individual resilience. This study was conducted with the approval of the Kobe university's ethics committee (No.684-2). The authors have no conflicts of interest to disclose.

Results: CgA levels were significantly higher on high-stress days compared to low-stress days ($F(1, 78) = 7.78, p < .01$), with the highest levels observed immediately after awakening ($F(2, 78) = 21.25, p < .001$). Subjective stress ratings were consistent, with significantly higher scores on high-stress days ($t = 4, df = 91, p < .001$). Linear mixed models revealed that daily stress was affected with lower satisfaction with sleep onset (Estimate = 0.12, SE = 0.04, $p = .003$) and reduced depth of sleep (Estimate = 0.11, SE = 0.04, $p = .004$). Daily stress also predicted higher systolic blood pressure at bedtime (Estimate = 1.21, SE = 0.53, $p = .002$). Multiple regression analysis, including BRS as a covariate, showed that cumulative stress scores were not significant predictors of either PSS or PSQI scores. However, higher resilience was significantly associated with lower perceived stress (Estimate = -0.43, 95% CI = -0.45 to -0.10, $p = .013$).

Conclusions: Day-to-day stress was linked to increased salivary CgA, elevated bedtime blood pressure, and decreased subjective sleep quality, indicating short-term physiological and behavioral responses. In contrast, cumulative stress did not significantly influence perceived stress or sleep quality over the two-week period. Rather, individual resilience played a protective role, being associated with lower perceived stress. These findings suggest that while daily stress manifests in short-term physiological responses, resilience may be a key factor in sustaining psychological well-being over time.

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Towards Standardized Diagnostic Tools in Sleep Medicine: A Comprehensive Analysis of Reliability, Symptom Overlap, and Screening Questionnaires

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Introduction: Sleep disorders, such as insomnia and obstructive sleep apnea (OSA), are defined by diagnostic criteria outlined in international classifications, including the ICSD and DSM. However, the reliability and clinical relevance of these criteria remain under discussion, partly due to the diversity and overlap of symptoms across assessment tools. This review synthesizes systematic analyses of screening questionnaires to better understand the complexity and limitations of current tools in sleep medicine.

Materials and methods: Four distinct methods were integrated:

1. A systematic review of studies evaluating the reliability of diagnostic criteria for sleep disorders using Cohen's kappa coefficient.
2. A content analysis of multiple sleep disorder screening questionnaires, assessing item overlap using the Jaccard Index.
3. A content analysis of insomnia questionnaires, focusing on their clinical dimensions and their ability to distinguish symptoms from related impairments.
4. A content analysis OSA questionnaires, examining the diversity and relevance of symptoms phenotypes covered by these tools.

Results: The systematic review of diagnostic criteria showed substantial reliability (mean kappa = 0.66), with a predominance of "test-retest" and "interrater" reliability methods. However, insomnia and parasomnia were overrepresented in the studies.

The analysis of multiple sleep disorder screening questionnaires revealed moderate similarity between symptoms (mean Jaccard Index = 0.44), with gaps in item harmonization. Insomnia questionnaires

identified 16 clinical manifestations but exhibited limited overlap (mean Jaccard Index = 0.409) and a lack of distinction between symptoms and impairments. Finally, the analysis of OSA questionnaires highlighted low content overlap (mean Jaccard Index = 0.224), with tools capturing heterogeneous phenotypic aspects of OSA and a risk of diagnostic biases.

Conclusions: These findings underscore significant gaps in the standardization of diagnostic criteria and screening tools for sleep disorders. The reliability of criteria is limited by an imbalance in studied disorders and the methods employed. Screening questionnaires suffer from heterogeneous content, low overlap, and poor differentiation between symptoms and consequences of disorders. These limitations call for the development of standardized tools that integrate broader clinical dimensions and differentiated approaches based on the phenotypes of sleep disorders. Greater harmonization of questionnaires and diagnostic criteria is essential to improve clinical validity and comparability across studies.

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Transdiagnostic Effects of a Chinese Herbal Formula DEP-2306 on Improving Sleep in Adults with Depressive Episode with Insufficient Symptoms: A Real-World Study

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Introduction: Sleep disturbances and depression frequently coexist, with most individuals experiencing depressive episodes reporting poor sleep quality, which can exacerbate mood dysregulation. Depressive Episode with Insufficient Symptoms (DEIS), characterized by symptoms that are subthreshold in severity or duration for a diagnosis of Major Depressive Disorder (MDD), represents a critical intervention window due to its heightened risk of progression to MDD and significant functional impairment. Pharmacological treatments, such as antidepressants, are often premature at this stage. Psychotherapy, although effective, faces barriers such as stigma and resource limitations. This highlights the need for effective, safe, and culturally acceptable alternatives. Leveraging thousands of years of holistic practice, Chinese herbal medicine has shown efficacy in alleviating depression in many clinical and preclinical studies. However, specific evidence for its transdiagnostic effects on sleep quality in DEIS is sparse. DEP-2306, a Chinese herbal formula designed to target DEIS treatment in mood, has demonstrated therapeutic potential in preliminary trials. This report extends prior work by analyzing its transdiagnostic effects on improving sleep in DEIS.

Materials and methods: A total of 67 DEIS patients received daily DEP-2306 for four weeks. The core ingredients include Curcuma Radix (Yujin), Paeoniae Radix Alba (Baishao), Triticum Aestivum (Fuxiaomai), and Acanthopanax Senticosus Radix et Rhizoma (Ciwujia). Main outcomes included sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI), and the 7 domains of PSQI, which include subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. A linear mixed model was used to analyze treatment effects, with statistical significance defined as $p < 0.05$.

Results: Among the 67 participants (mean age 37.3 ± 13.4 ; 70.1% female), significant improvements were observed in PSQI total scores, which decreased from 10.3 to 7.9 ($p < 0.01$, Cohen's d (d)=0.76). Significant improvements were also seen in subjective sleep quality, with a large effect size (d =0.83), moderate-to-large effects on sleep latency (d =0.73), and moderate effects on daytime dysfunction

($d=0.51$). Small to moderate effects were noted on sleep duration ($d=0.37$) and sleep disturbances ($d=0.47$). The tolerability rate, defined as the dropout rate due to adverse events, was very low, reported as 1.49%.

Conclusions: This study demonstrated that a 4-week DEP-2306 intervention is effective and safe for improving sleep quality in participants with DEIS. While the mean PSQI score reduction of 2.45 after 4 weeks of treatment fell slightly below the recommended minimal clinically important difference of 2.5, the short treatment duration may have limited its full therapeutic potential. Future research should employ longer intervention periods, placebo-controlled designs, and objective sleep measures to further validate these findings.

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Traumatic childhood experiences and objective sleep health in adults with insomnia symptoms

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Introduction: Childhood trauma is a profound adverse factor that may have lasting effect on a child's development and health problems that may persist into adulthood. Sleep disturbance is one of the critical areas that could directly be affected by these early adverse experiences. Prior research has found that traumatic childhood experience was associated with poor sleep in adults, albeit the evidence were mainly relied on subjective sleep measurements. Notably, objective sleep measures, particularly REM and NREM sleep, play distinct roles in processing memory regarding adverse experiences and emotional regulation. We aimed to examine the impact of childhood adversities on objective sleep architecture in adults who had already developed insomnia symptoms.

Materials and methods: A total of 228 participants with insomnia symptoms (Difficulty initiating sleep, Difficulty maintaining sleep, and/or Early morning awakening) were included. All participants underwent clinical interview that included the Structured Clinical Interview for DSM-5 Disorders - Clinician version (SCID-CV) and Diagnostic Interview for Sleep Patterns and Sleep Disorders (D.I.S.P). They also completed questionnaires for childhood trauma (Childhood Trauma Questionnaire short form), and subjective sleep characteristics that included sleep reactivity (FIRST), pre-sleep cognitive and somatic arousal (PSAS), and insomnia severity index (ISI). Sleep macrostructures were measured by ambulatory polysomnography (Nox A1s or Nox SAS solutions). Comparisons of sleep macrostructures between childhood trauma groups were conducted by t tests. Sleep parameters that showed significant difference between childhood trauma groups were selected in regression model, to further examine the associations with childhood trauma events. Confounders including age, sex, family income, educational level, psychiatric illnesses, and apnea-hypopnea index were adjusted.

Results: A percentage of 90.4% ($n=207$) of participants had reported at least one type of traumatic childhood experience (TCE). Adults with TCE had greater REM sleep proportion (TCE- vs TCE+: 19.77% < 24.83%, $p=0.04$) and probably longer REM sleep duration (TCE- vs TCE+: 74.52 min vs 92.81 min, $p=0.09$), as compared to those without TCE. Adults with TCE also had higher proportion of diagnosed insomnia disorder according to the DSM-V criteria (TCE- vs TCE+: 57.1% < 88.5%, $p=0.02$). Subjective sleep characteristics (sleep reactivity, pre-sleep arousal, and insomnia severity) and other sleep macrostructures (total sleep time, sleep efficiency, wake time after sleep onset, NREM sleep percentages and duration, AHI) were comparable between groups. In regression models, the traumatic childhood experience was also associated with higher probability of increasing REM sleep percentage ($\beta=6.83$, 95%CI: 1.53-12.13), and longer REM sleep duration ($\beta=27.90$, 95%CI: 5.07-50.72), when confounders were fully adjusted.

Conclusions: Traumatic childhood experiences were associated with excessive REM sleep in adults with insomnia symptoms. Future studies are warranted to better understand the underlying mechanism in childhood trauma and REM sleep in poor adult sleepers, to develop effective interventions.

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Uncovering Sleep-Linked Glucose Dynamics in Healthy Individuals Using Wearable Data

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Introduction: Sleep plays an important role in metabolic regulation, yet the glycemic dynamics that occur during sleep and their relationship with daytime glucose patterns remain poorly understood, particularly in healthy individuals. Glucose homeostasis, when disrupted, is known to contribute to oxidative stress, systemic inflammation, and cardiovascular risk. While glycemic patterns in diabetes have been well documented, the prevailing assumption that healthy individuals maintain stable glucose control across the day is increasingly being challenged. Emerging evidence suggests that transient hyperglycemia and elevated glycemic variability (GV) can occur even in normoglycemic individuals. Daytime glucose is influenced by behavioral factors such as meals and activity, whereas nocturnal glucose regulation is primarily governed by endogenous, autonomic processes. Thus, examining how sleep-time glucose patterns interact with daytime fluctuations may yield valuable insight into circadian metabolic stability, and potentially flag early anomalies before clinical symptoms emerge.

Materials and methods: We conducted a retrospective analysis of 5,124 hours of 24-hour continuous glucose monitoring (CGM) and wearable sleep data collected in naturalistic conditions from 12 healthy adults (mean age: 32.7 years, 50% male). Glucose levels were recorded every 15 minutes using the FreeStyle Libre system. Sleep onset and offset were captured using Fitbit Charge 3 wristbands worn on the non-dominant wrist. The CGM data were segmented into individualized in-sleep (GsleeP) and awake-time (Gawake) intervals based on Fitbit measured sleep onset and offset. A comprehensive set of short-term GV metrics (e.g., mean, max, standard deviation, MGN, CV, HBGI, LBGI) was computed for each segment. We applied Mann-Whitney U tests for between-state comparisons, repeated-measures correlation (rmcorr) to assess intra-individual associations over time, and quantitative association rule mining (ARM) with a novel post-filtering method to uncover high-confidence glycemic patterns.

Results: GV was consistently higher during wakefulness, while LBGI was significantly elevated during sleep. Strong, time-lagged associations emerged: LBGI_{sleep} on day N was strongly correlated with LBGI_{awake} of both the same day and previous day (rmcorr = 0.68–0.75), and negatively correlated with prior daytime mean and MGN. Similar reciprocal patterns were observed between meansleep and daytime GV. ARM revealed clinically meaningful rules linking low nocturnal glucose (≤ 54 mg/dL) to elevated LBGI the following day. These rules demonstrated high confidence (0.75–0.88) and lift (4.1–11.5), exceeding previous applications of ARM in metabolic data.

Conclusions: This study revealed significant and reciprocal associations between glycemic variability during sleep and daytime in normoglycemic adults. By integrating continuous glucose monitoring with wearable sleep tracking, we demonstrate that nocturnal glucose dynamics are closely linked to glycemic stability across the 24-hour cycle. While causal direction cannot be inferred, the observed bidirectional associations across sleep–wake cycles highlight the potential of combining CGM and wearable sleep data to characterize individual glucose variability over time. This may inform future research on early metabolic changes prior to disease onset.

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University students with classes before 8:30 AM exhibit short sleep and low attendance

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Introduction: Sleeping well and attending classes are important for learning performance in university students. However, many students struggle to obtain sufficient sleep. Early class start times may stand in the way of students reaching sleep and learning goals because they have to wake up much earlier than usual. Students may also skip early classes due to oversleeping or not wanting to wake up early. Here, we assessed the impact of early class start times on objective sleep behavior and daily self-reported class attendance in university students. We hypothesized that, for classes starting before 8:30

AM, (1) students would obtain shorter sleep on days they attended the class, and (2) students would be more likely to skip class compared with days when their first class started later.

Materials and methods: University students ($n=570$, 364 women) wore a wrist actigraphy device for 2 weeks during the school semester to track their sleep behavior. Daily diaries were used to record students' first class start time of the day, whether they attended the class, and their reasons for any absences. Mixed models were used to test associations of school start time with sleep duration (continuous variable) and class attendance (binary variable), adjusting for demographic variables, chronotype, commute time, and class format (i.e., in-person or online). The dataset used for analyses included 3,388 school nights and 4,551 non-school nights.

Results: On days when students attended their first class, their nocturnal sleep duration was more than an hour shorter ($\beta=-1.29$ h, 95% CI=-1.72 to -0.86 h, $P<0.001$) when class started before 8:30 AM ($M=5.87$ h, 95% CI=5.70 to 6.04 h) versus in the afternoon ($M=7.04$ h, 95% CI=6.97 to 7.12 h). When students skipped classes that started before 8:30 AM, however, their sleep duration ($M=7.42$ h, 95% CI=7.16 to 7.68 h) was comparable to non-school nights ($M=7.18$ h, 95% CI=7.14 to 7.23 h). Class attendance was about 20 percentage points lower when students' first class started before 8:30 AM (63.0%) compared with any time later in the day (ranging from 80.0% to 88.6%). The most common reasons cited for missing early morning classes were "I did not want to go" and "I overslept" (40.7% and 33.6% of skipped classes, respectively). The odds of being absent were 2-fold higher when students' first class started before 8:30 AM versus in the afternoon (adjusted OR=2.11, 95% CI=1.58 to 2.64).

Conclusions: In university students, early class start times were associated with short sleep and low class attendance. Students may face a trade-off where they either forego sleep to attend class, or skip class to obtain more sleep. Universities should consider avoiding mandatory classes that start before 8:30 AM in order to optimize sleep and learning.

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Unpacking the Discrepancy Between Subjective and Wearable-Measured Sleep: A Neurophysiological Perspective Using fNIRS

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Introduction: Discrepancies between subjective sleep experience and objective sleep metrics are well-documented in both clinical and consumer settings. While consumer sleep trackers like Fitbit provide convenient longitudinal monitoring of sleep structure using accelerometry and PPG, many users report that these data do not align with how they feel upon waking. These mismatches are often attributed to device inaccuracy, yet even gold-standard polysomnography (PSG) explains only a small fraction of the variance in subjective sleep quality. Despite this, little is known about the underlying neural basis of this divergence, particularly in the context of sleep-tracking technologies. This study aims to explore the neurophysiological correlates of subjective versus wearable-derived sleep assessments during the first sleep cycle, and to evaluate whether these reflect distinct patterns of prefrontal cortical activity.

Materials and methods: We conducted an N-of-1 pilot study with a healthy male in his 30s, free from diagnosed sleep or mental health conditions. Prefrontal cortical hemodynamics were recorded during the first 90 minutes of sleep using a 27-channel wearable fNIRS system (Brite 24, Artinis). Concurrently, sleep metrics were obtained from a Fitbit Sense (e.g., TST, WASO, sleep efficiency, light/deep/REM sleep ratios, and Fitbit's sleep score). Subjective sleep quality was self-rated on a 5-point Likert scale each morning. Eight hemodynamic features were derived from fNIRS data (i.e., mean, median, SD, skewness, kurtosis, total power, peak amplitude, peak ratio), and correlations were computed with both subjective ratings and Fitbit metrics.

Results: Subjective sleep ratings were moderately and positively correlated with median ΔO_2Hb and ΔHHb in specific prefrontal cortex (PFC) channels, suggesting that more stable or elevated hemodynamic activity during the first sleep cycle may support better perceived sleep. Negative correlations were observed between subjective ratings and the skewness and kurtosis of ΔO_2Hb , indicating that flatter or more symmetrical signal shapes may align with positive sleep perception. In contrast, Fitbit's sleep score showed strong negative correlations with the mean and standard deviation of ΔO_2Hb and ΔHHb in a different set of PFC channels ($r < -0.70$), implying that higher signal

amplitude or variability is linked to poorer device-rated sleep quality. Additional Fitbit metrics demonstrated distinct physiological signatures. Sleep continuity metrics—including sleep efficiency, WASO, wake ratio, and light sleep ratio—were positively associated with hemodynamic activity. Conversely, sleep quantity metrics like total sleep time and deep sleep ratio showed negative associations. REM sleep ratio exhibited weak or inconsistent correlations. Topographical analyses revealed little spatial overlap between channels linked to subjective ratings and those linked to Fitbit metrics.

Conclusions: Subjective and wearable-based sleep assessments appear to reflect different neurophysiological dimensions of early sleep cycle. The commonly observed mismatch is not merely a matter of device error but rather of measurement misalignment. These findings suggest a need to move beyond improving algorithmic accuracy and toward personalized, neuroscience-informed feedback in future sleep tracking technologies.

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Upper Airway Sleep Health and its Physiology

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Introduction: Billions of animals, from fish to humans, depend on rhythmic activation of upper airway muscles to accomplish “breathing”- the regulation of appropriate exchange of oxygen and carbon dioxide with the environment. Breathing interrupted by swallows or with speech involves a highly integrated neural control system which can dynamically maintain nasopharyngeal, oropharyngeal, and hypopharyngeal airway size and/or stiffness using structural feedback and controlled elements of muscle tension/orientation to switch functions.

Materials and methods: A literature review was conducted to address to identify whether neuromechanical features required to keep the airway during sleep are incrementally described either as controller or mechanical, crucial throughout development, and ignored until it fails.

Results: Bothersome increases in resistance, and decreases in flow are the result of unintentional airway narrowing and collapse during sleep, not seen in such proportions in few species, except perhaps bulldogs and elephant seals. In the condition called obstructive sleep apnea, the predominant theory is one of airway collapse, which we propose is an example of a failure of a little appreciated putative control system based in the brainstem. Supporting this to some extent are the new drug targets, based on sleep-influenced receptors on CN XII.

Conclusions: We propose a broader and testable view of functional health and disease for not only CN XII but also the other motor nerves to the upper airway, like CN IX. The unconventional idea is that OSA occurs in the context of a failure of neuromechanical control involving the palatal muscles attached to the base of the skull from which the upper airway, as well as the trachea and lungs, hang.

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Usage and effectiveness of sleep education apps among parents of infants in Japan

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Introduction: In Japan, the average duration of sleep for both children and adults is known to be shorter than many other countries in the world. It has also been pointed out that a lack of sleep during early childhood affects development and is a risk factor for later hyperactivity and impaired cognitive

function. Children's sleep disorders are also said to be related to parental stress and maternal depression, so early support of sleeping habits is necessary. Previous research in Japan has highlighted a lack of sleep education for parents, and therefore the necessity to provide sleep education to parents are raising young children. The sleep education app 'Nenne-navi' developed by Yoshizaki et al (2023; 2024) is being used in several municipalities in Japan, helping to create better sleep habits of parents and children, so that they can maintain improved lifestyles even after using the app. In previous studies reporting on the effectiveness of using such sleep education apps, the duration of use ranged from only a few times, to use for a whole year, and it is unclear what the most appropriate duration for use is. Therefore, in this study, we investigated the optimum duration for use for sleep education app use.

Materials and methods: Participants were recruited from infant health checkups and nursery schools targeting children aged 16 to 45 months in a countryside city in Japan. All participants installed the 'Nenne Navi' sleep education app on their mobile devices, entered their family's lifestyle habits, and their children's sleep challenges, and participated in pre- and post-surveys. The app provides participants with advice tailored to their lifestyle habits. The study was approved by the Ethical Research Review Committees of Osaka University and Kanazawa University on June 5th, 2020.

Results: Of the 56 participants who agreed to participate in the study, 20 used the app for 1 month, 16 used the app for between 2-5 months, and 20 used the app for between 6-12 months. The mean age of the participating mothers at the start was 27.56 with a range between 22-42 years. There was significant difference in variability of children's wake-up times, sleep onset latency, sleep duration, mothers' bedtimes, and SSR between the beginning and end of study. There was no correlation between age of children and duration of app use, however the presence of sleep challenges, such as late bedtime and a long time to fall asleep, had a slight effect on app-use continuation. On the other hand, those mothers who continued using for longer were more likely to show an improvement in anxiety.

Conclusions: The app may help reduce anxiety if used continuously by mothers of younger children. We will continue to collect data and analyze the relationship between continued use of the app and the knowledge of sleep and the confidence of mothers in their children and themselves to cope with sleep after using the app.

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Using the learnings from general practice nurse-delivered models of care for chronic conditions to inform the design of models of care for chronic insomnia and obstructive sleep apnea: a mixed-methods systematic review

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Introduction: The potential for new general practice nurse-delivered models of care to address obstructive sleep apnea and chronic insomnia have been explored in response to long wait times for the assessment and management of OSA and limited access to cognitive behavioural therapy for insomnia. Despite randomised controlled trials demonstrating evidence of efficacy, these models of care have not yet been widely integrated into clinical practice. Understanding the barriers and facilitators to implementation can inform the translation of complex interventions, such as models of care, however there is a scarcity of research exploring the implementation of general practice nurse-delivered models of care for chronic sleep disorders. With many years of research investigating the implementation of general practice nurse-delivered models of care for other chronic conditions, a systematic review focussed on the implementation of these models of care for chronic conditions was conducted to inform the design and implementation of future general practice nurse-delivered models of care for chronic sleep disorders.

Materials and methods: A mixed-methods JBI convergent integrated systematic review was conducted. The review utilised a framework synthesis approach informed by a conceptual framework for the implementation of complex interventions into primary care. Data were identified that did not fit the chosen framework, necessitating the development of an amended determinant framework – Factors influencing the Implementation of models of care for Chronic Conditions in General Practice (FICC-GP).

Results: Eighty-five records, published between 1995 and 2025, reported barriers and/or facilitators to implementation of models of care and were included in the review. Facilitators included an awareness of the benefits of the model of care by both patients and clinicians, general practice staff practicing effective teamwork, a collaborative relationship between general practice clinicians and specialist services, alignment with current work practices, and patient capability, such as adequate literacy and time to commit to the intervention. Barriers to implementation included lack of clarity about the roles and responsibilities of general practice team members and the scope of practice of general practice nurses, insufficient or inappropriate funding, such as funding that does not support multi-disciplinary care, and models of care that do not offer individualised patient centred care.

Conclusions: This review informs our understanding of the factors that influence the implementation of general practice nurse-delivered models of care for chronic conditions. The findings may be used to inform the design of future studies testing the implementation of general practice nurse-delivered models of care for chronic sleep disorders. Establishing a collaborative relationship between general practices and sleep specialist teams, ensuring that approaches to care are patient centred, and collaborating with patients to co-design models of care may lead to greater success when implementing new models of care for chronic sleep disorders in general practice.

Utility of the General Practice Sleep Scale “GPSS” among women in childbearing age in comparison to existing OSA screening tools

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Introduction: Background: The risk of developing obstructive sleep apnoea (OSA) increases during pregnancy. However, underdiagnosis of OSA during pregnancy continues and can have adverse maternal and fetal outcomes. Hence, it is vital in clinical practice to screen high risk women in childbearing age for presence of OSA.

Aims: In this study, we assessed the utility of the new OSA screening tool – the “GPSS” (General Practice Sleep Scale) among women in childbearing age in comparison to existing traditional OSA screening tools – the Epworth sleep scale (ESS) and STOP-Bang.

Materials and methods: Methods: This was a retrospective study including all women aged 18-35 years with either a completed GPSS/STOP-bang/ESS, or data available to retrospectively derive the GPSS/STOP-bang/ESS score, and who underwent diagnostic polysomnography (PSG) in the Northern Territory of Australia.

Results: Results: 30 women (median age 30.6 (IQR 26, 33.5), n=8 (26.7%) indigenous Australian, median apnoea hypopnea index (AHI) 9.5 (IQR 3.2, 12.9)) were included for analysis. 70% recorded OSA (50% mild, 6.7% moderate and 13% severe) with minor, non-significant differences in age and Indigenous status between those with OSA (median age 31.4 (IQR 26.6, 33.5), 28.6% Indigenous) and those without (median age 27 (IQR 26, 31), 22.2% Indigenous). Notably, the ESS was higher among patients without OSA than with (median 15 (IQR 12, 15) vs. 8 (IQR 6, 19), p=0.063) and frequency of a heightened ESS (ESS>8) was greater for those without OSA (77.8%) vs. those with (47.6%), showing a sensitivity and specificity of 47.6 & 22.2% respectively. The median STOP-bang score among those with OSA was 2 (IQR 2, 3) (47.6% moderate risk (score≥3)) vs. 1 (IQR 1, 3) (33.3% moderate risk) among those without, showing sensitivity and specificity of 47.6 & 66.7% respectively for a moderate risk score. The median GPSS score among those with OSA was 10 (IQR 7, 11) (76.2% moderate risk (score≥7)) vs. 8 (IQR 4, 10) (55.6% moderate risk) among those without, showing sensitivity and specificity of 76.2 & 44.4% respectively for a moderate risk.

Conclusions: This study illustrates a high prevalence of OSA in women of childbearing age. However, daytime symptoms appeared more commonly among those patients without OSA. The GPSS tool showed much higher sensitivity for OSA, while the STOP-bang showed higher specificity, indicating both may be of use in different clinical scenarios for this demographic. Further prospective studies are warranted to assess the performance of the GPSS amongst pregnant women.

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Validation of the reliability and validity of the 3-Dimensional Sleep Scale (3DSS), Japanese version, a measure of sleep phase, quality, and quantity

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Introduction: The Pittsburgh Sleep Quality Index (PSQI) and the Athens Insomnia Scale (AIS) are scales for evaluating sleep. These scales can assess the quality (e.g., sleep latency, sleep maintenance) and quantity (e.g., sleep duration, daytime sleepiness) of sleep, but cannot assess phase (e.g., sleep regularity, chronotype). We developed the 3-Dimensional Sleep Scale (3DSS) in 2015 to assess sleep phase along with quality and quantity. However, we encountered some problems, such as the small sample size at the time of validation and the classical methods for establishing reliability and validity. We therefore aimed to increase the sample size and update the statistical methods, to again validate the reliability and validity of the 3DSS.

Materials and methods: We conducted a web-based survey of approximately three thousand dayshift workers at four companies in Tokyo, Japan, between 2021 and 2022. The 15 questions of the 3DSS were tested for reliability and validity according to the COSMIN checklist, an international standard for scale development. The maximum likelihood method and promax rotation were selected for exploratory factor analysis. Reliability was tested by calculating the intraclass correlation coefficient and McDonald's ω reliability coefficient. To verify reproducibility, participants were asked to respond again within 2 weeks to the 15 items of the 3DSS, and the intraclass correlation coefficient between the first and second responses was calculated. Convergent and discriminant validity were verified by multi-trait multi-method analysis. As sleep phase indicators for convergent validity, holiday wake-up times and social jetlag were used. As sleep quality indicator for convergent validity, the total AIS Q1–5 score used. As sleep quantity indicators for convergent validity, the total AIS Q6–8 score and weekday sleep duration used. Cutoff values were verified using ROC curves and AUCs. We used "social jetlag ≥ 1 h" as the outcome when validating the cutoff value for the phase score. An "AIS score of 6 points or more" was set as the outcome when validating the cutoff values of the 3DSS sleep quality score and sleep quantity score. The author received a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology to conduct this research (grant no. 21K10507).

Results: A total of 2,605 participants (1,718 men, 887 women; mean age, 42.2 $\pm$ 11.7 years) were included in the analysis, after excluding non-responders, non-consenters, and absent employees. Exploratory factor analysis confirmed a three-factor structure of sleep phase, quality, and quantity, with reliability coefficients of 0.690, 0.786, and 0.710, respectively. The second dataset of responses was obtained from 402 participants to verify reproducibility. Intraclass correlation coefficients for reproducibility, close to or greater than 0.7, were observed for all items. For convergent and discriminant validity, ideal correlations were observed for all subscales, as hypothesized. AUCs for sleep phase, quality, and quantity were 0.747, 0.812, and 0.819, respectively.

Conclusions: The 3DSS demonstrated sufficient reliability and validity for use as a sleep assessment tool. As the world's first instrument to evaluate sleep phase, quality, and quantity within a single scale, the development of an English version is warranted.

Vascular Age Estimation Using a Consumer Wearable Sleep Tracker

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Introduction: Arterial stiffening, a hallmark of vascular aging, increases with age and is a proven biomarker of cardiovascular risk. However, instruments for its measurement are not suited for high frequency longitudinal measurement and not easily accessible outside of specialist settings. Nocturnal deployment of photoplethysmography (PPG) embedded in wearable consumer health trackers is a potential solution for recurrent longitudinal assessment of vascular aging at scale. Here, we assessed the ability of a sleep-tracking wearable (Oura Ring Gen 3) to detect age-related differences in key PPG features, comparing it to data from a clinical-grade pulse oximeter concurrently collected from the fingertip. We evaluated ring derived vascular age prediction performance using a featureless deep learning algorithm.

Materials and methods: Healthy adults (N=160; 78 males (49%), median age 31 years (IQR: 23)) underwent overnight polysomnography (PSG) in a sleep laboratory, during which fingertip photoplethysmography (PPG) and wearable ring PPG data were collected simultaneously. Pulse waveforms were extracted from both clinical and wearable sensors using a custom algorithm. Key PPG waveform features, crest time (CT), time difference between systolic and diastolic peaks (dT), and reflection index (RI), were used to assess waveform similarity across devices. Vascular age was estimated directly from PPG waveforms using a featureless deep learning approach based on a convolutional neural network (CNN). Model performance was compared between the fingertip and ring devices.

Results: Sleep PPG waveforms from fingertip and ring devices showed high overall similarity, with a median (IQR) cross-correlation of 0.97 (0.02) between devices. Age-related waveform changes were most strongly marked by PPG crest time ($r = 0.64$ and 0.62 for fingertip and wearable ring sensors respectively). The deep learning model similarly showed comparable prediction performance with mean absolute errors (MAE (SD)) of 6.28 (1.48) and 7.25 (1.29) years, and r (SD) of 0.84 (0.07) and 0.80 (0.10) for clinical-grade and consumer-grade sensors.

Conclusions: These findings support the feasibility of using wearable consumer devices to assess vascular age conveniently and frequently. Given the strong link between arterial stiffness and cardiovascular morbidity, these tools hold great promise for allowing persons to discover lifestyle changes that result in improvement in vascular health.

Virtual Reality–Assisted Sleep Bundle Intervention for Enhancing Sleep Outcomes in Critically Ill Patients

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Introduction: Sleep disturbance is a main complaint reported by critically ill patients, with an estimated prevalence of 66%. However, an effective intervention is still lacking in the current settings of intensive care units (ICUs). This study aimed to evaluate the effects of the virtual reality–assisted Sleep Bundle, comprising Supports Clustering, Light and Noise Reduction, Emotional Distress Relief, Eye Mask Use, and Pain Monitoring and Management, on sleep quality and quantity in critically ill patients.

Materials and methods: A two-arm, assessor-blinded randomized controlled trial was conducted in a surgical intensive care unit between April 2022 and May 2024. The primary outcomes were subjective sleep quality, assessed using the Traditional Chinese version of the Richards-Campbell Sleep Questionnaire, and objective sleep metrics measured via actigraphy. Secondary outcomes included anxiety and stress levels, evaluated using visual analogue scales. Generalized estimating equations were used to assess treatment effects over time.

Results: A total of 100 surgical ICU patients were randomized 1:1 to receive either the SLEEP intervention or standard care. After three days, patients in the experimental group demonstrated significantly better sleep quality, reduced percentage of stage 2 sleep, and increased stage 3 sleep compared to the control group (all $p < 0.05$).

Conclusions: The virtual reality-assisted sleep bundle program significantly improved subjective and objective sleep outcomes in critically ill surgical patients, supporting its implementation as a nonpharmacological strategy in ICU settings.

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Vision Transformer-based Per-Second Resolution Detection of Obstructive Sleep Apnea with Explainability

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Introduction: Manual, second-by-second scoring of polysomnography (PSG) remains the gold standard for obstructive sleep apnea (OSA) diagnosis but is resource-intensive and subject to variability among scorers. Current automated methods typically analyze fewer than three biosignal channels, providing only the coarse Apnea-Hypopnea Index (AHI) without second-level annotation, thus compromising clinical detail and interpretability. To address these limitations, we propose VOSA, a Vision Transformer (ViT)-based deep learning model designed to replicate a sleep technologist's visual diagnostic workflow using comprehensive, standardized PSG images.

Materials and methods: VOSA processes standardized PSG images, each containing 21 distinct biosignals utilizing specialized patch design and transformer blocks. The model performs per-second labeling of normal, hypopnea, or apnea events, calculates the Apnea-Hypopnea Index (AHI), and classifies OSA severity into four levels. Additionally, the ViT architecture provides visual explanations through attention heatmaps and well-calibrated confidence scores. Training and validation were conducted using the KISS dataset, comprising PSG data from 7,745 patients collected across four clinical centers. Model robustness was further tested on the independent, publicly available Sleep Heart Health Study-2 (SHHS-2) dataset.

Results: VOSA demonstrated robust performance with a per-second macro-F1 score of 82.6% and a severity classification macro-F1 of 73.5% in the KISS dataset, significantly outperforming baseline model. Importantly, 99.2% of patients were correctly classified into their actual or adjacent severity categories. Attention heatmap visualizations highlighted model alignment with established American Academy of Sleep Medicine (AASM) guidelines, confirming the clinical relevance. Reliability of VOSA's confidence score was evaluated by ECE (expected calibrated error), demonstrating near-perfect calibration of 0.005.

Conclusions: VOSA, leveraging comprehensive PSG image data and Vision Transformer-based architecture, provides second-level respiratory event predictions. By integrating visual explanations and calibrated confidence scores, VOSA represents a significant step towards scalable, interpretable, and precise diagnostic workflows in sleep medicine.

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Where You Live Shapes How You Sleep: Geographic and Cultural Influences on Sleep Duration in Global Data Measured by the Galaxy Watch

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Introduction: Endogenous circadian rhythms regulate human sleep but are also influenced by environmental light exposure and sociocultural factors. The widespread adoption of wearable devices has enabled the acquisition of large-scale, population-level sleep data across diverse geographic and socioeconomic contexts, including regions previously underrepresented in sleep research. In this study, we analyzed sleep data collected globally from Samsung Galaxy Watch devices to examine variations in nocturnal sleep duration and timing, and their alignment with local sunrise and sunset times, in relation to latitude, season, and cultural context.

Materials and methods: We analyzed 475 million sleep records obtained in 2023 from users in 101 countries. Sleep metrics included sleep onset time (SO), total sleep time (TST), sleep offset time (SF),

and wake after sleep onset (WASO). Sleep timing was evaluated to local sunrise and sunset, assuming device registration reflected users' locations. Countries were classified into five latitude-based climate zones—tropical, dry, temperate/continental, and polar—based on the Köppen-Geiger climate classification.

Results: Total sleep time increased with latitude, with the shortest durations observed near the equator (15°N to 15°S) and the longest in Arctic regions (66.5°N to 90°N). Countries within the temperate and continental zones (approximately 30° to 60° latitude) exhibited consistently later sleep onset and offset times than countries in other climate zones. Sleep timing patterns were notably similar among culturally related or geographically adjacent countries, suggesting sociocultural influences on sleep behavior.

Conclusions: Sleep duration and timing can be shaped by a combination of latitude, seasonal variation in natural light, and cultural context. These findings underscore the importance of developing region-specific strategies for public health messaging and sleep education.

Why do people miss their optimal sleep window? Adherence to a personalized sleep-wake recommendation delivered with a mobile application

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Introduction: The physiological benefits of aligning sleep with the body's natural circadian rhythms has been extensively documented in the literature. Despite this understanding, a substantial portion of the population struggles to adhere to a consistent sleep schedule that aligns with their internal chronotype. This study investigated the real-world application and adherence of SleepWake, a mobile application that recommends an individualized and optimal sleep-wake window.

Materials and methods: Participants in this study (n=77) received a real-time, personalized sleep recommendation delivered by the SleepWake mobile application. The SleepWake app implements a previously developed framework for dynamic tracking of sleep homeostasis and circadian rhythms using a mathematical model, provided to all participants after 14 days of monitoring sleep and wake times. Throughout the intervention period (14~28 days), the app continuously generated and delivered individualized sleep and wake recommendations based on accumulated sleep deficits and personalized sleep phase alignment optimized for individual sleep patterns. Sleep indices included sleep duration, sleep regularity, and sleep timing. Insomnia symptoms (measured by the Insomnia Severity Index; ISI) and excessive daytime sleepiness (Epworth Sleepiness Scale; ESS) were also measured. Sleep period agreement was calculated based on the proportion of observed sleep compared to suggested sleep, with values allowed to exceed 1 if the participant slept longer than the suggested sleep time.

Results: Participants (mean age = 33.7±7.1 years, 19.5% female, 44.2% shift workers). A total of 1,048 sleep records were analyzed. Sleep period agreement was on average 67% (range 45% – 96%). Among the analyzed sleep records, 41.3% (n=433) indicated participants slept more than one hour later than the suggested bedtime, with the average discrepancy being 67 minutes later (ranging from 90 minutes earlier to 287 minutes later). Smaller discrepancies between suggested and actual bedtime were associated with longer sleep duration (nocturnal sleep + naps; $r=.52$, $p=.001$). Discrepancies between suggested and actual bedtime were not associated with age, sex, shift work, ISI scores, or ESS scores.

Conclusions: Despite the promise of informing participants of their biologically aligned sleep timing, adherence to the recommended sleep-wake schedule was moderate. Notably, a large proportion of users delayed their bedtime beyond the suggested window, underscoring the persistent gap between ideal and actual sleep behavior, even when armed with real-time, individualized guidance. Future research should explore strategies to enhance user engagement and behavioral compliance, as well as assess long-term outcomes associated with adherence to biologically informed sleep schedules.

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“You need to be better than this” : Using an intersectional lens to examine sleep and healthcare access in marginalised communities in Australia

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Introduction: Sleep health disparities are under-recognised, yet are a critical marker of health inequities. Marginalised and underrepresented communities often experience unique and compounded barriers to healthy sleep. Interactions between racial discrimination, gender, socioeconomic factors, housing stability, and cultural misalignment with Western sleep norms are some factors that can contribute to these sleep disparities. However, intersectional approaches, such as the compounded effects of multiple personal, social, financial, environmental and cultural identities are not meaningfully incorporated in sleep research and practice. This exploratory study used an intersectional lens to: a) examine prevalence of sleep disorders in multicultural communities; b) explore contextual narratives and perspectives surrounding sleep and healthcare accessibility.

Materials and methods: The study used a mixed-methods approach. A cross-sectional, weighted survey of 1829 individuals representing key multicultural communities in Australia (e.g. South Asians, Southeast Asians, East Asians, Middle Eastern communities) captured quantitative data on demographics, work patterns (including shift work), sleep health (Insomnia Severity Index or ISI, Shift Work Disorder Questionnaire or SWDQ), mental health (Patient Health Questionnaire – 4), and experiences of discrimination (Intersectional Discrimination Index). In-depth interviews were conducted with 25 individuals representing a subset of community members and key stakeholders (clinicians, educators, researchers, policy makers) to examine facilitators, barriers and culturally embedded perspectives on sleep.

Results:

Over 52% of participants from multicultural communities screened positive for insomnia, a rate that is double the general population estimates 5. 37.6% were shift workers, double general population, with 1 in 2 meeting the criteria for Shift Work Disorder. Elevated anxiety ($r = 0.57$), depression symptoms ($r = 0.54$), and experiences of intersectional discrimination ($r = 0.31$) were correlated with greater insomnia symptoms (all $p < .001$). Greater resilience was correlated with decreased insomnia symptoms ($r = -0.34$, $p < .001$). Interviews identified complex multilevel influences on sleep across individual, familial, community, clinician, and systemic domains:

1. Sleep norms – Dominant sleep narratives were described as Western-centric, overlooking communal and integrative sleep practices, and collectivistic values. Sleep was often stigmatised as ‘laziness’, reinforcing extended wakefulness for productivity.
2. Minority Stress – Interviewees described sleep as being impacted by unique stressors, including loneliness, familial disconnection, racism, and migration processes and trauma.
3. Sleep is a Privilege – Sleep was identified as a privileged experience, with broader systemic barriers, such as overcrowded housing, cost of living, public transportation and infrastructure deficits, long and irregular work schedules, knowledge inaccessibility, and tokenistic political support.
4. Clinician Awareness – Clinicians-cited inadequate training and tools. Community members reported experiences of discrimination and emphasised the value of clinician self-disclosure and shared lived experience in fostering trust.
5. Community-led Strategies – Peer advocacy and culturally grounded supports, particularly through local government, were considered key facilitators of good sleep.

Conclusions: Improving sleep health requires a shift in narrative: from individual responsibility to system-level support. Embedding an intersectional lens in research, practice and policy making can address compounded impacts of marginalisation. Community-led interventions, investment in culturally-safe, accessible services, and delivery of integrative, holistic clinical education can promote more inclusive health outcomes for our communities.

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Technology/Technical

Actigraphy from sensor-level acceleration measurement

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Introduction: As actigraphy advances, standardised reporting methods become essential. Transitioning from traditional counts per minute to sensor-level, raw acceleration (m/s^2) enhances data transparency, reproducibility, and consistency across disciplines. However, maintaining backward compatibility remains essential to preserve continuity with decades of legacy data from now-discontinued devices. We developed an open-access web tool that processes and analyses sleep data in the Actiwatch-compatible AWD file format. This allows data from devices like GENEActiv to be converted and analysed in a historical format, facilitating cross-device compatibility and supporting long-term data integration.

Materials and methods: The core of the system is an open AWD conversion algorithm designed to approximate AWD-equivalent outputs from raw GENEActiv acceleration and light data. The algorithm was implemented independently in R and C# for cross-verification. Validation was conducted by collecting GENEActiv and Actiwatch data simultaneously, converting GENEActiv files to AWD format, and comparing the results.

We built a web-based application incorporating Actiware's open sleep scoring algorithm. Usability was assessed through moderated sessions with sleep clinicians. Clinicians completed task-based evaluations while narrating their experience, focusing on familiarity to existing workflows, ease of navigation, and value of individual features.

Internal validation compared rest intervals marked using the web toolkit with those analysed in Actiware. Validation efforts included determining the best GENEActiv and web toolkit configuration for closest equivalence to Actiwatch outputs.

Clinicians with prior experience using Actiware and performing sleep scoring were recruited for usability testing. To assess cross-platform compatibility, the group included two Mac and four Windows users.

Results: Clinicians responded positively to the toolkit, describing it as intuitive, quick, easy to navigate, and convenient for its web-based nature. The interval mark-up feature was considered straightforward and well-suited to their analytical needs, contributing to an overall efficient user experience.

Validation of the AWD conversion demonstrated a strong equivalence between the converted GENEActiv data and Actiwatch AWD files. Zero-count rates for the data from the two systems differed by only a few percent of each other and a linear regression of time-matched non-zero epochs yielded a slope near 1, confirming high alignment. GENEActiv data sampled at 50 Hz analysed at a wake threshold of 60 counts provided the closest match to Actiwatch outputs. This configuration slightly overestimated total sleep time by 4.91 minutes and sleep efficiency by 0.80%, while underestimating sleep onset latency by 4.23 minutes, wake after sleep onset (WASO) by 0.09 minutes, and number of awakenings by 1.95. Although based on a single participant, these results support the potential of this approach for future validation with larger datasets.

Conclusions: This project addresses the challenges of the discontinuation of legacy actigraphy systems. By developing an AWD file conversion algorithm and a user-friendly, web-based toolkit, we enable clinicians to maintain continuity between historical data and new data from modern GENEActiv devices. Clinician feedback highlighted the tool's accessibility and ease of use, and early validation results demonstrate strong equivalence between converted and original datasets. Together, these tools offer a scalable solution for cross-platform sleep data analysis and establish a foundation for expanded validation studies involving more diverse populations.

Adenosine-Mediated Sleep Enhancement via Transcranial Near-Infrared Photobiomodulation: Translational Evidence from Animal and Human Studies

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Introduction: Adenosine is a well-established neuromodulator implicated in sleep homeostasis, particularly in the promotion of non-rapid eye movement (NREM) sleep. However, modulation of adenosine itself has not yet been successfully developed as a therapeutic modality for insomnia. Near-infrared (NIR) photobiomodulation (PBM) enhances mitochondrial activity and ATP production, potentially leading to increased extracellular adenosine levels. Based on this mechanistic hypothesis, we conducted a translational investigation comprising both animal and human studies to evaluate the sleep-promoting effects of NIR PBM.

Materials and methods:

In the animal study, mice were implanted with a fiberoptic cannula on the skull surface fixed with dental cement, allowing localized delivery of 810 nm filtered NIR light. EEG recordings were obtained to assess sleep architecture. Intracerebral levels of adenosine were measured by microdialysis and cytochrome c oxidase activity of the illuminated area of brain was quantified. For a randomized sham-controlled double-blind clinical trial (RCT), a wearable PBM device consisting of 32 NIR LEDs (810 nm) was developed for application to the forehead. Forty participants with subthreshold insomnia (defined by Insomnia Severity Index, ISI) were randomly assigned to either PBM or sham stimulation groups. Following a 2-week baseline period, participants received 1 week of nightly intervention. Subjective sleep quality was evaluated using the ISI, Pittsburgh Sleep Quality Index (PSQI), and Epworth Sleepiness Scale (ESS). Objective sleep parameters were monitored via actigraphy using a wearable watch and a data collection system (Labfront Research Tool: www.labfront.com). A two-way repeated measures ANOVA was employed to analyze the main effects of Time, Group, and Time × Group interaction.

Results:

In the animal study, NIR PBM significantly increased NREM sleep duration and delta power on EEG. Biochemical assays confirmed elevated adenosine levels and enhanced cytochrome c oxidase activity, supporting increased mitochondrial function. In the RCT, the PBM group demonstrated statistically significant reductions in ISI, PSQI, and ESS scores after the intervention with large effect sizes (Cohen's $d = 1.08$ and 0.78 for ISI and PSQI, respectively), while the sham group showed non-significant changes. Notably, ISI and PSQI scores exhibited significant Time × Group interactions ($P = 0.007$ and 0.011 , respectively), indicating a differential improvement in the PBM group over time. Actigraphy-based sleep analysis is ongoing.

Conclusions: This translational study provides converging preclinical and clinical evidence that transcranial NIR photobiomodulation enhances sleep, potentially via increased adenosine signaling. The findings support the feasibility of NIR PBM as a non-pharmacological intervention for sleep enhancement and warrant further trials in patients with clinically diagnosed insomnia.

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AI-Based Contactless Sleep Monitoring for Early Detection of Mood Dysregulation in Hospitalized Patients

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Introduction: Sleep disturbances are both a symptom and an early warning sign for mood disorders, including depression and bipolar disorders. Poor sleep quality not only impairs recovery but is also associated with increased risks of emotional instability, aggression, and suicide. These sleep-related issues are often underrecognized in psychiatric wards. Early and continuous monitoring of sleep may provide crucial opportunities for proactive intervention in vulnerable patients. This study aims to

develop a contactless, AI-driven sleep monitoring system based on smart mattress technology to detect physiological changes associated with mood disorder exacerbation. The goal is to enhance early detection of emotional dysregulation and support timely psychiatric intervention.

Materials and methods: This study consists of two phases. In the first phase, the smart mattress system (Huijia Health Life Corporation) will be calibrated against gold-standard polysomnography (PSG) in healthy individuals to evaluate its validity and sensitivity for sleep stage detection and physiological signal reliability. In the second phase, psychiatric inpatients diagnosed with depression or bipolar disorder will undergo continuous overnight monitoring using the smart mattress, which captures heart rate, respiration, and body movement. Supervised machine learning algorithms will be used to model the association between sleep dynamics and clinical indicators of mood instability. SHAP will be applied to interpret model outputs and determine key contributing features.

Results: We anticipate developing a validated supervised learning model capable of detecting early changes in sleep patterns that indicate deterioration of mood disorders. The system is expected to provide real-time insights to assist clinical teams in decision-making and intervention planning.

Conclusions: Integrating AI-assisted, contactless sleep monitoring into psychiatric care may significantly improve early detection and clinical management of mood disorders. This approach has the potential to enhance patient safety, support timely treatment, and improve the overall quality of psychiatric care.

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AI-based Prediction Model of Alzheimer's Disease From Polysomnographic Records: A Preliminary Study

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia, primarily affecting memory, cognitive function, and behavior. Thus, a convenient and accurate screening method is critical for the early detection of AD. This study aimed to develop an AI-based prediction model for prescreening Alzheimer's disease using nocturnal polysomnographic (PSG) recordings.

Materials and methods: Real-world clinical PSG data were collected from 150 subjects (100 controls and 50 with AD) from the MrOS sleep study. We proposed a hybrid deep learning model that combines convolutional and recurrent neural network architectures, optimized through dropout and batch normalization. The model extracted and analyzed complex patterns from nocturnal EEG signals. PSG data were preprocessed, segmented into 30-second intervals, and evaluated using 5-fold cross-validation.

Results: The AI-based prediction model showed promising performance, achieving an accuracy of 76.19%, a sensitivity of 77.35%, and a specificity of 74.73% in screening for AD.

Conclusions: Our preliminary results demonstrate the feasibility of using AI-based PSG analysis for AD prescreening. The proposed model has potential as a practical and non-invasive tool for early detection and monitoring of neurodegenerative disorders.

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An innovative solution to positional therapy for obstructive sleep apnea - Pilot Study

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Introduction: Obstructive sleep apnea (OSA) is a prevalent global health issue, with a significant subset, positional OSA (POSA), affecting up to 60% of patients. While continuous positive airway pressure

(CPAP) is the gold standard treatment, poor compliance due to discomfort remains a major limitation. Existing positional therapies often act as aversive stimuli, leading to suboptimal long-term adherence. This pilot study evaluated a novel, comfort-focused approach using a commercially available G-shaped maternity pillow as a positional therapy device for POSA, hypothesizing that its supportive design would effectively maintain lateral sleep positioning and improve respiratory outcomes.

Materials and methods: In this prospective pilot study, 18 adult patients with confirmed POSA (per Cartwright's criteria) were enrolled. The study protocol involved: (1) a baseline inpatient polysomnography (PSG) without intervention; (2) a two-week actigraphy period to establish baseline sleep patterns; (3) a subsequent inpatient PSG with the G-shaped maternity pillow; (4) Psychomotor Vigilance Task (PVT) testing pre- and post-intervention; and (5) validated sleep questionnaires (Karolinska Sleepiness Scale, Samn-Perelli Fatigue Scale, PANAS) to assess subjective sleep quality, alertness, and mood. Respiratory indices, sleep architecture, and sleep position data from the two PSGs were compared using paired statistical tests.

Results: Use of the maternity pillow resulted in a significant improvement in respiratory parameters. The median apnea-hypopnea index (AHI) decreased from 17.5 to 8.92 events/hour ($p<0.01$) and the oxygen desaturation index (ODI) from 14.8 to 6.41 events/hour ($p<0.01$). The pillow was highly effective in enforcing lateral sleep, increasing the median lateral sleep time from 19.7% to 84.2% of total sleep time ($p<0.01$). Although total sleep time and sleep efficiency decreased during the single-night intervention, participants demonstrated improved morning alertness on PVT testing (faster response times, $p=0.03$) and reported less fatigue ($p=0.02$). Patient acceptance was notably high, with 83.3% preferring the pillow over CPAP and 61.1% continuing its use post-study.

Conclusions: These preliminary findings suggest that a G-shaped maternity pillow is an effective and well-tolerated positional therapy for POSA, significantly reducing AHI and ODI by successfully promoting lateral sleep. Its high acceptance rate highlights its potential as a comfortable and accessible alternative for CPAP-intolerant patients. This study introduces a promising new category of positional therapy based on positive support rather than aversion. Larger, long-term trials with an acclimatization period are warranted to confirm these efficacy and compliance findings in a real-world setting.

An Integrated EEG-Respiratory Home Sleep Monitoring System for Sleep Staging and Arousal Detection in Obstructive Sleep Apnea Screening

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Introduction: Obstructive sleep apnea (OSA) has a high prevalence and is associated with serious health risks, yet patients in Taiwan often face waiting periods exceeding six months for a polysomnography (PSG) test due to limited bed availability at sleep centers. Home sleep test offers an alternative approach to address this issue; however, current devices typically measure only respiratory parameters. The absence of EEG signals prevents the detection of arousal events, leading to an underestimation of the Apnea-Hypopnea Index (AHI). Moreover, without EEG data, it is difficult to objectively assess sleep quality impacted by OSA. Therefore, a home sleep monitoring system that integrates EEG and respiratory signals is highly desirable.

Materials and methods: We developed an integrated home-based sleep monitoring system combining a self developed EEG eye mask to capture Fp1, E2, and F3 channels with ApneaLink Air to measure airflow, respiratory effort, and oxygen saturation. This system enables synchronized, high-quality recording of both brain and respiratory signals over eight hour sleep periods. A scoring platform was also developed that integrates a web based scoring interface and assisted labeling of events and wave candidates for manual scoring. A validation study was conducted at National Cheng Kung University Hospital and the data from 21 participants (aged 25-67 years, AHI range: 5.8-72.6 events/hour) undergoing simultaneous overnight recordings using both our system and standard PSG. Sleep staging and arousal events were manually scored by clinical technicians. Agreement between the scoring results of the eye masks and the PSG was evaluated using mean differences for key sleep indices: Total Sleep Time (TST), Wake After Sleep Onset (WASO), Sleep Onset Latency (SOL), and Sleep Efficiency

(SE), kappa and average agreement for sleep staging, and correlation analysis for the arousal Index. These metrics were used to assess measurement consistency and potential bias.

Results: The mean differences between our system and PSG measurements were SOL = 0.07 minutes, WASO = 6.26 minutes, SE = -1.72%, and TST = -6.90 minutes. For sleep staging between our system and PSG, kappa = 0.81 with an agreement of 90.3%, based on a four-stage classification: Wake, Light sleep (combining N1 and N2), N3, and REM. A strong correlation ($r = 0.83$) was also observed for the arousal index. Furthermore, our system demonstrated significantly higher AHI and HI values compared to ApneaLink ($p < 0.001$), as the integration of EEG-based arousal detection enabled more accurate identification of respiratory-related events.

Conclusions: We propose an integrated EEG-respiratory home sleep monitoring system to enable synchronized, high-quality recording of brain and respiratory signals over eight-hour sleep periods. The validation experiments demonstrated high agreement between the proposed system and standard PSG across subjects with varying AHI severities. In addition, the EEG signals support the detection of arousal events, leading to more accurate AHI estimation. This system is expected to improve the quality of sleep diagnostics and help reduce wait times for sleep testing in the near future.

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A novel ECG-Based Machine Learning Pipeline for Screening Major Depressive Episodes in Sleep Disorder Patients

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Introduction: Major Depressive Episodes are a significant global health challenge, often co-occurring with sleep disorders. Accurate and efficient screening for current MDE (cMDE) in patients undergoing evaluation for sleep disturbances could improve diagnostic efficiency and treatment outcomes. Traditional diagnostic methods for cMDE, such as clinical interviews and questionnaires, are resource-intensive and require significant clinical expertise.

Advances in machine learning (ML) and physiological data analysis have opened new avenues for leveraging objective signals like ECG to screen for cMDE. Polysomnography routinely captures ECG signals, providing a unique opportunity to explore their potential in identifying autonomic and sleep-related patterns indicative of depressive symptoms.

This project aims to investigate the accuracy of a pipeline of ML algorithms that allow screening for cMDE using only ECG as a physiological signal in subjects undergoing in-patient polysomnography.

Materials and methods: 296 subjects from a recently completed prospective, single-arm, non-randomized cohort study have been used to investigate the screening performance of the cMDE determination pipeline compared to the MINI neuropsychiatric interview. All subjects recruited in this study were referred for inpatient polysomnography due to suspected sleep disorders.

The cMDE determination pipeline begins with a deep learning algorithm that classifies sleep stages using only the lead-II ECG signal. Subsequently, heart rate (HR) and heart rate variability (HRV) metrics are computed across the identified sleep stages, and macrostructure indices derived from the ECG-based sleep staging are calculated. Finally, HR and HRV metrics and macrostructure indices are combined with the responses to items 1 and 2 of the PHQ-9 questionnaire and used as input for an ML algorithm to perform the final cMDE determination.

Results: The observed sensitivity relative to the MINI cMDE determination was 80.85% (95% CI: 66.74%-90.85%), the specificity was 71.37% (95% CI: 65.31%-76.91%), the positive predictive value was 34.86% (95% CI: 25.99%-44.58%), and the negative predictive value was 95.16% (95% CI: 91.01%-97.76%).

Conclusions: The proposed machine learning pipeline leveraging the ECG as a physiological signal demonstrates promising potential as a screening tool for cMDE in patients undergoing polysomnography for suspected sleep disorders.

A novel, wearable, in-ear EEG technology to assess sleep and daytime sleepiness

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Introduction: In laboratory polysomnography (PSG) is the gold standard for assessing sleep and excessive daytime sleepiness (EDS), but is time, labor, and cost intensive and has limited diagnostic utility. Thus, a substantial unmet clinical need persists for measures that are more readily accessible and accurate for detecting sleep and EDS. Here, we describe the usability and validity of an in-ear electroencephalogram (Ear-EEG) device alongside PSG and maintenance of wakefulness testing (MWT) in healthy participants (NCT05114616), and participants with narcolepsy (NT) or idiopathic hypersomnia (IH), both on and off their wake-promoting medications (NCT05066009).

Materials and methods: Eight clinic patients with NT/IH underwent standard MWTs during two visits while wearing NextSense's Ear-EEG device, one during a site-blinded, randomized drug holiday to assess treatment effect. Sixteen healthy participants underwent 4-hour sleep-restricted PSG to assess increased sleep pressure during MWT. Subjective sleepiness (Karolinska Sleepiness Scale) was assessed post-MWT, whereas objective vigilance and working memory were assessed only after sessions 1 and 3 by Psychomotor Vigilance Task (PVT) and NBack Trials, respectively. Device comfort and usability were assessed by questionnaire. PSG and Ear-EEG recordings were scored for sleep stages independently by three scorers blind to subject and condition. Within-and-between rater agreement between PSG and Ear-EEG-based sleep staging was in accordance with AASM standards. Pre-trained SleepTransformer model was adapted to Ear-EEG via direct transfer and fine-tuning, with performance evaluated using Macro-F1 (MF1) and Cohen's Kappa. Mixed models were used to analyze sleep-related and treatment-related outcomes.

Results: There was high agreement between the accuracy of the 3 raters (82.7%) in healthy controls. The Nextsense Ear-EEG device demonstrated robust agreement with PSG for Wake (90%) and N2 (83%); moderate agreement for REM-sleep (74%), N3 (66%), and slightly lower for N1 (56%). Automatic scoring using the Sleep Transformer adapted to Ear-EEG resulted in a MF1 score of 80.0%, a Kappa coefficient of 85.8% with human scorers, and an accuracy (90.9%) superior to human annotators. Most metrics (SOL, TST, REM, N2/N3 durations and latencies, WASO, and SE) were similar between PSG-EEG and Ear-EEG (all $p > 0.05$), except that 5.63 min more N1 sleep was derived via Ear-EEG ($p = 0.0025$). The mean difference in SOLs during MWTs was small (-0.68 min, $p = 0.7321$), and even lower for overnight SOLs in healthy participants (-0.16 min, $p = 0.9034$). SOLs did not differ significantly between PSG-EEG or Ear-EEG, $p > 0.05$. In NT/IH, SOL was greater On-Drug compared to Off-Drug (21.49 ± 15.24 vs 7.93 ± 7.96 , $p = 2 \times 10^{-16}$). Vigilance was greater and less variable On-Drug than Off-Drug with these changes being associated with SOL (Interaction with Slowest 10% $p = 0.0003$ and Lapses $p = 0.003$). Working memory was faster but less accurate On-Drug than Off-Drug and associated with SOL (Interaction with Accuracy $p = .002$ and Correct RT $p = 2.59 \times 10^{-12}$). Participants reported the Ear-EEG as very comfortable on a 10-point scale (Healthy: 7.9 ± 1.3 , NT/IH: 8.7 ± 1.1).

Conclusions: NextSense's Ear-EEG device advances the collection of accurate sleep-wake state metrics reflective of clinically relevant signs and symptoms (e.g., sleepiness, vigilance, and memory). It offers a comfortable, accurate alternative to PSG for assessing sleep and daytime sleepiness.

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Apnea Detector Across Multiple Cohorts Reaches Expert Level Performance

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Introduction: Sleep disordered breathing (SDB), the repeated occurrence breathing events like obstructive apneas (OA), central apneas (CA), and hypopneas (HYPO), affects millions globally and contributes to significant morbidity. Diagnosing SDB requires manual scoring of polysomnography (PSG) recordings, a labor-intensive process marked by high inter-rater variability and inconsistent application of scoring rules. Despite the availability of automated scoring tools, most have limited

generalizability due to training on single-center datasets and an inability to distinguish among event subtypes. We developed the Apneic Breathing Event Detector (ABED), a deep learning-based tool designed to detect and classify OA, CA, HYPO, and isolated respiratory events without arousals or desaturations (IREs). ABED aims to increase accuracy, reduce scoring burden, and enable more consistent, scalable SDB evaluation across centers.

Materials and methods: ABED was trained on 5,456 full-night PSGs from four large cohorts available through the National Sleep Research Resource. An independent test set of 1,099 PSGs, spanning all four cohorts, was used for evaluation. In addition, ABED was tested on two external datasets including 113 subjects scored by multiple independent experts. Input channels included cannula flow, oral thermistor, thoracic and abdominal effort, SpO₂, and probabilities of wake and arousal derived from previously validated EEG-based models. Each PSG was processed in overlapping 240-second windows. ABED's deep learning architecture combined convolutional layers (based on a modified ResNet50), bi-directional LSTMs, and YOLO detection heads for event classification and localization.

Results: Across all test cohorts, ABED achieved a mean F1 score of 0.78 for apnea event detection, with specific F1 scores of 0.71 for OA, 0.51 for CA, and 0.65 for HYPO. The model also detected IREs, capturing events with clear respiratory effort reductions but no associated desaturations or arousals. Predicted apnea-hypopnea index (AHI) values strongly correlated with expert annotations ($R^2 = 0.84$), and ABED correctly classified sleep apnea severity in 75.3% of cases. In external, expert-scored datasets, ABED performed comparably or better than individual scorers, matching human-level detection accuracy across event types. Performance was robust to differences in scoring criteria and generalizable across sites and populations. Signal quality analysis revealed ABED maintained stable performance across a range of signal conditions, with mild degradation only for poor-quality thoracic excursions and EEG signals.

Conclusions: ABED is a robust and generalizable deep learning model for expert level automated detection and classification of SDB events, including less commonly recognized IREs. Its performance is consistent across diverse cohorts, hypopnea scoring definitions, and expert annotations, offering a scalable solution to address the current challenges of manual PSG scoring.

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Apnea-Hypopnea Event Detection from 10-Second Sleep Audio Clips: A Machine Learning Model

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Introduction: Sleep apnea is a prevalent sleep disorder with serious health consequences, underscoring the need for accurate and accessible detection methods. Current diagnostic standards, such as overnight polysomnography (PSG), are expensive and inconvenient. We propose a novel machine learning approach that utilizes pre-trained large audio models to analyze raw audio waveforms—such as 10-second segments of breathing or snoring sounds—for apnea detection. To enhance performance, we introduce a multi-task learning framework that addresses both apnea detection and sleep stage classification, leveraging the physiological relevance of sleep stages. This combination of a pre-trained audio encoder and multi-task learning is designed to improve generalization and robustness in identifying apnea events.

Materials and methods: The proposed framework comprises two main components: a pre-trained audio encoder and a multi-task classifier. We use HuBERT, a state-of-the-art self-supervised audio model, to convert raw 10-second waveform segments into compact feature embeddings. These embeddings serve as input to a downstream classifier consisting of a shared feature extractor ("bottom" network) followed by two task-specific branches: one for binary apnea classification (apnea vs. no-apnea) and another for sleep stage classification (Wake, REM, NREM). Each branch includes a lightweight task-specific encoder and prediction head built atop the shared representation. The model is trained end-to-end in a multi-task learning (MTL) setup, optimizing a combined loss from both tasks.

Incorporating sleep stage information provides important physiological context—for example, certain sleep stages may correlate with higher apnea occurrence—thereby guiding the model to learn more robust features that improve apnea detection.

Results: Preliminary evaluation on a held-out test set yielded promising performance. The proposed multi-task model achieved an accuracy of 84.8% and an area under the curve (AUC) of 0.810 for binary apnea classification. These results demonstrate that our model can reliably distinguish apnea events from normal breathing using only short audio segments. Importantly, incorporating sleep stage classification as an auxiliary task improved overall apnea detection performance compared to a single-task baseline, confirming the benefits of multi-task learning. We also employed a dynamic loss weighting strategy to balance optimization between the two tasks, which further enhanced training stability and performance. The current model architecture—comprising a HuBERT-based audio encoder and a shared-bottom, task-specific multi-task classifier—proved effective in learning generalizable audio features and context-aware physiological representations.

Conclusions: In conclusion, this study demonstrates that combining pre-trained large audio models with multi-task learning offers a promising approach for automatic sleep apnea detection. By leveraging HuBERT as an acoustic feature extractor and jointly training on apnea detection and sleep stage classification, the model captures both general audio patterns and context-specific physiological cues. The resulting accuracy and AUC indicate that this audio-based method can serve as a non-invasive, efficient tool for sleep apnea screening in both clinical and home settings. Future work will explore alternative foundation audio models, incorporate additional physiological signals, and validate the approach on larger and more diverse populations to support real-world deployment.

A randomized controlled trial to evaluate digital cognitive behavioral therapy for insomnia (CBT-I) with artificial intelligence chatbot for youth with insomnia: Preliminary results

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Introduction: Digital cognitive behavioral therapy for insomnia (CBT-I) has shown to be effective in improving insomnia among youths. Research suggests that digital interventions are more effective when they incorporate interactive elements. Artificial intelligence (AI) chatbots have the potential to transform digital CBT-I into an interactive, conversational tool. This randomized controlled trial aims to evaluate the efficacy of an app-based CBT-I with an AI chatbot in alleviating insomnia symptoms in youths compared to an app-based CBT-I without an AI chatbot.

Materials and methods: The study was a randomized controlled trial that recruited participants aged 18-25 years with moderate to severe insomnia, as indicated by a score of 14 or higher on the Insomnia Severity Index (ISI), and meeting DSM-IV-TR criteria for insomnia disorder. Exclusion criteria encompassed a history of sleep disorders other than insomnia, mental retardation, serious suicidality, current pharmacological treatment, structured psychotherapy, or recent shiftwork/trans-meridian travel. Eligible participants were randomly assigned to either the intervention group, receiving an app-based CBT-I with AI chatbot, or the control group with an app-based CBT-I without AI chatbot, in a 1:1 ratio using permuted block randomization with block sizes of 2, 4, or 6 participants, stratified by gender and insomnia severity. Both interventions lasted for 28 days, with participants progressing through four CBT-I modules (28 daily units) sequentially. In the intervention group, participants interacted with the chatbot through free-text input or predefined response options, with the chatbot providing standardized statements and follow-up questions. Assessments were conducted at baseline (T0), 2-week interim (T1), post-intervention (T2), 3-month follow-up (T3), and 6-month follow-up (T4). An intent-to-treat analysis using a mixed-effects model for repeated measures was utilized to evaluate the effect on the primary outcome, the ISI.

Results: Among the 87 participants recruited, 44 participants (mean age=21.3±2.24 years; 61.4% female) were assigned to the intervention group, while 43 participants (mean age=21.0±2.29 years; 60.5% female) were allocated to the control group. Both groups exhibited significant improvements in

ISI scores at post-intervention ($d=2.15-2.41$, $p<.001$). However, the intervention did not yield a better treatment outcome compared to the control group ($d=0.37$, $p=.36$). Over the follow-up periods, the effect in the control group remained stable ($d=2.30-2.74$, $p<.001$), while the effect in the intervention group continued to increase ($d=3.53-3.71$, $p<.001$). By T4, a significant difference emerged between the control group (mean ISI= 12.0 ± 6.16) and the intervention group (mean ISI= 6.00 ± 4.83), indicating that the intervention group had more significant improvement (effect size $d=1.47$, $p=.04$). A significant time x group interaction effect ($\beta=-4.80$, 95% CI: -9.59 to -0.01 , $p=.04$) were observed.

Conclusions: The study is currently in progress with the goal of recruiting 168 participants. Preliminary findings suggest that utilizing an AI chatbot as a new tool to deliver digital CBT-I shows potential by providing interactive features and enhancing efficacy. This approach may increase service accessibility at a lower cost, potentially alleviating the worldwide impact of insomnia.

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Are different Transcutaneous Carbon Dioxide (TcCO₂) monitor brands in positive correlation and agreement?

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Introduction: Transcutaneous carbon dioxide (TcCO₂) measurement is essential for the diagnosis of nocturnal hypoventilation. These measurements however have a wide margin of error, with the literature stipulating the clinically acceptable range of TcCO₂ measurement being $\pm 7.5\text{mmHg}$ ($\pm 1\text{kPa}$). Sleep laboratories largely utilise the Sentec SDM™ or Radiometer TCM5™ for TcCO₂ measurement. To date, there are no studies that have investigated the agreement of these devices against each other. In this study, we investigated whether the TcCO₂ values derived from the Sentec SDM™ monitor correlated with the Radiometer TCM5, and comparing these measures to PCO₂ derived from Capillary Blood Gas (CBG). We also assessed how well these values agreed with each other. We hypothesised that there would be strong positive correlations between TcCO₂ measurements and PCO₂, and agreement would be observed between these measures.

Materials and methods: 59 patient measurements of TcCO₂ from Sentec™ and Radiometer™ probes were collected. The measurement site for the TcCO₂ probes was inferior to the clavicle, as recommended by Sentec™ and Radiometer™. PCO₂ was sampled via lancet prick at the earlobe for confirmation of TcCO₂ readings once stabilised prior to sleep study commencement (PM), and immediately on termination of the sleep study (AM). Data was assessed for normality. Correlation between metrics was assessed via Pearson and Spearman correlation coefficients. Agreement was assessed via Bland-Altman plots.

Results: Strong positive correlations were demonstrated between metrics (Correlation values ranged from 0.741-0.888, all p values < 0.001). Close agreement was demonstrated across all metrics.

Conclusions: This study demonstrated that TcCO₂ measured via Sentec SDM™ and the Radiometer TCM5™ were in strong positive correlation with each other and PCO₂, with these measurements showing agreement within the sleep laboratory context. This provides confidence to sleep laboratories that TcCO₂ monitor choice should not affect the quality of the data being collected. Most samples collected in this study however were normocapnic. Further investigation of agreement between these devices in cases of nocturnal hypoventilation is required to ensure condition diagnosis is consistent irrespective of the TcCO₂ monitor being used.

Acknowledgments: Thanks to Sentec for the provision of their SDM monitors for the study.

A Screening Alternative for Depressive Episodes in COMISA: A Comparative Evaluation of a Novel Software Compared to Neuropsychometric Assessments

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Introduction: In recent years, numerous studies have focused on enhancing the understanding of sleep disorders within military, veteran, and civilian populations. Among these, insomnia and obstructive sleep apnea (OSA) have emerged as the two most prevalent sleep disorders affecting both military personnel and civilians.

The term COMISA was introduced to describe the co-occurrence of insomnia and OSA, highlighting the significant burden associated with this dual condition. Research has shown that COMISA is associated with more severe mental health challenges compared to insomnia or OSA alone.

The aim of this study is to investigate the agreement between the determination for current Major Depressive Episodes (cMDE) made by the MEB-001 software (Medibio Limited) and the MINI's cMDE diagnosis across specific clinical subgroups. These include individuals with suspected insomnia but no confirmed sleep apnea, individuals with confirmed sleep apnea but no suspected insomnia, and those with COMISA.

Materials and methods: This study analyzes data from the recently completed prospective, single-arm, non-randomized cohort study. The subjects recruited in this study were referred for an inpatient polysomnography for suspected sleep disorders.

Results: In a preliminary analysis, in the subgroup of subjects with insomnia but no confirmed sleep apnea (n=55), the observed sensitivity relative to the MINI cMDE determination was 90.91% (95% CI: 58.72%-99.97%), the specificity was 61.36% (95% CI: 45.50%-75.64%), the PPV was 34.17% (95% CI: 9.69%-53.48%), and the NPV was 96.43% (95% CI: 81.65%-99.91%). Instead, in the COMISA subgroup (n=147), the observed sensitivity relative to the MINI cMDE determination was 88.46% (95% CI: 69.85%-97.55%), the specificity was 71.07% (95% CI: 62.13%-78.95%), the PPV was 39.66% (95% CI: 27.05%-53.36%) and the NPV was 96.63% (95% CI: 90.46%-99.30%).

Conclusions: The MEB-001 software demonstrated strong sensitivity and high negative predictive value for detecting current Major Depressive Episodes (cMDE) across clinical subgroups, particularly in individuals with COMISA and insomnia without sleep apnea.

A Smartphone-based Intervention to Improve Light Exposure in Young Adults

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Introduction: Light exposure patterns play a critical role in regulating circadian rhythms and promoting optimal sleep quality. Modern lifestyles often involve insufficient daytime sunlight exposure and excessive artificial light at night, disrupting sleep-wake cycles and impairing alertness and cognitive performance. Smartphone-based behavioural interventions offer a promising scalable approach to optimize individual light exposure and health. In this study, we introduce a novel, digital, smartphone-based intervention that tunes behaviour to optimize light exposure—enhancing daytime light intake while reducing nighttime exposure—with the goal of improving sleep quality and daytime functioning in young adults.

Materials and methods: Seventeen healthy young male adults (average age $\pm$ SD = 28.1 $\pm$ 4.5 years) participated in this study comprising a baseline and an intervention phase (10–14 days each). Light exposure was measured using wearable sensors with a 1-min sampling rate, for the continuous quantification of illuminance, spectral composition of light, and melanopic Equivalent Daylight Illuminance (mEDI). Daytime outdoor time (7AM–7PM) was estimated using a machine learning model trained to classify light data as indoor or outdoor. Sleep quality and duration were monitored using the same devices and sleep diaries. Baseline sleep quality and daytime sleepiness were assessed using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS), respectively. During the intervention phase, participants received personalized WhatsApp nudges encouraging greater daytime exposure and reduced evening exposure to light. Evening nudges were sent three hours before baseline average bedtime. Outcome measures included time spent outdoors and above the recommended 250 mEDI (in minutes and as a percentage of wear time), average mEDI levels during daytime, as well as sleep metrics (e.g. Bed time, Get up time, Time in bed, Sleep efficiency, number of awakenings, etc.).

Results: At baseline, participants reported a mean PSQI score of 5.6 $\pm$ 3.3 and an ESS score of 7.2 $\pm$ 3.3. The digital intervention successfully enhanced outdoor time in 14 out of 18 participants (77.8%).

That increment ranged between 4 to 78 minutes of outdoor time per day with improvements being more pronounced on weekdays compared to weekends. On average, on weekdays, daily outdoor time was increased from 84.6 ± 48.9 (at baseline) to 100.5 ± 51.7 minutes ($p = 0.03$). Accounting for the sensor's wear time, this translated to an increase from $12.6 \pm 7.2\%$ to $15.6 \pm 7.1\%$ ($p = 0.01$) of outdoor time during daytime. Time spent above 250 mEDI was also increased from $15.0 \pm 8.9\%$ to $18.7 \pm 9.2\%$ ($p = 0.008$). Additionally, mEDI levels increased marginally from 350.6 ± 280.2 lx to 470 ± 272.7 lx ($p=0.07$) during waketime. These outcome measures were not different between baseline and intervention on weekends. Nighttime mEDI levels and most sleep metrics were comparable between conditions, with fewer maximum awakenings during the intervention ($p=0.04$).

Conclusions: Our findings demonstrate the potential of a scalable smartphone-based intervention to enhance weekday light diets in young adults living busy, modern lifestyles. By significantly increasing daytime light exposure and mEDI, our approach holds promise for enhancing circadian alignment, reducing daytime sleepiness and performance, and improving nighttime sleep.

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A technical and clinical validation of ElvySense Medical for sleep apnea diagnostics

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Introduction: Sleep apnea is a highly prevalent but underdiagnosed disease. Sleep registrations needed to confirm sleep apnea diagnosis require a high amount of manual labour, and currently these methods do not allow continuous follow-up measurements. In this study, we performed a technical and clinical validation for ElvySense Medical system that is a self-applied stand-alone device for sleep apnea detection. The device consists of a pressure-sensitive electromechanical film-like sensor placed under the mattress, an oximeter, a separate control device and an automated analysis software. It aims to fill current diagnostic gaps providing respiratory and associated event scoring and the possibility to use the device as an easy-to-use diagnostic and screening tool as well as a follow-up monitor.

Materials and methods: We recruited and measured 56 individuals (34.0% female, mean (SD) age = 51.6 (12.1), mean (SD) BMI = 30.8 (5.5)) based on clinical home sleep apnea test (HSAT) done at Kuopio University Hospital aiming at equal number of volunteers for each sleep apnea severity group. Based on baseline HSAT, 9 had no, 16 had mild, 16 had moderate and 15 had severe sleep apnea based on apnea-hypopnea index (AHI). The volunteers underwent type I polysomnography (PSG) at SmartSleep Laboratory (University of Eastern Finland, Kuopio, Finland) and simultaneous ElvySense Medical measurement before their possible treatment initiation. After scoring, the performance of ElvySense Medical was evaluated by first comparing the number of scored events and estimated sleep time. Second, we utilized Pearson's r and Wilcoxon's signed-rank to test the agreement of the PSG AHI and ElvySense Medical AHI. Third, we calculated the sensitivity and specificity of the ElvySense Medical in detecting moderate-to-severe sleep apnea.

Results: Measurements had 95% success rate: three measurements out of the total 56 failed due to a technical issue in the ElvySense Medical, leaving 53 recordings for the data analyses. Based on in-lab PSG, 6 had no, 12 had mild, 12 had moderate and 24 had severe sleep apnea. The median PSG AHI and ElvySense Medical AHI did not differ significantly (25.5 vs. 23.3, $p=0.13$) and the correlation between them was 0.79 ($p<0.01$). The ElvySense Medical differentiated those with $AHI \geq 15$ with a sensitivity of 94.3% and specificity of 72.2%. On average, ElvySense Medical scored 40.2 apneas more and 7.9 hypopneas less than was scored to PSG, utilizing 2.02 hours longer estimated sleep time than PSG-based total sleep time.

Conclusions: The ElvySense Medical system shows high sensitivity and acceptable specificity in differentiating individuals having moderate-to-severe sleep apnea from those being healthy or having mild sleep apnea with only a few failed measurements. The strong positive correlation between the AHI's indicates diagnostic accuracy comparable to standard HSAT with considerably less manual labour.

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Automated distinctive apnea type analysis from pulseoximetry signal only

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Introduction: The use of pulseoximetry and the signal of arterial oxygen saturation for early detection and screening of sleep disordered breathing based on the number of oxygen desaturations (ODI), the mean oxygen saturation and the time of oxygen saturation below 90% is widely acknowledged since the 1990's. In 2001 we presented in an overview in the journal Chest with figures of the different shapes of the oxygen saturation curve with the different types of apneas and hypopneas. At this time this was meant as an add on for the manual visual analysis of apneas and hypopneas. Now, with the increasing possibilities of AI supported automated analysis even in wearables it was time to consider using the findings of 2001 for a much advanced automated analysis of the oxygen saturation curve. The idea arose to use the angle of the uprising leg of the oxygen curve after the apneic dip to determine a mathematical value usable for further automated calculation.

Materials and methods: We put an angle on the visually recorded 50 each consecutive central, complex, and obstructive apneas as well as hypopneas from the polysomnographs (Sleep Doc Porti, Fenyves und Gut, Rangendingen, Germany) of five different male patients (mean age 62,4 years) and analyzed the mean difference of the angles of the different apnea types via T-test in MS Excel as well as we calculated the mean angles for the different apnea type.

Results: The angles of the uprising leg after desaturation dip of the different apnea types and hypopneas differ significantly ($p < 0.05$). The mean of the angle on the uprising leg of the oxygen saturation curve after a desaturation dip of central apneas is the most flat with an average of 27°. The average angles of obstructive apneas was the steepest with 79°, complex respectively mixed apneas had an average angle of 65° and hypopneas an significantly flatter angle of 33°.

Conclusions: The differentiation of the angles of the uprising leg of the oxygen saturation curve after a desaturation dip can most likely be used for an analysis of different apnea types without the need of the respiratory curves of respiratory belts or the the flow from a nasal thermistor or nasal pressure recording. With the help the learning possibilities (generative pretraining) of artificial intelligence and the use of such a technology built in wearables the distinction of central and obstructive sleep apnea, so far not possible without polygraphy or polysomnography, could be possible in the near future.

Automatic Nap Detection During MSLT and MWT Using Wearable Sensors in Patients with Sleep Disorders

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Introduction: Short daytime sleep episodes, or naps, are increasingly recognized as valuable biomarkers for hypersomnolence and neurodegenerative conditions. Their accurate detection is important for diagnosis and disease monitoring. In clinical settings, naps are assessed via polysomnography (PSG) during the Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness Test (MWT). While well-established, these procedures are labor-intensive and limited to single-day hospital-based recordings. Wearable devices offer a promising alternative for nap detection in real-life conditions. However, most existing algorithms are optimized for long-duration nocturnal sleep and perform poorly on shorter naps than one hour. This study aims for automatic short nap detection using data from a wristband (Empatica E4) recorded in parallel with PSG during MSLT and MWT in sleep patients with sleep disorders.

Materials and methods: Patients were recruited at the University Hospital of Bern, Switzerland. The dataset includes 188 Empatica recordings from 35 individuals with suspected or diagnosed sleep disorders, amounting to approximately 80 hours of raw signal data, including manual sleep staging by

clinical experts. The wristband provided 32 Hz accelerometer data and 1 Hz heart rate data, which were downsampled and combined to simulate the lower-resolution inputs typical of consumer-grade devices. To classify 30-second epochs as sleep or wake, we implemented a compact Temporal Convolutional Network. Inputs were structured into 270-second windows with a 30-second stride, and the network processed 1 Hz activity and heart rate signals through seven residual blocks using dilated convolutions, batch normalization, rectified linear unit activation function, and dropout. A time-distributed linear layer outputs a sleep probability for each epoch. The model was trained against manual sleep staging using class-weighted binary cross-entropy, the Adam optimizer, and early stopping. A 10% holdout set was reserved for final evaluation, while the remaining 90% was used for 5-fold cross-validation and hyperparameter tuning.

Results: On the independent holdout set, the model achieved an accuracy of 0.75, a precision of 0.67, a recall of 0.78, and an F1 score of 0.72 for the detection of short naps with an average duration of 15 minutes. These results demonstrate a clear improvement over naive baselines ("always wake," "always sleep," and class-balanced random), whose F1 scores ranged from 0 to 0.55. Performance was robust across participants, with the model successfully identifying short naps despite the subtle physiological changes and minimal movement typical of MSLT and MWT sessions.

Conclusions: The dataset poses inherent challenges: during MSLT and MWT, participants often remain physically still while awake, making activity-based sleep detection difficult; furthermore, heart rate changes may be subtle. Nevertheless, the model achieved strong performance under these conditions, suggesting good potential for generalization. Importantly, this approach uses only low-resolution features from widely used consumer wearables, making the model easily transferable to large datasets collected outside clinical settings. These encouraging results support future testing on larger, more diverse populations and in free-living conditions, with the potential to enhance large-scale nap detection from commercial devices. This model lays the foundation for real-world ambulatory monitoring of hypersomnolence and related disorders using wearable technologies.

A Web3-Based System for Decentralized Sleep and Circadian Health Data Sharing

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Introduction: Sleep research is increasingly powered by wearable technology, yet data privacy, siloed storage, and limited participant agency remain challenges. We introduce a Web3-based platform that encrypts and decentralizes wearable-derived sleep data, allowing individuals to retain ownership while contributing anonymized datasets to collaborative research.

Materials and methods: We designed a pilot framework integrating wearable sleep tracking (commercial and custom devices) with decentralized storage via IPFS and public blockchain indexing. Users access personalized insights through AI-generated dashboards while retaining control over data-sharing permissions via smart contracts. A simulated cohort of 10 individuals was used to test feasibility, with live-user recruitment underway.

Results: System-level testing demonstrated successful data encryption, indexing, and retrieval across platforms. Users were able to view circadian alignment feedback and authorize selective data access. Early user feedback suggests interest in both the privacy-preserving model and personalized insights, though usability testing is ongoing.

Conclusions:

This technology demonstrates the feasibility of integrating Web3 infrastructure with sleep and circadian monitoring. While full-scale deployment is in progress, this prototype points to a future of participant-driven research ecosystems with increased transparency, scalability, and trust. We anticipate expanding to real-world trials and open-science collaborations in 2025–2026.

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Benchmarking Reveals Shared Biases in Sleep-Staging Algorithms and Points to Age-Aware Solutions

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Introduction: Deep learning (DL) algorithms (models) hold promise for automating the labor-intensive task of sleep-staging. Yet, clinical adoption remains limited due to inter-scorer variability, partly stemming from ambiguities in AASM guidelines¹, which constrains model performance and hinders translation. Debates over optimal DL architectures are further complicated by heterogeneous datasets and inconsistent validation protocols. While standardized benchmarking is key, it must be paired with subgroup-specific performance analysis. To address this, we trained state-of-the-art DL-models within a harmonized, large-scale benchmarking framework and evaluated them using a robust, distribution-aware approach to quantify systematic biases.

Materials and methods: We leveraged DL-models from the SLEEPYLAND² benchmarking platform (U-Sleep³, DeepResNet⁴, SleepTransformer⁵), pre-trained on over 27,000 harmonized PSGs from 17 public datasets using standardized pipelines to ensure comparability. These models were then evaluated on 6,633 out-of-distribution PSGs from the Bern Sleep-Wake Registry⁶, spanning ages 0-88 and diverse clinical conditions. To assess bias in individual sleep-scoring models, we applied a GAMLSS-based framework^{7,8} that quantifies the full distribution of both model performance metrics (e.g., macro- or stage-specific F1-score) and errors in prediction-derived clinical markers (e.g., sleep-stage durations, number of stage-transitions). This approach captures non-linear effects of age while adjusting for covariates such as gender, AHI, and PLMI, characterizing individual health status. Beyond mean trends, it quantifies variability and extremes, and enables formal testing of how these variables shape model behavior, offering a comprehensive view of clinically relevant, variable-driven biases.

Results: Despite architectural differences, all models showed similar average performance (macro-F1 $\approx$ 0.75) and exhibited consistent bias patterns. Performance declined markedly at age extremes, especially in children, reflecting underrepresentation in training data and differences in AASM scoring rules. Non-linear age-related biases were observed across all performance metrics and prediction-derived clinical markers. Higher AHI and PLMI were associated with greater errors and variability, likely due to fragmented sleep and signal artifacts. Among stages, N1 remained the most challenging (F1 $\approx$ 0.45), while REM and wake were the most reliable. All models consistently overestimated WASO, and consequently the number of awakenings, and underestimated N3 duration, with the strongest biases observed in younger and high-AHI subgroups. Notably, stage transitions were systematically undercounted, producing overly smoothed hypnograms, likely a result of loss functions used during DL-model optimization.

Conclusions: Our analysis shows that performance and marker biases in DL-based sleep-staging are consistent across architectures and primarily driven by demographic and clinical factors, rather than model design. These findings underscore the need for structured validation of algorithm behavior across real-world subgroups. Our GAMLSS-based framework supports this by quantifying full distributions of performance and marker errors, and identifying sources of systematic bias. Strong non-linear age effects, likely reflecting AASM scoring differences between pediatric and adult populations, suggest that future DL-models could benefit from incorporating age as their input. Additionally, training strategies such as targeted upsampling of underrepresented groups may help mitigate imbalance-driven bias. Given the consistency of bias patterns across models, future progress in automated sleep-staging should prioritize subgroup-aware mitigation strategies over further architectural innovation, to ensure fair and clinically reliable deployment.

Acknowledgments:

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1. <https://jcsn.aasm.org/doi/10.5664/jcsn.5176>
2. <https://github.com/biomedical-signal-processing/sleepyland>
3. [10.1038/s41746-021-00440-5](https://doi.org/10.1038/s41746-021-00440-5)
4. [10.1093/sleep/zsaa161](https://doi.org/10.1093/sleep/zsaa161)
5. [10.1109/TBME.2022.3147187](https://doi.org/10.1109/TBME.2022.3147187)
6. [10.3390/ctn8010014](https://doi.org/10.3390/ctn8010014)

7. [10.1109/SDS60720.2024.00045](#)
8. [10.21203/rs.3.rs-6278214/v1](#)

Beyond Conventional Sleep: Modelling Diverse Sleep Behaviours Using Personalized Sleep Probability

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Introduction: Traditional sleep research has largely focused on the assessment of a single, consolidated nocturnal sleep period. While mostly effective for individuals with conventional sleep patterns, current data pre-processing / processing approaches are often unsuitable for persons with irregular or unconventional sleep schedules, such as shift workers or those with polyphasic sleep habits who often do not have a well-defined “main” sleep period. To more accurately capture such non-canonical sleep in community dwelling individuals, we propose a novel method that utilizes a personalized sleep probability model for identifying main sleep periods across individuals.

Materials and methods: For each individual, a 24-hour mean sleep probability profile is first constructed using multiple days of wearable-derived sleep-wake data, i.e., the likelihood that someone is asleep at any time of the day (15min resolution), including main sleep and naps. The mean sleep probability captures an individual's sleep habit over time. Sleep episodes detected are then weighted according to the individual's mean sleep probability profile, matched to the time-of-day at which they occur. Sleep episodes separated by short wake gaps during typical sleep periods (i.e., high mean sleep probability) are concatenated. For each day, the sleep episode occurring between 1800h the previous day and 1759h the current day with the highest cumulative sleep probability weighted TST is then identified as the main sleep period. This method accounts for both intra- and inter-individual variability in sleep patterns without assuming a fixed circadian timing.

Results: This approach was validated in a diverse sample of 2351 individuals (1268 female, 53.9%) across varying age groups, from 18 to 80 years old (mean 52.0, S.D. 23.8), including university students, working adults, and older adults. Here, our method demonstrated robustness in identifying main sleep periods across heterogeneous sleep patterns, with preference given to sleep episodes during an individual's typical sleep hours, but also accommodating deviations on irregular days. Multiple sleep episodes may be detected within an individual's typical sleep window, particularly among older adults experiencing high sleep fragmentation. The sleep probability model effectively identified and merged these fragmented episodes, capturing them as components of a single, extended sleep period.

Conclusions: This personalized 24-hour sleep probability framework provides a standardized yet adaptable method for identifying main sleep periods in wearable- or nearable- based sleep studies. It enables comparability of main sleep periods across individuals with irregular sleep behaviours to support the characterization of sleep in a broader and more diverse population. While the current evaluation focused on retrospective analyses, the approach can be readily adapted for prospective applications. For example, baseline or moving-window sleep probability can inform wearables when to increase sensor sensitivity to facilitate detection of the Time an individual is Attempting to Sleep (TATS Start Time), or to distinguish between transient wakefulness and the true end of a sleep episode. Sleep probability modelling can also be used to track seasonal shifts in sleep timing.

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Bright White Light Reduces Early Afternoon Alertness Decline in Healthy Adults

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Introduction: Decreased alertness impairs individual judgment, leading to more human errors, decreased work efficiency, and even increased risk of accidents. Light exposure has been shown to

modulate alertness, but the optimal intensity for afternoon settings remains unclear. This study aimed to examine the effects of different light intensities on afternoon alertness in healthy adults.

Materials and methods: 82 healthy subjects aged 18 to 45 years were enrolled and block-randomly assigned to four light intensity groups: 2500 lux group (n = 21), 5000 lux group (n = 20), 7500 lux group (n = 21), and 10000 lux group (n = 20). Two subjects who violated the protocol were excluded, and finally 80 subjects (20 in each group) were included in the statistical analysis. The experiment was completed within two consecutive days (baseline day and intervention day). On the baseline day, the starting time point of the subjects' afternoon sleepiness was set as the 0 minute. During the subsequent 90 minutes, subjective alertness scoring (Karolinska Sleepiness Scale, KSS), objective alertness testing (10-minute Psychomotor Vigilance Task, PVT) and saliva cortisol collection were carried out every 30 minutes. On the intervention day, continuous light exposure for 30 minutes was given starting from the 0th minute. The procedures for collecting subjective and objective alertness and saliva cortisol were exactly the same as those on the baseline day.

Results: Statistical analyses were performed using two-way repeated measures ANOVA to assess the effects of light intensity and time on alertness. Results showed significant between-group differences in the slowest 10% reaction speed of the PVT ($F(3, 76) = 4.100, p = 0.009$). Post hoc analysis revealed that the reaction speed in the 10000 lux group was significantly lower than that in the other three groups, and the group×time interaction effect was significant ($F(3, 76) = 2.056, p = 0.031$). No significant differences were observed in KSS scores or cortisol levels among groups. Subsequently, using paired t-tests, the study found that compared with the baseline day: In the 2500 lux group, the KSS scores decreased significantly at 90 min ($t = 2.595, p = 0.018$). In the 5000 lux group, the KSS scores decreased significantly at 30 min ($t = 2.223, p = 0.039$), and the slowest 10% PVT reaction speed decreased significantly at 30 min ($t = 3.399, p = 0.003$) and 90 min ($t = 2.602, p = 0.018$). In the 10000 lux group, the KSS scores at 30 min ($t = 2.517, p = 0.021$) and 90 min ($t = 3.559, p = 0.002$) were significantly decreased, and the slowest 10% PVT reaction speed at the onset of light exposure ($t = 3.216, p = 0.005$) was significantly decreased.

Conclusions: The study concludes that 2500 lux, 5000 lux, and 10000 lux light exposure reduce subjective alertness decline, and the higher the intensity, the faster the effect. The 10000 lux light exposure has the most pronounced impact on objective alertness in the early afternoon. Future research should explore the underlying mechanisms and long-term effects of high-intensity light exposure.

Can Large language models be used to perform clinical evaluation for patients reporting sleep disorders ? A proof of concept comparing human versus LLM performed medical diagnosis

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Introduction: Sleep related disorders are increasingly prevalent worldwide, yet there remains a significant gap between clinical needs and physicians availability. To help address this, advances in Large Language Models (LLMs) offer promising tools for supporting sleep doctors in clinical diagnosis. LLMs have been successfully applied to clinical tasks such as information extraction and patient report summarization. The DSM-5 R criteria provide a structured and standardized system for diagnosing sleep related disorders, with clear guidelines on symptom classification across various syndromes or pathologies. A diagnostic tool that incorporates DSM-5 R criteria and LLMs could theoretically assist clinicians in identifying sleep related symptoms and disorders more efficiently and consistently.

Materials and methods: We collected clinical interviews of 67 patients performed by 2 sleep specialists from the sleep department of the University Hospital of Bordeaux. The interviews were de-identified, transcribed, and independently analyzed by both clinicians, who assigned diagnoses following a list of twelve sleep-related disorders defined by the DSM-5 R classification. We developed a total of 36 large language model (LLM)-based systems to generate diagnostic hypotheses from clinical interview transcripts. Each system integrates one of 12 distinct LLMs—ranging from the smallest (LLaMA 3.1 with 8 million parameters) to the largest (GPT-4o)—and implements one of three prompting strategies. These include: (1) zero-shot prompting, which directly poses the diagnostic question to the model; (2) chain-of-thought prompting, which guides the model through a structured reasoning process; and (3) prompt chaining, which simulates a multi-agent dialogue. This experimental design allows for a robust

comparative analysis of both the diagnostic capabilities of the LLMs and the impact of the prompting strategies. To evaluate performance, we compared each system's diagnostic outputs with clinical assessments provided by human specialists.

Results: Our preliminary findings demonstrate a clear influence of LLM size on the diagnostic performance of our systems. Small-scale models (approximately 8 million parameters) yield poor results, frequently producing hallucinations by suggesting pathologies not identified by clinicians. In contrast, medium-sized models (ranging from 24 million to 70 million parameters) achieve sensitivity and specificity scores exceeding 70%. The largest models, such as GPT-4o, attain scores above 90% for both metrics. Interestingly, our initial analysis indicates that the choice of prompting strategy has a minor impact on diagnostic accuracy. Contrary to expectations, the most straightforward approach—zero-shot prompting—consistently outperforms more complex methods. This suggests that allowing the LLM to operate with minimal guidance may be more effective in this context.

Conclusions:

Our proof of concept demonstrates that large language models can approach or even match specialists-level performance in diagnosing sleep disorders from transcribed patient interviews. While prompting strategy has a limited effect, model size plays a critical role in diagnostic accuracy. These findings raise important ethical questions. While larger LLMs show superior diagnostic performance, their reliance on cloud-based infrastructure poses challenges for clinical deployment. This trade-off between performance and privacy highlights the need for further development of high-performing models that can run securely in local clinical environments.

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Can the alpha power of the electroencephalogram (EEG) signal during the eyes-closed calibration of the Multiple Sleep Latency Test (MSLT) first nap predict daytime hypersomnolence?

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Introduction: Hypersomnolence poses significant medical risks, including driving risks. A sleep latency of 8 minutes or less, as measured by the Multiple Sleep Latency Test (MSLT), indicates clinical sleepiness. However, MSLT is time-consuming and resource intensive. An alternative, simple method would be valuable.

This study evaluates whether EEG total alpha power (TAP) from the 20-second eyes closed calibration exercise conducted before the start of nap 1 of the MSLT can predict sleep latency (MSL) as a measure of daytime hypersomnolence

Materials and methods: We retrospectively collected data from 400 consecutive polysomnography (PSG) and MSLT sleep studies conducted between January 2022 and February 2025 at an Australian tertiary hospital. Participants were prohibited from alcohol and caffeine during the tests as per the laboratory standard procedure. Exclusions included PSG reports with an Apnea-Hypopnea Index (AHI) ≥ 15 , Total Sleep Time (TST) < 6 hours, or Sleep Efficiency (SE) $< 75\%$ ($n=156$), and MSLT data with poor EEG quality and different montages ($n=37$).

We extracted alpha frequency components of EEG from the occipital (O1 & O2) and frontal (F3 & F4) lobes using digital filtering (filter settings of 8 Hz for the low pass and 12 Hz for the high pass).

To calculate total alpha power (TAP), alpha waves were transformed using a Fast Fourier Transformation algorithm (LabChart8, ADInstruments) before generating TAP values from each of the 4 signals using the 20-second segment of the eyes-closed manoeuvre at the start of nap 1. We averaged, then categorized TAP values from the frontal channels (F-TAP) and occipital channels (O-TAP) into 3 groups of low TAP ($< 20 \mu V^2$), medium TAP ($20-40 \mu V^2$), and high TAP ($> 40 \mu V^2$). Mean sleep latency

was compared to the 3 groups using a one-way ANOVA and post hoc tests ($p < 0.05$). Analyses were conducted using IBM SPSS Version 30.

Results: After exclusion, PSG/MSLT data were analyzed for 207 participants, age range 16-68 years, 65% were female ($n=134$).

The MSL mean values increased by F-TAP groups: low F-TAP ($n=92$) 8.35 ± 4.62 , medium F-TAP ($n=66$) 8.62 ± 5.09 , and high F-TAP ($n=49$) 9.76 ± 5.13 .

Similarly, the MSL mean values increased by O-TAP groups: low O-TAP ($n=55$) 8.21 ± 4.64 , medium O-TAP ($n=43$) 8.94 ± 5.03 , and high O-TAP ($n=109$) 8.99 ± 5.00 .

However, the one-way ANOVA analyses showed no significant difference in the mean of MSL between the 3 groups of F-TAP ($p = 0.26$) or O-TAP ($p = 0.616$), nor were significant differences found in post-hoc pairwise comparisons.

A correlation was observed between MSL and F3_TAP ($p=0.015$), but not with the other channels (F4_TAP $p=0.186$; O1_TAP $p=0.855$; O2_TAP $p=0.588$).

Conclusions: We observed some evidence that higher alpha power from the frontal lobe may be associated with increased sleep latency, though this finding requires more data and further examination of the impact of various medications and incorporating an arousal index threshold into the exclusion criteria.

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Chaos Theory Mathematically Characterizes EEG Brain Wave Patterns of Emotions

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Introduction: What is “chaos theory”?

“Chaos” is when an observer perceives a dynamic system (e.g., weather or global economy) to be unpredictable and complex, noisy or disorderly. However, under the “chaos” are deterministic laws that give rise to structures and patterns.

A popular phrase within chaos theory is “the butterfly effect” where a tiny change in the atmosphere can lead to large-scale changes in weather e.g., hurricane.

The brain, a dynamic system, can be evaluated using 62-dimensions (or leads) of EEG data. On the surface, this can look “chaotic,” however, under the “chaos” are deterministic laws e.g., effect of sympathetic response during a nightmare on sleep/wake, daytime fatigue or hypertension. These deterministic laws give rise to specific brain structures and collectively, patterns.

Why we care about developing a methodology to identify emotions using 62-lead EEG data?

Emotions are a clear outcome that allows us to quickly develop methods to analyze high dimensional data captured by 62-dimensions of EEG data.

Once optimized, these methods can be adapted for clinical use, where big, high dimensional, dynamic data is collected. This includes the ICU, polysomnograms, 30-day Holter Monitors, wearables (over years/decades), and even histological slides.

Objective

To develop a novel methodology that uses chaos theory to mathematically describe (e.g., quantitative metrics) complex interactions and patterns of the brain using 62-lead EEG data. Then use AI to analyze the metrics to find patterns that correlate to 4 specific emotions (e.g., neutral, sad, fear, happy). Each step should be optimized to RETAIN all high dimensional data (nonlinear, unbiased) while balancing computing power (keeping it low).

Materials and methods: The proposed methodology was evaluated using the SJTU-SEED IV database. We first applied uniform manifold approximation and projection (UMAP) for manifold embedding of the

62-lead EEG signals into a lower-dimensional space. We then developed MHRA to characterize the complex recurrence dynamics of brain activity across multiple transition levels. Finally, we employed tree-based ensemble learning methods to classify four emotions (neutral, sad, fear, happy) based on the extracted MHRA features.

Results: Our approach achieved high performance, with an accuracy of 0.7885 and an AUC of 0.7552, outperforming existing methods on the same dataset. Additionally, our methodology provided the most consistent recognition performance across different emotions. Sensitivity analysis revealed specific MHRA metrics that were strongly associated with each emotion, offering valuable insights into the underlying neural dynamics.

Conclusions: 1. We developed a novel methodology, Multilevel Heterogeneous Recurrence Analysis (MHRA), which embeds the interactions underlying 62 dimensions of data to 4 dimensions, extract dynamic features of the pattern of interactions, derive thousands of quantitative metrics that describe the patterns and use ensemble learning to find patterns that classify 4 emotions.

2. Implication for the sleep field: MRHA outperforms Deep Learning alone in terms of Accuracy to identify 4 emotions. This will allow us to quantitate subtle, complex patterns within brain activity that can be applied to dynamic EEG polysomnogram data.

Clinical Application of a Polysomnography Report with an AI-Assisted Summary

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Introduction: The interpretation of polysomnography (PSG) reports in clinical practice traditionally focuses on the Apnea-Hypopnea Index (AHI), often overlooking the complex interplay of underlying pathophysiological traits that define a patient's Obstructive Sleep Apnea (OSA). The Phenotyping Using Polysomnography (PUP) approach allows for the non-invasive estimation of these traits—including Loop Gain (LG), Arousal Threshold (AT), Anatomical Collapsibility (Pcrit), and Pharyngeal Compensation. However, manual calculation and interpretation of these traits are complex and not widely integrated into routine clinical workflows. We aimed to develop a novel tool to bridge this gap.

Materials and methods: We developed a web-based application utilizing a multimodal AI model (Google's Gemini) to automate the analysis of PSG reports during the study period of 2025/May/1 to 2025/Jun/26. The tool's workflow involves: (1) user upload of a standard PSG report image; (2) AI-powered extraction of key parameters (AHI, respiratory event counts, SaO₂, arousal index, sleep architecture); (3) execution of a rule-based algorithm, informed by recent literature, to score and rank the four primary PUP traits based on the extracted data; and (4) dynamic generation of a structured, downloadable PDF report that presents the data and a prioritized analysis of the likely pathophysiological drivers for the specific case. It is important to note that all figures and data transferred to the Large Language Model (LLM) for calculation are anonymous and free from any personal information to ensure patient privacy.

Results: The AI-assisted tool successfully automates the translation of a static PSG report image into a dynamic, interpretable summary. It generates an instantaneous analysis that prioritizes the patient's likely OSA endotypes. The final report provides clinicians with a clear, ranked list of the contributing physiological traits (e.g., "1. High Loop Gain," "2. Low Arousal Threshold"), along with data-driven justifications for the ranking. This output facilitates a more nuanced understanding of the individual patient's disease beyond a single AHI value.

Conclusions: This AI-assisted application demonstrates a practical and rapid method for integrating advanced PUP-based phenotyping into routine clinical practice. By automating the data extraction and analysis process, this tool has the potential to enhance clinical decision-making, facilitate the development of personalized treatment strategies for OSA, and ultimately improve patient outcomes by connecting complex sleep physiology research with day-to-day clinical care.

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Comparative Study of Polysomnography and HSAT levels in Diagnosis of Sleep Apnea and Analysis of Subsequent Treatment Uptake in 300 Patients

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Introduction: Obstructive Sleep Apnea (OSA) is a common but frequently underdiagnosed sleep disorder with significant health consequences, including increased risk of cardiovascular disease, metabolic dysfunction, and impaired quality of life. Early and accurate diagnosis, followed by prompt initiation of appropriate therapy, is essential for mitigating these risks and improving patient outcomes. Sleep studies-ranging from in-lab polysomnography (PSG) to home-based testing-are the cornerstone of OSA diagnosis. However, the pathway from diagnosis to treatment can be influenced by the type of diagnostic modality used, patient engagement, and the structure of follow-up care. This study aims to evaluate the distribution of sleep study types and analyse treatment initiation rates at SleepMed Solutions, a tertiary sleep centre in Bengaluru, India.

Materials and methods: • **Study Design:** Retrospective analysis

• **Setting:** SleepMed Solutions, Bengaluru, Karnataka, India

• **Study Period:** January 2024 – January 2025

• **Total Sleep Studies:** 301

• **Modalities:**

Level 1: In-lab polysomnography (n=61)

Level 2: Home polysomnography (n=132)

Level 3: Home Sleep Apnea Test (HSAT) (n=108)

• **Data Collected:** Number of studies by type, number of patients initiating treatment, number not taking treatment, number not meeting doctor post-diagnosis.

• **Analysis:** Calculation of treatment initiation rates by modality.

Results: In a study of 301 patients, the distribution of sleep study modalities was as follows: 61 patients underwent in-lab polysomnography (Level 1), 132 had home polysomnography (Level 2), and 108 completed home sleep apnea testing (HSAT, Level 3).

The rates of treatment initiation varied significantly by modality. In-lab polysomnography (Level 1) had the highest treatment uptake, with 70.49% of patients starting therapy after diagnosis; this equated to 43 patients out of 61. Home polysomnography (Level 2) showed a moderate initiation rate of 57.58%, with 76 patients taking treatment out of 132. In contrast, HSAT (Level 3) had the lowest uptake at 44.44%, with 48 patients out of 108 beginning treatment.

Overall, the treatment initiation rate across all modalities was 55.48%. Notably, 281 patients met with a doctor following their diagnosis, while 20 did not attend a post-diagnostic consultation.

These findings indicate that patients diagnosed through in-lab polysomnography are more likely to initiate treatment compared to those diagnosed via home-based modalities. This could be attributed to the comprehensive nature of in-lab studies, structured patient counselling, and immediate access to healthcare providers. Conversely, the lower uptake rates in home-based studies, particularly HSAT, may reflect milder disease severity, reduced patient engagement, or logistical challenges in follow-up. These disparities highlight the importance of providing robust post-diagnostic support and patient education, especially for those undergoing home-based testing.

Conclusions: In-lab polysomnography is associated with the highest rates of treatment initiation among patients diagnosed with OSA at SleepMed Solutions. Home-based diagnostic modalities, while increasing accessibility, are linked to lower treatment uptake. To enhance overall outcomes in OSA management, targeted interventions to improve patient engagement and follow-up after home-based diagnoses are warranted.

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COMPARISON AMONG GUIDELINES AND FRAMEWORKS FOR THE VALIDATION OF NEW SLEEP TECHNOLOGIES

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Introduction: Sleep medicine is witnessing a revolution in the development and implementation of new sleep technologies (NSTs), including both consumer sleep technologies and those directed to healthcare professionals. Despite the rising trust in NSTs, concerns have been raised regarding their diagnostic accuracy, therapeutic effectiveness, and overall reliability. Due to concerns about the low methodological quality of the validation studies, there is a need for structured guidelines and recommendations to standardize the development and validation processes of NSTs. The current work overviews the currently available guidelines for the development and validation of NSTs.

Materials and methods: NSTs were contextualized as those that fulfil the following criteria: 1. Are not currently considered as gold-standard procedures, 2. Are innovative technologies, or significant improvements in standard technologies, 3. Are intended to be used either by the consumer/patient or by healthcare professionals, and 4. Are mainly related to software or hardware developments. Based on a literature review, guidelines and methodological frameworks for the development and validation of NSTs were identified. Information was extracted regarding the coverage of these guidelines, their targeted sleep condition, targeted type of NST, involvement of stakeholders, and methodological approaches for issuing recommendations.

Results: Five guidelines related to the development of NSTs were found, published since 2020, which demonstrate that the field is still in development. Regarding targeted sleep conditions, two were devoted to sleep scoring, one to point-of-care obstructive sleep apnea (OSA) screening, and two to overall sleep monitoring. Altogether, all guidelines were related to diagnostic technologies, while none were devoted to the validation of therapeutic technologies (such as digital cognitive-behavioral therapy for insomnia (CBT-I), or treatment devices for OSA). Regarding the targeted type of NST, all were devoted to consumer sleep technologies, with two being specifically directed to wearable devices. None were directed to the standardization of medical-grade NSTs. Three of them involved the participation of important stakeholders in sleep research (Sleep Research Society, the Sleep Health Journal, and the World Sleep Society). Regarding the methodological approach, most of them are unclear or have not followed standard procedures for evidence synthesis or the establishment of consensus.

Conclusions: As NSTs have become widely accessible and are utilized by consumers and healthcare providers, the process of development and validation of these technologies should follow rigorous methodological standards. The guidelines analyzed provide actionable items to assist researchers and manufacturers, and represent valuable contributions towards the standardization of the development and validation of NSTs. However, significant challenges persist, including the absence of guidelines for therapeutic technologies (e.g. CBT-I apps and OSA treatment devices) and medical-grade devices, and the non-adherence to standard guidelines or consensus development techniques.

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Comparison of cardiovascular disease mortality outcomes using oximetry event desaturation transient area-based methods

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Introduction: Desaturation area-based parameters derived from oximetry have recently emerged as novel predictors of cardiovascular disease (CVD) mortality in the context of obstructive sleep apnoea (OSA). Recent studies have proposed a novel desaturation area-based parameter, which may provide better prediction of CVD outcomes in community population and chronic heart failure-free population. Desaturation area-based parameters measure the desaturation event transient area under the oximetry trace during sleep but there are different variations in calculations. These different calculation methods can be categorised by their dependence on respiratory event scoring, the definition of sampling window, or their choice of baseline. Among parameters based on manually scored respiratory events, hypoxic burden (HB) and respiratory event desaturation transient area (REDTA) have been used for predicting CVD outcomes. HB is calculated by an event-specific baseline and a record-specific sampling window, while the sampling window and baseline of REDTA are fixed for all recordings and events.

Materials and methods: We evaluated the six possible combinations of baseline (event-specific, record-specific, or fixed) and sampling window (record-specific or fixed) to find an easy-to-calculate yet effective method area for predicting CVD mortality. The Sleep Heart Health Study data and corresponding CVD mortality outcomes were utilized. The predictive performance of each method was assessed by Cox proportional hazard regression analysis with adjustment for relevant covariates. To enable direct comparison of the areas, each area was normalised to a z-score. Normalization was performed by subtracting the mean value of each set of desaturation areas and dividing by its standard deviation accordingly. Based on normalised area values, the corresponding hazard ratios (HR) were calculated by the adjusted and unadjusted Cox proportional hazard regression models. The performance of each area-based method in predicting CVD mortality was compared based on the hazard ratios and the p-values.

Results: Results show that an area method using a record-specific baseline and a fixed sampling window and an area method using a record-specific baseline and sampling window performed the best.

Conclusions: We explored different calculation methods for desaturation area-based parameters and comprehensively compared their performance in predicting CVD mortality. The results show that a method using a fixed sampling window and a record-specific baseline to prevent noise interference and reduce computational complexity had the best performance.

Comparison of conventional and extended middle meatal antrostomy for the treatment of antrochoanal polyps with snore

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Introduction: Objective: The objective was to compare the recurrence rate and complications between endoscopic middle meatal antrostomy (MMA) and extended MMA for the treatment of antrochoanal polyps with (ACPs) with snore.

Materials and methods: Methods and materials: 95 ACPs were prospectively enrolled to undergo MMA (n=48) or extended MMA (n=47). The recurrence rate and complications were compared between these groups.

Results: Results: All patients completed 24 months of follow-up. The recurrence of ACP was demonstrated by only endoscope at 6 and 12 months postoperatively but at 24 months postoperatively by endoscope and CT. Rates of recurrence of ACP differed between groups and significance at postoperative month 6 (7/48 patients in the MMA group and 0/47 patients in the extended MMA group, $P=0.02$), month 12 (16/48 vs. 2/47, $P<0.01$) and month 24 (21/48 vs. 3/47, $P<0.01$). No MMA closure was found in any group, 19.15% (9/47) patients complained of cheek numbness in the extended MMA group, however, no major complications were observed in both groups.

Conclusions: Conclusions: Extended MMA via antidromic extended medial wall of MS may effectively reduce the recurrence of ACP with lower complications.

Contactless objective sleep monitoring of inpatients at a psychiatric hospital

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Introduction: Patient monitoring in acute psychiatric settings has remained largely unchanged for over a century, relying heavily on subjective staff observations. Low tolerance for on-body sensor equipment and high demands for sensitivity and privacy has made objective monitoring in this setting particularly challenging. There has been a critical gap in the use of objective tools to assess patients' physiological states and symptom trajectories. This study examines one way of performing objective characterization of sleep among acutely admitted psychiatric inpatients through the use of contactless, unobtrusive movement data measured with a radar sensor. The aim of this study was to explore radar technology as a tool for objective monitoring and characterization of sleep of psychiatric inpatients.

Materials and methods: All 40 bedrooms of an acute psychiatric hospital were equipped with contactless ceiling-mounted radar sensors able to record the movement of patients within the rooms and provide objective estimates of their sleep. In total, 1791 days of radar data were recorded from 327 unique hospital admissions (age 36.4 ± 13.9 (mean $\pm$ SD), 43% male, days admitted 6.4 ± 7.6). Primary diagnosis from hospital records were used to categorize patients in four groups: Severe depressive episode, psychosis, manic episode, and "other diagnoses".

An actigraphy-inspired model was applied to estimate the sleep/wake state of the patients from their radar-recorded body movement, and a heuristic sleep onset/offset search was performed to estimate their primary sleep period. Total sleep time (TST) was calculated as the patient's total duration of sleep within the primary sleep period for each day of the admission. A linear mixed model was used to evaluate TST over the course of admissions for the four diagnostic groups.

Results: At admission, the "other diagnosis" group (N=237, mean duration of admission 4.3 ± 4.8 days) had an estimated mean TST of 8.8 hours (95% confidence interval (CI) [8.5, 9.3]). Patients in a manic episode (N=17, mean duration of admission 17.2 ± 11.6 days), had 4.7 hours (95%CI [6.0, 3.3], $p < 0.001$) lower estimated mean TST at admission compared with the "other diagnosis" group, with an increase in TST per day of the admission of 12.7 minutes (CI [3.8, 21.7], $p < 0.001$). There were no significant differences for the depression or the psychosis subgroups compared with the "other diagnosis" group.

Conclusions: Clinically meaningful differences in sleep patterns can be detected in a feasible way using ceiling mounted radar sensors. We observe that both the amount of sleep at admission and the trajectory of sleep across an acute admission differs between distinct diagnostic groups.

Contactless Oxygen Desaturation Prediction and ODI Estimation from Nocturnal Breathing Sounds via Deep Learning

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Introduction:

Intermittent hypoxemia in obstructive sleep apnea (OSA), often termed "hypoxic burden," has emerged as a superior predictor of cardiovascular morbidity and mortality compared to the Apnea-Hypopnea Index (AHI). Although direct measurement of hypoxic burden requires high-resolution oximetry, the Oxygen Desaturation Index (ODI) - the average number of $\geq 4\%$ desaturation events per hour - serves as a well-validated proxy that correlates with cardiovascular outcomes. Conventional ODI assessment necessitates pulse oximetry during full polysomnography (PSG), limiting its scalability for home screening of at-risk populations. Given that apneas and hypopneas commonly lead to oxygen desaturation, and building on our previous work predicting OSA events using a sound-based AI model, we developed an AI model to directly detect desaturation events from nocturnal breathing sounds. This

approach aims to broaden access and enable contactless estimation of hypoxic burden via its surrogate, the ODI.

Materials and methods: We trained our binary classifier on 2,973 nights of synchronized PSG recordings - both hospital- and home-based - with audio captured via smartphone and PSG equipment. Ground-truth ODI values for the independent test cohort of 802 anonymized subjects (mean age 50.5 ± 15.4 years; BMI 25.5 ± 3.6 ; male:female = 530:272) were derived from oximetry during PSG. For each 30-second epoch, the model processes 80 consecutive Mel-spectrogram frames to decide whether a desaturation event occurred. By counting the number of epochs predicted as desaturation per hour, we obtain an estimated ODI for each night. Model performance was assessed at the epoch level using sensitivity, specificity, precision, recall, and F1 score; overall classification accuracy and macro-averaged F1; and agreement between estimated ODI and ground truth ODI was quantified via Pearson correlation and Bland-Altman analysis.

Results: On the test set, our model achieved a sensitivity of 0.79 and specificity of 0.95 for the desaturation detection, with a corresponding precision of 0.78 and an F1 score of 0.79 via each 30-second epoch by epoch evaluation. Overall classification accuracy reached 0.92, with a macro F1 of 0.87. Estimated ODI correlated strongly with ground-truth ODI (Pearson $r = 0.93$, $p < 0.001$). The mean true ODI was 17.71 events/hour, versus a mean estimated ODI of 17.92 events/hour. Bland-Altman analysis showed a mean difference of -0.21 events/hour (SD of differences: 6.91), with 95% limits of agreement from -13.75 to 13.32 events/hour. In binary classification, for ODI cutoff values of 5, 15, and 30 events/hr, the sensitivity was 0.92, 0.86, and 0.82, respectively, and the specificity was 0.89, 0.92, and 0.96, respectively.

Conclusions:

Our sound-based AI model achieves high accuracy in desaturation detection and reliable ODI estimation, matching oximetry-derived measures at the group level. By eliminating contact sensors, it enables scalable home screening for intermittent hypoxemia - a key factor in cardiovascular risk assessment. Integrating this approach with simultaneous AHI inference could deliver a comprehensive, non-contact sleep assessment platform. Future work will target individual-level precision improvements and prospective validation in community settings.

Deep Learning-based Detection of Atrial Fibrillation in Patients with Suspected Obstructive Sleep Apnea Undergoing Portable Sleep Monitoring

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Introduction: Atrial fibrillation (AF) is the most common arrhythmia and is associated with increased cardiac risk. Its prevalence is notably higher among patients with obstructive sleep apnea (OSA). However, systematic AF screening during sleep monitoring remains uncommon. This study aimed to: 1) develop and validate a deep neural network (DNN) algorithm for automated AF detection using electrocardiogram (ECG)-derived RR intervals, and 2) evaluate its applicability to pulse-to-pulse (PP) intervals derived from photoplethysmography (PPG) in patients with suspected OSA undergoing portable sleep monitoring with the Biologix system.

Materials and methods: The study consisted of two phases. **Phase 1** involved developing a DNN model using four public long-duration ECG databases (MIT-BIH Atrial Fibrillation, MIT-BIH Normal Sinus Rhythm, Normal Sinus Rhythm RR Interval, and IRIDIA-AF), totaling 40.14 million annotated heartbeats from 249 subjects, including 10.56 million AF-labeled beats (26.31%). The model architecture comprised stacked bidirectional long short-term memory (biLSTM) layers, max pooling, and fully connected ReLU-activated layers. It classified windows of 60 consecutive RR intervals as AF or non-AF, requiring six cumulative minutes of AF-positive segments to classify a patient exam as positive, a threshold set to reduce false positives from transient irregularities. The dataset was split into training (90%) and hold-out test (10%) sets. Performance was evaluated over the training set via 10-fold cross-validation stratified by patient and validated on the independent test set. Beat-level performance was further

stratified by heart rate (HR): bradycardia (<60 bpm), normal (60–100 bpm), and tachycardia (>100 bpm). **Phase 2** involved testing the algorithm developed in Phase 1 in patients who underwent simultaneous type 1 polysomnography (PSG) and monitoring with Biologix oximeter (Oxistar™, Biologix Sistemas S.A., Brazil), which consists of a high-resolution oximeter with a built-in accelerometer, a smartphone app for recording snoring, and cloud-based analysis. AF detection using PPG signals from the Biologix oximeter was compared with single-lead ECG from PSG.

Results: Phase 1: Cross-validation showed strong beat-level performance, with an area under the curve (AUC) of 0.994 ± 0.003 , sensitivity of $96.6\% \pm 2.2\%$, specificity of $97.6\% \pm 1.0\%$, and accuracy of $97.4\% \pm 0.6\%$. Sensitivity across HR ranges was 94.5% (<60 bpm), 96.6% (60–100 bpm), and 96.7% (>100 bpm); corresponding specificities were 98.9%, 98.5%, and 89.9%, respectively. Patient-level analysis yielded an AUC of 0.957 ± 0.029 , sensitivity of $91.3\% \pm 5.8\%$, specificity of 100%, and accuracy of $94.1\% \pm 3.8\%$. On the hold-out test set, beat-level AUC was 0.994 with an accuracy of 99.4%, while patient-level AUC was 0.971, sensitivity 94.1%, and specificity 100%. **Phase 2:** PSG and Biologix assessments were conducted simultaneously in 220 patients with suspected OSA. All seven ECG-confirmed AF cases were correctly identified by PPG-based classification. Sensitivity, specificity, and accuracy for PPG detection were each 100%.

Conclusions: The proposed DNN algorithm reliably detects AF from PPG-derived PP intervals acquired by the Biologix system, enabling systematic AF screening during sleep assessments in patients with suspected OSA.

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DeepSpecFusion: Early Fusion Transformer for sleep staging using PSG

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Introduction: Sleep stage classification is a crucial component in assessing sleep quality and associated pathologies. Manual sleep staging is an inefficient process requiring significant time and labor investment. Recent studies have employed late fusion architectures to extract information from multiple PSG channels including EEG, EOG, and EMG. However, cognitive psychology and neuroscience research demonstrates that multimodal fusion can occur early in the perceptual stack, enabling deeper integration of modalities. In this study, we propose DeepSpecFusion, an early fusion transformer-based model for automatic sleep staging using polysomnographic records.

Materials and methods: The DeepSpecFusion model employs a multi-channel fusion encoder based on transformer architecture that tokenizes along the time axis. We utilized continuous wavelet transform (CWT) instead of short-time Fourier transform (STFT) to generate spectrograms for improved sleep stage classification. The core mechanism involves random initialized fusion tokens updated through factorized channel interactions using cross-attention mechanisms. Pre-training was conducted using masked autoencoder (MAE) methodology, masking and restoring 50% of tokens to learn complex inter-channel interactions. Two public datasets were used: SleepEDF-78 (78 subjects, Fpz-Cz EEG/Pz-Oz EEG/ROC-LOC EOG) and SHHS (300 subjects, C3/C4 EEG/EOG_L/EOG_R/Chin EMG). Performance was evaluated using accuracy, macro F1-score, and sensitivity metrics.

Results: The proposed DeepSpecFusion model demonstrated superior performance compared to MultichannelSleepNet baseline across both datasets. On SleepEDF-78, we achieved accuracy of 82.69%, F1-score of 80.93%, and sensitivity of 82.93% versus baseline performance of 81.67%, 73.54%, and 73.75%, respectively. On SHHS dataset, our model achieved accuracy of 87.03%, F1-score of 80.83%, and sensitivity of 86.21% compared to baseline performance of 86.94%, 80.07%, and 81.63%, respectively. The model showed particularly improved performance in N1 stage classification across all sleep stages.

Conclusions: We demonstrated that early fusion transformer architecture successfully integrates multi-channel PSG features, yielding improved classification performance across all sleep stages, especially N1, relative to late fusion approaches. However, N1/N2 classification remains challenging for both baseline and proposed models, requiring further investigation to resolve class confusion. Our results

represent the potential of early fusion paradigms for enhanced sleep stage classification using polysomnographic signals.

Delivering Sleep Hygiene Interventions through Smartwatch-based Serious Sleep Games

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Introduction: Sleep hygiene is a foundational element of cognitive behavioral therapy for insomnia (CBT-I). There is established evidence that sleep hygiene can positively impact sleep quality, with effects that often sustain beyond the intervention period. However, existing sleep hygiene programs largely rely on instruction and user self-discipline, which poses engagement challenges, especially among younger populations. The objective of this study is to explore alternative medium for delivering interventions so that it becomes easier for young users to follow through.

Materials and methods: We adopted an interdisciplinary approach integrating the sleep hygiene components of the CBT-I protocol, serious game design principles, and co-design methodology. This approach ensures that the intervention remains clinically aligned while enhancing user engagement through gamified experiences. Smartwatches were selected as the delivery platform, given their low blue-light emission and minimal sleep disruption compared to smartphones or large computer displays.

Results: The study progressed in two phases. Phase-I involved three empathy workshops with 51 university students aged 18 to 35. These workshops identified key factors contributing to sleep disturbances, including excessive screen time, stress, anxiety, irregular sleep schedules, poor eating habits, and uncomfortable sleep environments. These findings align with previous research. However, an interesting insight was that participants did not always view late-night disruptions as negative. For some, staying up late was a choice for creativity or productivity, not just procrastination. This challenges the conventional view that sleep disruptions should always be avoided, emphasizing the value of the co-design approach. The workshops generated design ideas to address these sleep disturbances and improve existing technologies. Proposed solutions included automated sleep environment optimization, screen time regulation, relaxation techniques, AI-driven sleep induction, and smoother transitions from sleep to wakefulness. These ideas emphasized actionable interventions targeting behavioral and psychological changes. Based on these insights, the research team developed three sleep game prototypes. In phase-II, a design workshop collected feedback on the three prototypes: Hero's Sleep Journey, Sleep Tamagochi, and Sleepland. We found that Hero's Sleep Journey was the most popular game, but Sleep Tamagochi was considered the most effective for improving sleep health. We also found that the preferred timing for interacting with each sleep game features varies depending on users' availability, their situated context, and the perceived functions of the feature.

Conclusions: Our findings suggest that smartwatch serious games can serve as a promising medium to foster sleep hygiene in young populations. Future designs should create games that resonate with users' personal lives, health goals, and situational contexts. A variety of game genres and features should be offered to cater to diverse needs. Moreover, allowing users to customize their experience and set technology boundaries will help foster a sense of control and autonomy in improving sleep hygiene.

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Detection of Arousal Epochs During Sleep Using a Sound-Based AI Model

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Introduction: This study investigates the feasibility of detecting arousals using a sound-based AI model for sleep analysis. Arousals - brief awakenings during sleep marked by abrupt EEG shifts lasting at least 3 seconds - are clinically important indicators of sleep quality and are commonly used in diagnosing sleep disorders. However, their detection currently relies on polysomnography (PSG), which is costly, time-consuming, and impractical for long-term home-based monitoring. Previously, we demonstrated that our sound-based AI model accurately predicts sleep stages and sleep apnea events. Given that arousals are accompanied by characteristic changes in breathing - such as transient increases in ventilation and reduced inspiratory duration due to sympathetic activation - we hypothesized that nocturnal breathing sounds could also be used to infer arousal events.

Materials and methods: We developed a single-task classifier for arousal detection. The model processes 80 consecutive Mel spectrograms, each representing a 30-second epoch, to extract breathing-related acoustic features, and performs a three-class classification (sleep, wake, arousal). The training dataset included 2,973 nights comprising hospital PSG recordings (with PSG equipment audio or smartphone audio) and home PSG recordings (with smartphone audio). An independent test set of 802 nights was used for evaluation (mean age: 50.5 ± 15.4 years; BMI: 25.5 ± 3.6 ; AHI: 21.2 ± 20.6 ; male:female = 530:272). Model performance was evaluated on an epoch-by-epoch basis using sensitivity, specificity, F1 score, and area under the precision-recall curve (AUPRC) and receiver operating characteristic curve (AUROC). In addition, nightly arousal epoch counts predicted by the model were compared with PSG-derived reference counts.

Results: For detecting arousal-containing epochs, the model achieved a sensitivity of 0.65, specificity of 0.91, and an F1 score of 0.63. The AUPRC and AUROC for arousal detection were 0.64 and 0.88, respectively. For wake and sleep epochs, the model showed sensitivity, specificity, and F1 scores of 0.75 / 0.96 / 0.80 and 0.89 / 0.78 / 0.88, respectively. Overall three-stage classification resulted in an accuracy of 82.52% and a macro F1 score of 0.77. Predicted nightly arousal epoch counts correlated strongly with PSG-derived counts ($r = 0.92$), with mean predicted and actual values of 160.5 and 150.8, respectively.

Conclusions: Accurate estimation of arousal significantly enhances the capabilities of sound-based AI models for comprehensive sleep monitoring, particularly as a cost-effective, contactless home-based solution. The approach provides valuable insights into sleep quality by enriching diagnostic detail. Future developments will focus on improving the temporal resolution to capture brief arousal events effectively, enhancing the precision of arousal index predictions essential for detailed sleep assessments.

Development of a battery-free, wirelessly-controlled system for optogenetic stimulation of hypoglossal nucleus in mouse models of obstructive sleep apnea

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Introduction: Obstructive sleep apnea (OSA) is characterized by upper airway obstruction, usually caused by muscle hypotonia during sleep, especially REM sleep. Obstruction can be prevented by inducing contraction of these muscles during REM sleep. An innovative approach, testable on OSA murine models, is the activation of hypoglossal innervated muscles by optogenetic stimulation of their motoneurons. However, optogenetic currently available devices may impact on mouse sleep behaviour and are hardly compatible with use inside a whole-body plethysmograph, necessary for continuous monitoring of respiration. The aim of this study was to design a wireless power transfer (WPT) system based on a subcutaneous device to be used on mouse models of OSA.

Materials and methods: This system is based on an inductive coupling operating at a frequency of 13.56 MHz. It features a multi-coil array transmitter (TX) integrated into the semi-cylindrical wall of an

experimental chamber (height and radius = 50 mm). The TX array consists of 5 series-connected coils, 4 of which are made up of 2 rectangular turns and are located on the lateral wall; the fifth, a circular coil with a radius of 35 mm, is positioned at the bottom of the chamber. The receiver (RX), implantable subcutaneously in the mouse, consists of two identical rectangular coils, each composed of 5 turns, with dimensions of 14 x 15 mm². The shape, size and arrangement of the TX and RX coils have been optimized to obtain an omnidirectional and uniform distribution of the magnetic field inside the chamber, and to maximize the collected power independently of the movements or orientation of the mouse. This results in reliable operation of the selected optogenetic LED (wavelength = 470 nm).

Results: The system was first simulated and optimized using circuit simulation software to meet the power consumption requirements of the selected LED. Next, the fabricated prototype was tested with the RX device moving in six different positions with a transmitted power of approximately 740 mW. The worst-case scenario corresponds to the RX device at the edge of the TX system, far from the side coils and significantly misaligned compared to the one on the floor. In this case, the measured available rectified power is 14.7 mW.

Conclusions: Our system consistently meets the power demand and can maintain uninterrupted operation of the LEDs for effective optogenetic neurostimulation, even under the most challenging mouse positioning and orientation conditions. From a translational perspective, it may lead to the development of innovative therapeutic approaches for OSA.

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Development of a Machine Learning Model to Estimate Psychomotor Vigilance Response Speed from Eyelid Opening Degree

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Introduction: Responsiveness to stimuli declines under conditions such as sleepiness, leading to errors and reduced performance in tasks like driving. We previously developed a machine learning model to estimate response speed in the Psychomotor Vigilance Test (PVT)–quantified as reciprocal reaction time (RRT)–using eyelid opening degree measured by non-contact eye-tracking cameras under daily sleep conditions (Noguchi et al., 2024, ASSM). The present study aimed to improve the model's estimation accuracy by expanding the training dataset. Additionally, we evaluated whether the updated model could estimate PVT RRT under sleep deprivation. Since the PVT does not require eye movements, we also investigated whether estimated PVT RRT would similarly decrease during a visual search task (VST), which involves eye movements, under sleep-deprived conditions.

Materials and methods: We previously constructed a dataset comprising eyelid opening measurements from 98 healthy participants during a 40-minute PVT under daily sleep conditions, collected via eye-tracking camera (Taniguchi & Noguchi et al., 2023). To enhance estimation accuracy, we conducted hyperparameter tuning for a Gradient Boosting Decision Tree (GBDT) model across 100 randomized runs, selecting the most frequently occurring optimal hyperparameters to build the final model. For validation, 18 healthy participants (16 males; mean age 23.7 ± 6.4 years) completed a 10-minute PVT and an 8-minute VST before and after a night of either 8-hour normal sleep or total sleep deprivation. Eyelid opening degrees, collected during both tasks, were used to estimate PVT RRT.

Results: When the model trained on daily sleep condition data was applied to both normal sleep and sleep-deprived conditions, the intraclass correlation coefficient (ICC) between observed and estimated PVT RRT was 0.52, indicating moderate agreement. In the PVT, both observed and estimated PVT RRT significantly decreased after sleep deprivation compared to normal sleep ($p < 0.001$ for both). Similarly, in the VST, both observed VST RRT and estimated PVT RRT significantly decreased after sleep deprivation ($p < 0.001$ for both).

Conclusions: The model achieved moderate estimation accuracy, as indicated by the ICC. Notably, estimated PVT RRT significantly declined under sleep deprivation during both the PVT and VST, supporting the model's applicability under sleep-deprived conditions and in tasks involving eye

movements. Incorporating sleep deprivation data into the training set may further improve model performance in future studies.

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DREEMER: Toolbox to manage and process Waveband data locally

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Introduction: The Beacon Biosignals Waveband allows for easy home-based EEG-derived sleep monitoring. Although the Waveband does not use the typical electrode montage, the Waveband staging algorithm has been shown to have an accuracy of 95.02% (Ong et. al., 2024). Raw sleep and staging data are available for download from Beacon servers. However, the file formats and naming conventions can be difficult to work with. Artifact detection methods as well as power spectral analyses are also not readily available. As such, we developed a toolbox to address these issues.

Materials and methods: Our team had previously conducted 2 studies using the Waveband. Currently, there are 5 different files to download for each recording: 1) complete raw data (h5 format), 2) PDF report based off the Waveband onboard processing, 3) lightly processed set of data (edf file), 4) sleep staging (text file), 5) a sleep report (csv file) generated from the Beacon servers. The file names of item 1 and 2 are the record ID, while files 3, 4, and 5 are named using the account ID and recording time stamp. Sorting these files is a time-consuming and error-prone process, therefore we developed a toolbox to automate this. We show an example extraction process from a recently completed multi-night (up to 12 nights) study with 60 participants with a total of 2502 files. In addition, detailed sleep staging overview can also be accessed through a plotting function which allows users to quickly highlight abnormalities in the data. Finally, artifact detection and power spectral analyses were also performed using Buckelmueller's (2005) method.

Results: We developed a toolbox in MATLAB to organize and process DHB recordings after they have been manually downloaded from the Beacon Biosignal servers. At the current development stage, the toolbox is able to:

1. Automatically read files and create a summary csv pulling data from individual report. Users can manually add study identifiers and the toolbox will update the file structure and consolidate files under individual participant folders and subfolders for each recording.
2. Plot staging data and save it, to allow for quick visual look at the data.
3. Convert raw h5 data into edf format.
3. Calculate and plot artifact-free power spectra of the recordings using EEGLAB.

Conclusions: Automation of data processing pipelines packaged into a toolbox can help users effectively manage, visualize and analyze large streams of Waveband data.

Effect of CPAP on cardiac function: Echocardiographic analysis using Speckle Tracking

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Introduction: Obstructive sleep apnea syndrome (OSAS) is associated with an increased risk of cardiovascular morbidity and mortality. The objective of our study was to analyze using echocardiography and speckle tracking imaging right and left ventricular functions of OSA patients at baseline and cardiac changes with CPAP treatment.

Materials and methods: We prospectively included 36 OSAS patients (diagnosed by polygraphy or polysomnography). Patient underwent transthoracic echocardiography (TTE) with conventional 2D analysis, pulsed, continuous, and tissue Doppler analysis, and a strain study using the Speckle Tracking

technique. Systolic and diastolic functions were analysed. Echocardiographic measurements were performed at baseline and repeated at one month and six months of CPAP treatment.

Results: We included mainly men (69%), aged 56 ± 12 years, and obese (73%) with a mean BMI of 35.1 ± 7.4 kg/m², all presented severe OSAS (RDI > 30/h). Echocardiographic parameters were as follow: we found significant improvement of right heart function with improvement in global and regional contractility: TAPSE (mm) increased from 22 ± 3 to 23 ± 3 ; $p < 0.05$, speckle tracking of right ventricle improved from 173.9 ± 89 to 119 ± 55.9 ms, $p < 0.05$. Left ventricular ejection fraction (61 ± 8 vs 63 ± 6 %) and LV diastolic function remains (1.2 ± 0.4 vs 1.2 ± 0.5) stable over 6 months of CPAP treatment.

Conclusions: We found significant improvement in RV global and regional contraction after one month of CPAP for OSAS. This beneficial effect of CPAP on right heart contraction was persistent at 6 months.

Estimating Daytime Productivity from Sleep-Time Biosignals with a Reduced Feature Set

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Introduction: Inadequate or poor-quality sleep erodes next-day alertness, psychomotor speed, and working-memory accuracy, all of which translate directly into lost productivity and safety risks. Conventional metrics such as total sleep time or stage proportions capture only fragments of sleep physiology and require cumbersome polysomnography. We therefore investigated whether a compact overnight biosignal array could directly forecast three concrete daytime outcomes—subjective sleepiness, psychomotor vigilance, and working-memory performance—and, if so, how few sensors were sufficient.

Materials and methods: After two adaptation nights, twenty healthy men (28.4 ± 4.9 y) spent four experimental nights in the laboratory (lights-off 22:00, lights-on 06:00); 59 recordings remained after artefact rejection and signal-quality screening. Signals were sampled at 1 kHz via a Biosignalsplux hub: 3-lead ECG, respiratory-inductance belt, palmar electrodermal activity (EDA) and bilateral external-oblique EMG. Twenty-five features—heart-rate-variability indices (pNN20, RMSSD, LF/HF, etc.), respiration rate/amplitude, EDA burst counts/amplitudes and EMG RMS—were z-scored participant-wise and fed to a three-layer Transformer encoder (d_model = 64, eight heads, cosine-decay Adam, early stopping at 100 epochs). At 06:00, 07:00 and 09:00 participants completed (i) the Stanford Sleepiness Scale (SSS) for self-rated alertness, (ii) a 5-min psychomotor vigilance task (PVT-B) for median reaction time, and (iii) a 3-back task for percent-correct working-memory accuracy. Four-fold cross-validation quantified performance. Shapley values ranked feature importance and guided two ablation routes: (i) dropping low-value sensors and (ii) dropping only low-value features.

Results: The full model explained $R^2 = 0.68$ – 0.77 of variance in median PVT reaction time and up to 0.76 in 3-back accuracy across the three test times; SSS sleepiness classification peaked at $F1 = 0.81$ at 07:00 (06:00 = 0.70 , 09:00 = 0.71). Approximate 95 % confidence intervals confirmed robustness (reaction-time R^2 0.64 – 0.80). HRV indices reflecting parasympathetic tone (pNN20, RMSSD) and sympatho-vagal balance (LF/HF), together with EDA burst counts, dominated psychomotor-speed prediction, whereas respiratory-stability metrics (mean RR, RR SD) emerged alongside HRV for working-memory accuracy. Removing the respiration belt and EMG electrodes—retaining only ECG and EDA—reduced reaction-time R^2 by < 0.20 while preserving ≥ 85 % of baseline performance, demonstrating a practical two-sensor solution.

Conclusions: An overnight recording of only heart-rate and skin-conductance signals can accurately forecast next-morning alertness (SSS score), psychomotor speed (median PVT reaction time), and working-memory accuracy (3-back percent correct) without explicit sleep-stage scoring. Transformer models capture long-range physiological patterns, and Shapley-guided pruning reveals that a two-channel wearable is enough for reliable early-shift screening of cognitive readiness. These findings support applications in shift-work fatigue management, driver vigilance checks, and remote-operator scheduling. Limitations include an all-male sample, controlled laboratory conditions, and a restricted cognitive battery. Future work will expand validation to larger, gender-balanced cohorts, real-world environments, and broader cognitive tasks, paving the way for longitudinal occupational deployment.

Evaluation of a Contactless Sleep Monitoring Device for Sleep Stage Detection against Home Polysomnography in a Healthy Population

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Introduction: Sleep is essential for overall health and well-being, but assessing sleep architecture and quality is often costly and time-consuming, relying primarily on polysomnography (PSG). Wearable and nearable devices offer potential alternatives, but they regularly lack rigorous validation, especially in real-world settings.

Materials and methods: This study evaluates the accuracy and reliability of Withings Sleep Analyzer (WSA), a contactless sleep monitoring device, compared to PSG in a home setting using a large and diverse cohort of healthy individuals. A total of 117 participants (69 women; 39.9 ± 11.4 years, mean $\pm$ std) underwent home-based polysomnography (PSG) and simultaneous WSA recording. Data analysis focused on evaluating sleep-wake distinction and sleep stage identification using standard classification metrics.

Results:

WSA demonstrates high sensitivity (93%) for sleep detection and moderate sensitivity (73%) for wakefulness, achieving an overall accuracy of 87% for sleep-wake distinction. The device showed consistent performance across various demographic subgroups, including different age, BMI, mattress and sleep arrangements (with or without bed partner) categories. Challenges were noted in accurately classifying specific sleep stages, particularly in distinguishing between light and deep sleep, with a mean accuracy of 63% and a Cohen's Kappa of 0.49. The WSA tended to overestimate total sleep time (+20 min) and light sleep (+1h21 min) while underestimating REM (-15 min) and deep sleep (-46 min) durations. Disagreements between expert reviewers, particularly between light and deep sleep stages, mirrored in part the WSA's misclassifications. Participants reported significantly altered perceived sleep quality during the night with the PSG, suggesting potential discomfort during sleep.

Conclusions: WSA offers a promising approach to sleep monitoring in natural home environments. Being contactless and placed under the mattress, the WSA's allows for long-term monitoring of sleep measures. It shows competitive performance in sleep-wake and sleep stage identification compared to other consumer devices. Progress in wearable and nearable devices is necessary to enhance their accuracy to better support the monitoring of populations with strongly impaired sleep, although limited by an imperfect gold standard. This work also emphasizes the importance of using large, diverse, and challenging datasets, as well as the need for a standardized methodology for accurate sleep stage classification.

Feasibility and Application of a Novel Home-Based EEG Eye Mask for Personalized Sleep Pattern Modeling in an Elite Athlete: A Case Study

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Introduction: For athletes, appropriate training periodization is critical for performance optimization, yet leveraging objective sleep metrics to support periodization remains a challenge. The clinical gold standard, Polysomnography (PSG), is unfeasible for routine use due to its prohibitive cost and extensive waiting periods. Athletes often rely on subjective questionnaires and consumer-grade wearables, which

lack the electroencephalogram (EEG) signals required to analyze sleep architecture. Therefore, a portable home-based sleep monitoring device that provides valid and objective sleep metrics is highly desirable to bridge the gap between practical usability and reliable physiological measurement.

Materials and methods: This case study examined the relationship between daytime training stress and nighttime sleep patterns in a 27-year-old elite male triathlete across 38 consecutive days. Data acquisition involved two parallel streams: sleep data were recorded using a novel, self-applied EEG eye mask developed at National Cheng Kung University, while training data were quantified objectively via Training Stress Score (TSS) by the Garmin watch and subjectively via a four-tier intensity scale. To control for confounders, Obstructive Sleep Apnea (OSA) was screened using an ApneaLink Air device. Following data collection, raw EEG data exceeding four hours in duration were manually scored by sleep technicians to obtain precise and objective sleep metrics, including total sleep time (TST), sleep efficiency (SE), sleep onset latency (SOL), wake after sleep onset (WASO), arousal index, wake-sleep transitions, and stage transitions. These metrics, foundational for personalized sleep modeling, were also evaluated in relation to clinical normative thresholds. The primary objective was to validate a feasible home-based sleep monitoring methodology and establish a practical framework for personalized sleep pattern modeling in athletic populations.

Results: In evaluating the feasibility of home-based sleep monitoring, 27 of 38 nights (71%) resulted in successful data acquisition. Recordings of less than 4 hours ($n=7$) were excluded, along with 11 nights due to participant non-adherence ($n=8$) and poor signal quality ($n=3$). Sleep metrics across 20 nights showed the following distributions: $TST=354.9\pm54.9$ min, $SE=90.2\pm6.1\%$, $SOL=15.9\pm14.4$ min, $WASO=16.6\pm14.2$ min, arousal index= 14.2 ± 10.2 events/hour, wake-sleep transitions= 24.8 ± 9.7 counts, and stage transitions= 90.8 ± 33.2 counts. These values mostly fell in established clinical normative ranges. Analysis of threshold exceedances showed that SE fell below 85% in 1 of 20 nights (5%), SOL exceeded 30 minutes in 2 nights (10%), WASO exceeded 30 minutes in 3 nights (15%), and arousal index exceeding 14 events/hour in 6 nights (30%).

Conclusions: This study demonstrated the feasibility of the novel EEG eye mask as a portable sleep monitoring solution for an elite athlete, achieving a 71% data acquisition success rate. In addition, the personalized modeling approach revealed athlete-specific sleep patterns, underscoring the discrepancy between clinical norms and practical monitoring needs of athletic populations. Crucially, the integration of sleep-based modeling with training load data establishes a foundation for a data-driven framework, providing athletes and coaches with reliable metrics to optimize training periodization.

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Hemodynamic spectral signatures across vigilance states: a whole-night EEG/fNIRS investigation

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Introduction: Sleep is not only characterized by Electroencephalography (EEG) signatures, but also by specificities in brain hemodynamic activity, measurable with functional Magnetic Resonance Imaging (fMRI) or functional Near-Infrared Spectroscopy (fNIRS). EEG/fMRI studies revealed distinct oscillations in regional blood-oxygen-level-dependent signal during N2 and N3 sleep, correlated with sleep spindles and slow waves. An enhancement in vasomotor (~0.1Hz) and respiratory (~0.2Hz) oscillations has also been reported during non-rapid-eye-movement (NREM) sleep which was linked to increased EEG slow oscillations. However, REM findings remain absent, highlighting the necessity of

whole-night investigations. Despite these insights, EEG/fMRI sleep studies are limited in duration due to immobility constraints and the acoustic noise impedes reliable investigation of REM phasic/tonic microstructure. Alternatively, fNIRS emerged as a promising approach for prolonged sleep monitoring, allowing measurement of hemodynamic fluctuations by estimating cortical oxygenated and deoxygenated hemoglobin concentration changes. We propose whole-night EEG/fNIRS, using an optimized locally dense montage to maximize fNIRS sensitivity to targeted bilateral frontoparietal regions, allowing to investigate sleep-state-specific and region-specific patterns of oxyhemoglobin oscillations in healthy subjects.

Materials and methods: Whole-night simultaneous EEG-fNIRS were recorded from 13 healthy young adults together with auxiliary signals (respiratory belt, pulse oximetry and mean arterial pressure (MAP)), monitoring systemic physiology. EEG sleep staging, including REM phasic/tonic states, followed the American Academy of Sleep Medicine manual. Our personalized fNIRS optimal montage, targeting bilateral frontoparietal regions (2 light-sources and 4 detectors per region) were computed for each participant using individual anatomical information to optimize fNIRS optodes placement (Delaire et al 2025). Standard fNIRS pre-processing included: filtering (0.002-0.5Hz), short distance channel regression, oxy/deoxyhemoglobin estimation. We then applied Morse analytical wavelet time-frequency analysis and disentangled oscillatory from aperiodic (1/f) components of hemodynamic signals. Oxyhemoglobin power spectra were estimated for each stable sleep state—including REM phasic/tonic, using the time-frequency maps. To assess whether relative changes of hemodynamic power during each sleep state (vs wakefulness) were significant, time-frequency results were normalized frequency-bin-by-frequency-bin to wake segments, before applying a t-test on the logarithm of such ratio. Similar time-frequency analysis was applied to auxiliary signals.

Results: Our results, based on 13 subjects (6 females, 18-35 years, mean sleep efficiency:90.3%), show sleep-state-specific signatures of hemodynamic oscillations in frontal and parietal regions. In frontal region, compared to wakefulness, N3 showed increase oxyhemoglobin power in respiratory band (~0.2Hz) and reduced power around 0.004-0.013Hz. N2 exhibited increased oscillatory power in respiratory band ~0.2Hz. REM sleep was characterized by overall increases in frequencies <0.15 Hz and respiratory-band oscillations. Both REM tonic and phasic states exhibited increased power in (<0.15 Hz) and respiratory band, with tonic REM showing a larger peak around 0.2Hz. Complementary analysis of auxiliary signals revealed dominant oscillatory component in pulse oximetry at ~0.2Hz and cardiac band (~1Hz), MAP at vasomotor ~0.1Hz and respiration belt at ~0.2Hz, suggesting that sleep-stage-specific hemodynamic oscillations were not solely driven by systemic physiology.

Conclusions: Whole-night personalized EEG/fNIRS appears as a new promising modality to study sleep physiology, suggesting that sleep-stage-specific hemodynamic signatures could be used to further characterize NREM and REM sleep in healthy and pathological conditions.

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Impact of lifestyles and daily experiences on nocturnal heart rate variability and heart rate among 100,000 adults

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Introduction: Both heart rate (HR) and heart rate variability (HRV) can be used to assess autonomic function. Lifestyle choices, such as alcohol use and smoking, may impact autonomic activity at night. However, it is unclear how nocturnal HRV and HR are impacted by these and other daily behaviors. Cutting-edge sleep technologies provide an opportunity to address this gap; in the current study, we do so using a large, real-world sample comprising adult users of an under-mattress sleep monitor.

Materials and methods: We assessed nocturnal HR and HRV using Sleeptracker-AI Monitors (Fullpower Technologies Inc., California, USA), which use under-mattress piezo-electric sensors. HRV measures included SDNN (overall HRV) and RMSSD (an index of parasympathetic activity). Each day, subjects self-reported alcohol use, smoking, eating habits, stress, caffeine use, sleep quality, and exercise. Data was collected from 9/1/2023-9/30/2024. We used mixed effects models with participant as a random effect to obtain estimated marginal mean (EMM) HR, SDNN, and RMSSD for

each response category of the self-report questions. We performed pairwise comparisons to assess the differences in EMMs across categories. Additionally, we examined the effects of age and gender adjustment and performed a completely within-subjects analysis in which we excluded participants who answered questions only one way, minimizing the effects of between-subject variability.

Results: Data availability differed by self-report question and HR/HRV metric, so analyses differed in sample size. Across all participants (47.3% female), the mean (standard deviation) age was 48.9 (13.2) years. The largest analysis (HR by exercise) included 100,990 participants (1,765,500 nights) and the smallest analysis (RMSSD by smoking) included 1,145 participants (12,519 nights). The mean analysis size was 35,120 participants (571,650 nights). All pairwise comparisons, except leisurely vs. no exercise for HR ($p: 0.09$), were significant ($p < 0.001$). On nights after which participants reported alcohol use (vs. non-use), participants had decreased SDNN (EMM: 37.3 vs. 40.6 ms) and RMSSD (EMM: 28.6 vs. 31.9 ms), and increased HR (EMM: 66.5 vs. 62.7 bpm). Similarly, self-reported smoking (vs. non-smoking) was associated with lower HRV (EMM, SDNN: 38.1 vs. 41.4 ms; RMSSD: 32.1 vs. 34.7 ms) and higher HR (EMM: 67.4 vs. 64.4 bpm) during the night. Additionally, SDNN and RMSSD were lower, while HR was higher, on nights after which participants reported caffeine non-use vs. use, having a stressful vs. normal vs. stress-free day, exercising at high intensity vs. leisurely vs. not exercising, eating a meal vs. a snack vs. not eating within two hours of bedtime, and sleeping not well vs. normally vs. well. For all metrics, alcohol use and smoking showed the largest effect sizes. Results were similar after age/gender adjustment and in the completely-within subjects analysis.

Conclusions: Decreased nocturnal HRV and increased nocturnal HR were linked to drinking alcohol, smoking, eating before bedtime, stress, caffeine non-use, self-reported poor sleep, and exercise. Nocturnal autonomic function may be particularly impacted by lifestyle choices such as drinking alcohol and smoking. Noninvasive sleep technologies will be invaluable in further uncovering the relationship between daily behaviors and nighttime autonomic function.

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Implementation of the AI-Powered Belun Ring to Streamline Sleep Disorder Assessment in Primary Care: A Real-World Community Study

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Introduction: The global increase in sleep disorders—driven by an aging population and rising obesity presents a significant public health challenge. Despite their high prevalence and association with cardiovascular, metabolic, and mental health conditions, many sleep disorders remain undiagnosed, contributing to increased healthcare utilization and socioeconomic burden. The delay in diagnosis and treatment is largely due to the long waiting time for diagnostic test (PSG) in public healthcare system as well as costly tests in private health care setting. Wearable sleep technologies offer a scalable and cost-effective alternative to traditional testing; however, their adoption in primary care remains limited. This study evaluated the use of the AI-powered Belun Ring (BR), a medical-grade wearable, to characterize sleep phenotypes and compare outcomes between individuals referred by primary care physicians (PCPs) and specialists in a real-world clinical setting.

Materials and methods: This retrospective study included 347 adults referred for sleep assessment at The Chinese University of Hong Kong (CUHK) Medical Clinics between June 2020 and June 2025. Participants completed at least three nights of home sleep monitoring using the BR, with ≥ 60 minutes of total sleep time per night required for data inclusion. The device generated objective sleep metrics, including the apnea-hypopnea index (bAHI4%, AASM 1B rule) and sleep efficiency (bSE). Based on these measures, participants were categorized into four sleep phenotypes: normal (bAHI4% <15 & bSE ≥ 80), obstructive sleep apnea (OSA: bAHI4% ≥ 15 & bSE ≥ 80), insomnia (bAHI4% <15 & bSE <80), and COMISA (bAHI4% ≥ 15 & bSE <80). A multinomial logistic regression model was used to assess the association between referral type (PCP vs. specialist) and sleep phenotype, adjusting for age, sex, and BMI.

Results: Of the 347 referred patients, 287 (83%) met data quality criteria. Among these, 53% screened positive for a sleep disorder phenotype: 30% met criteria for OSA, 16% for insomnia, and 6% for COMISA. PCP referrals accounted for 85% of the cohort. There were no statistically significant

differences in sleep phenotype distribution between PCP and specialist referrals (COMISA: Odds Ratio=2.34, 95% CI=0.67–8.14; insomnia: 1.40, 0.54–3.64; OSA: 0.86, 0.35–2.08). Age was significantly associated with increased odds of all three sleep disorder phenotypes (COMISA: 1.13; insomnia: 1.10; OSA: 1.05). Higher BMI was associated with increased odds of COMISA (1.31, 1.14–1.52) and OSA (1.26, 1.15–1.39), but not insomnia. Female sex was associated with lower odds of OSA (0.31, 0.14–0.67).

Conclusions: This study is among the first to demonstrate the feasibility and public health value of integrating AI-driven wearable technology into primary care for sleep disorder risk assessment. The comparable phenotype distributions between PCP and specialist referrals support the use of the BR as a frontline tool for identifying individuals at risk and triaging them for further evaluation. Integrating medical-grade wearables into primary care workflows could play a critical role in addressing the substantial burden of undiagnosed sleep disorders, reduce demand on specialist services, and enabling earlier care for at-risk individuals in community settings.

Improving Inter-Scorer Reliability in Polysomnography Interpretation: A Multi-Year, Case-Driven, Cloud-Based Training Program

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Introduction: Accurate interpretation of polysomnography (PSG) is essential for diagnosing sleep disorders, yet inter-scorer variability persists due to differences in patient presentations, scorer backgrounds, and application of American Academy of Sleep Medicine (AASM) standards. To address this, we developed a cloud-based platform, and, since 2021, have conducted annual workshops that utilize PSG and Multiple Sleep Latency Test (MSLT) case reviews, platform tools, and standards discussions to systematically improve inter-scorer consistency.

Materials and methods: This ongoing training program (2021–2025), conducted in collaboration with the Taiwan Society of Sleep Medicine, hosts annual sleep workshops on the cloud-based platform. The platform provides full-length PSG and MSLT recordings, supports online annotation of sleep stages and events, features an autosave function, and allows location-independent access. The workflow comprises a participant pre-test, an expert review of common errors, and interactive lectures covering AASM standards, and interpretation strategies. Participants then complete a post-test on the same data set; upon submission, the platform generates individualized reports summarizing overall agreement, and stage-specific concordance.

From 2021 to 2024, the workshop participants were primarily sleep technicians and physicians (n=70 in 2021; n=34 in 2022; n=13 in 2023; n=23 in 2024). To address diverse clinical challenges, each workshop centered on a specific case. The 2021 workshop focused on a 50-year-old male patient with a moderate apnea-hypopnea index (17.7). The 2022 session targeted an 80-year-old male with a severe sleep disorder and significant leg movements. The 2023 workshop addressed sleep fragmentation in an 85-year-old female patient. The 2024 case involved a 59-year-old male with severe nocturnal apnea (AHI=57.4) and daytime sleepiness, and the platform also incorporated a novel automated slow-wave (0.5–2 Hz) detection system (recall=0.979; precision=0.963). The upcoming 2025 workshop will focus on narcolepsy, featuring a 46-year-old male and adding new functions for REM sleep without atonia (RWA) annotation, integrated PSG/MSLT visualization, and MSLT light markers.

Results: The workshops have consistently improved scoring agreement over the years. In 2021, the median sleep stage agreement increased from 74.6% to 82.3% (P < .001 for N1, N2, N3, and overall), and the proportion of scorers achieving ≥ 80% agreement increased from 20.0% to 58.6%. For 2022 significant limb movement cases, sleep stage agreement improved from 71.6% to 80.8%, and periodic limb movements (PLMS) event agreement from 83.2% to 87.5%. In the 2023 study of complex elderly cases, stage agreement rose from 79.1% to 84.0% (P < .05 for N2 and overall). In 2024, with slow-wave detection to assist in scoring a case of severe sleep-disordered breathing, stage agreement improved from 65.7% to 72.7% (P = .00012), and respiratory event agreement increased from 72.8% to 89.4% (P = .00014).

Conclusions: This case-driven, cloud-based training paradigm effectively improves inter-scorer reliability for the interpretation of PSG and MSLT across diverse clinical scenarios by combining tailored instruction with advanced signal-detection tools. The transition to a global, online workshop in 2025 is expected to extend these benefits internationally, thereby promoting standardized sleep scoring practices.

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Improving Sleep and Well-being Through VR Mindfulness: Evidence from a 5-Session Program

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Introduction: Virtual Reality (VR)-based mindfulness interventions have demonstrated promising effects on emotional well-being, including stress reduction and improved emotional regulation. However, few empirical studies have specifically examined the impact of VR mindfulness programs on sleep quality, a key indicator of psychological and physiological health. This study aimed to investigate the effects of a structured VR mindfulness program on sleep quality, perceived stress, and negative affect.

Materials and methods:

control group (n = 35). The experimental group participated in five 45-minute VR mindfulness sessions using *TRIPP* over two weeks. Each session consisted of a 10-minute check-in and emotional awareness activity, a 10-minute guided mindfulness meditation using *TRIPP*, a 10-minute mindfulness session with 360-degree natural landscape immersion, and a brief wrap-up and reflection. The control group received no intervention during the study period. Sleep quality was measured using two methods: the Pittsburgh Sleep Quality Index (PSQI) for self-reported sleep quality and smartwatch-based actigraphy using Galaxy Watch, which recorded sleep duration, onset latency, wake time, and sleep efficiency. Participants wore the Galaxy Watch overnight at three time points—pre-intervention, post-intervention, and follow-up (two weeks post-intervention). Perceived stress and negative affect were assessed using validated self-report questionnaires administered at the same time points.

Results: Repeated-measures ANOVA revealed significant interaction effects between time and group for all three outcome variables. Compared to the control group, the experimental group showed significant improvement in sleep quality, as indicated by lower PSQI scores and increased sleep efficiency recorded by the Galaxy Watch. Additionally, participants in the experimental group reported reduced perceived stress and decreased negative affect. These positive effects were evident immediately after the intervention and were maintained at the follow-up assessment.

Conclusions: This study demonstrates that a short-term, VR-based mindfulness program can effectively improve sleep quality and reduce psychological distress. The combination of self-report measures and objective data collected through the Galaxy Watch supports the reliability of these findings. VR meditation may offer a useful and engaging tool for promoting mental health and enhancing sleep in daily life.

Improving Sleep Stage Classification from Consumer Wearables Using a Two-Level Machine Learning Framework with Selective Correction

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Introduction: Measuring sleep across extended periods is critical for capturing day-to-day variability in sleep dynamics. While polysomnography (PSG) remains the gold standard, its high cost and intrusiveness limit feasibility for longitudinal, real-world monitoring. Consumer-grade wearable activity trackers such as Fitbit are increasingly adopted in research due to their affordability, scalability, and ease of use. However, these devices are known to have limited accuracy in detecting sleep stages. This study proposes and validates a novel two-level machine learning framework that selectively corrects

Fitbit-derived sleep stage labels using only processed, readily available data. The aim is to improve sleep staging accuracy in free-living environments.

Materials and methods: A three-night, in-home sleep monitoring study was conducted with 23 healthy adults (mean age = 24.8 ± 4.4 years). Sleep was recorded using Fitbit Charge 2 and a medical-grade portable EEG (Sleep Scope). To minimize the first-night effect, data from the second night were primarily used. Fitbit-provided sleep stages, heart rate, and aggregated metrics (e.g., total sleep time, sleep efficiency) were synchronized with medical-grade labels. We constructed 21 features from Fitbit and questionnaire data, divided into static (e.g., age, PSQI, sleep summaries) and dynamic (e.g., epoch-wise heart rate changes, adjacent sleep stages) feature groups.

Each 30-second epoch received two labels: a binary label indicating Fitbit classification correctness (level-I), and a multi-class label representing the true sleep stage (level-II). Level-I classifiers (SVM, RF, NB) identified misclassified epochs, while level-II reclassified them using XGBoost. To address class imbalance, random up- and down-sampling techniques were applied at level-II. Models were evaluated using nested leave-one-subject-out cross-validation (LOSO-CV) and assessed via both microscopic (e.g., accuracy, kappa, MMCC) and macroscopic (e.g., normalized absolute bias [MAB]) performance metrics.

Results: The two-level models consistently outperformed Fitbit and one-level baselines. SVM + XGBoost with up sampling (SVM + XGBu) achieved the best per-epoch classification accuracy (0.731 ± 0.119), while RF + XGB with down sampling (RF + XGBd) showed the best agreement in total sleep stage durations (lowest MAB = 0.010, <1% of baseline error). SVM + XGBd achieved a balance between the two. Light sleep classification reached up to 89.6% accuracy, although accuracy for deep sleep remained lower. Compared to Fitbit, the models reduced misclassification between adjacent sleep stages, notably for REM and wakefulness. Performance was influenced by class imbalance and dataset shift, with resampling improving accuracy but also increasing sensitivity to inter-individual variability. Down sampling led to better generalizability, while up sampling improved detection of underrepresented stages at the cost of distribution shift.

Conclusions: This study demonstrates that accurate sleep stage classification is achievable using only processed outputs from consumer wearables, without relying on raw data or specialized equipment. The proposed two-level correction framework improves both per-epoch accuracy and stage-level duration estimates. These findings support the use of enhanced machine learning techniques to extend the utility of wearables in sleep research and digital sleep medicine.

In-lab experience with an AASM-certified AI for sleep staging using polysomnography data

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Introduction: In sleep laboratories, polysomnographic recordings are routinely evaluated manually, especially when it comes to sleep stage classification.

Often several scorers are employed in sleep laboratories, and discrepancies between them are common due to the subjective nature of visual scoring, even when standardized guidelines are followed. Sleep staging remains one of the most time-consuming tasks, accounting for approximately 50 to 80% of the total evaluation time. With the AASM-certified DOMINO-AI (SOMNOmedics AG, Germany), a scoring tool is now available that promises time-efficient sleep staging. This study compares AI-based staging with two human scorers (S1 and S2) in our sleep lab, assessing agreement, interrater variability, and efficiency.

Materials and methods: In a total of 26 patients (16 male; mean age 51.8 ± 15 years; 10 mild, 5 moderate, 5 severe obstructive sleep apnea (OSA); 15 periodic limb movement disorder (PLMD); 9 subjects presented comorbidity) standard polysomnography (SOMNO HD, SOMNOmedics AG, Germany) during diagnostic nights (four patients with mandibular advancement device, MAD) were performed. Recordings were scored independently according to current AASM guidelines by two qualified scorers (S1, S2) as well as by DOMINO-AI (Fig. 1). The results of S1 (default scorer) were compared with DOMINO-AI and S2. Agreement between AI and human scorers and the interrater variability between the two scorers was analyzed epoch-to-epoch (in total 21358 epochs, epochs with artefact excluded) using confusion matrices, Cohen's Kappa, F1 score.

Results: The interrater reliability between the manual scorer S1 and the AI-conducted analysis on average across all patients was $82.7 \pm 6.3\%$, between the two manual scorers the agreement was

80.8±6.2% (Fig.2). In the epoch-to-epoch evaluation of artefact-free epochs Cohen's kappa was 0.75 and F1 score 0.815 (Table 1). The comparison of S1 and S2 showed a Cohen's kappa of 0.71 and a F1 score of 0.787. The regression of the evaluated epochs (E) for S1 vs. AI and S1 vs. S2, respectively, was as follows (Table 2): Wake phases (W): $R^2 = 0.925$ and $R^2 = 0.963$; N1/N2: $R^2 = 0.789$ and $R^2 = 0.737$; N3: $R^2 = 0.813$ and $R^2 = 0.737$; REM sleep (REM): $R^2 = 0.812$ and $R^2 = 0.745$.

Conclusions: The AI-based analysis showed an agreement of 80%, which was slightly higher than the agreement observed between the two in-lab scorers (S1 vs. S2: 79%). The inter-rater reliability between AI and S1 was substantial (Cohen's kappa = 0.75, F1 score = 0.815), indicating a strong level of agreement in sleep staging– slightly higher than the agreement between the two manual scorers (Cohen's kappa = 0.71, F1 score = 0.787). The level of agreement, Cohen's Kappa, and F1 score are in the same range as reported in the literature^{1,2,3}. These results are particularly notable given the challenging nature of the dataset, which included fragmented sleep patterns due to conditions such as OSA and PLMD. Given its sufficient accuracy, better than our in-lab rater variability and significant time savings, the AI-based pre-analysis proves to be a valuable tool for routine use in our sleep laboratory.

Management of adult laryngeal hemangioma with snore using low-temperature plasma radiofrequency coblation

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Introduction: Objective: This study investigated the therapeutic effects of low-temperature plasma radiofrequency (LPRF) coblation on adult laryngeal hemangiomas (ALHs) with snore using suspension laryngoscopy.

Materials and methods: Material and Methods: The clinical data of 23 patients with ALH with snore treated by LPRF coblation were analyzed retrospectively. All patients underwent edge coagulation before ablation resection. Postoperative voice and swallowing were assessed.

Results: Results: The 23 ALHs were diagnosed clinically as 6 cavernous hemangiomas and 17 capillary fibroangiomas. All 23 cases achieved success after a single LPRF coblation, and there was no postoperative bleeding, dyspnea, dysphagia, dysphonia, or other complications. None required postoperative tracheotomy. The patients were followed for 1 year without recurrence. Before surgical intervention, only 2 (8.7%) of the 23 patients had mild (n = 1) or moderate (n = 1) dysphagia. Postoperative dysphagia was assessed at the 1- and 3-month follow-ups. At 1 month, 5 (21.7%) of 23 patients had mild dysphagia, including 3 (13.0%) reporting new mild dysphagia. However, at 3 months postoperatively, none of patients had any dysphagia. The mean Voice Handicap Index was 11.2 ± 3.7 preoperatively, 7.1 ± 2.8 at 1 month postoperatively, and 4.8 ± 3.1 at 3 months postoperatively; the mean maximum phonation time was 10.8 ± 3.7 s preoperatively and 12.6 ± 1.8 and 14.1 ± 3.9 s at 1 and 3 months postoperatively, respectively.

Conclusions: Conclusions: LPRF coblation is an effective minimally invasive method for treating ALHs with snore with better voice and swallowing recovery. Edge coagulation before ablation resection may reduce intraoperative bleeding.

Manual Versus Automated Polysomnography Scoring: Inter-rater Accuracy in a Single-Center Thai Cohort

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Introduction: The demand for trained sleep study personnel is rising, but the relative accuracy of advanced sleep technicians (ASTs), sleep disorder specialists (SDSs), and commercial autoscoring

software (AUTO) has not been quantified in Thailand. We evaluated inter-rater agreement, scorer bias, and clinical comparability among these three methods.

Materials and methods: A retrospective analysis was performed on 250 consecutive diagnostic polysomnography (PSG) studies recorded between September 2022 and February 2023 (102 women, 148 men; mean age 48.5 ± 17.5 y; BMI 29.1 ± 6.6 kg/m²). Each record was independently scored by a randomly assigned certified AST (n = 10), a blinded SDS and AUTO (default settings). Sleep stages, respiratory events and derived indices were extracted. Categorical agreement was assessed with Cohen's κ ; continuous agreement with intraclass-correlation coefficients (ICC, two-way random, absolute agreement). Bias and limits of agreement were evaluated using Bland–Altman analysis. Apnoea–hypopnoea index (AHI), arousal index (ARI) and sleep efficiency (SE) were compared across raters with repeated-measures ANOVA and Tukey post-hoc tests ($\alpha = 0.05$).

Results: AST–SDS staging agreement was almost perfect ($\kappa = 0.832$ – 0.980). In contrast, AST–AUTO agreement ranged from slight for NREM1 ($\kappa = 0.081$) to moderate for wake ($\kappa = 0.599$), producing stage-specific differences between AST–SDS and AST–AUTO for every stage except NREM2 (overall $p < 0.0001$; NREM2 $p = 0.099$). For respiratory events, AST–SDS reliability was substantial to perfect (ICC = 0.684 for central apnoea; 0.945–0.998 otherwise), whereas AST–AUTO reliability spanned poor (central apnoea, ICC = 0.023) to strong (mixed apnoea, ICC = 0.869). The same pattern emerged for derived indices: AST–SDS ICCs were excellent for AHI (0.982), ARI (0.982) and periodic limb movements (PLMs, 0.965); AST–AUTO ICCs were moderate for AHI (0.564) and ARI (0.496) and poor for PLMs (0.149). Bland–Altman plots showed significant bias across all variables ($p \leq 0.0487$). Repeated-measures ANOVA revealed significant rater effects for AHI ($p = 0.042$) and ARI ($p = 0.028$); SE differed for seven of ten ASTs ($p < 0.006$). Post-hoc tests confirmed AST differed from AUTO for AHI ($p = 0.013$) and ARI ($p = 0.030$) but not from SDS.

Conclusions: Manual scoring conducted by ASTs and SDSs, following the AASM 2020 guidelines, shows a strong level of agreement and minimal bias. In contrast, the commercial AUTO algorithm demonstrates lower reliability and clinically significant discrepancies, particularly regarding NREM1 sleep, central apnoea, and periodic limb movement detection. Therefore, expert review remains crucial until the performance of these algorithms is improved. This data serves as a foundation for national training standards and identifies specific areas for improvement, including NREM1, PLMs, and CA discrimination, to guide the development of future AI-enhanced autoscoring tools.

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Monitoring the motor fingerprint of the nocturnal sleep period and its cardiovascular correlates with a wearable multi-sensor array

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Introduction: Wearable technology allows for unobtrusive monitoring of cardiovascular and motor function. We explored the feasibility of characterizing the motor fingerprint of the nocturnal sleep period and its cardiovascular correlates using an array of wearable sensors.

Materials and methods: Twelve healthy adult volunteers (6 females) from the LOOKING-GLASS MIAR study were monitored at home throughout their self-reported sleep period with simultaneous use of Axivity AX6 accelerometers at five body segments (both wrists, both ankles, and the lower back), a Polar H10 ECG chest strap, and a Polar Verity Sense photoplethysmography arm band. The two Polar sensors were connected via Bluetooth to a smartphone with a custom-built app (VEGA). Movements were detected with a threshold-crossing algorithm based on the envelopes of the accelerometer signal magnitude vector over time. The algorithm was validated against visual scoring based on raw acceleration recordings. Movements were categorized as segmental, regional, or global if occurring in 1, 2–4, or 5 body segments, respectively. Changes in cardiovascular control associated with movements were assessed based on heart rate (HR) and pulse wave amplitude (PWA) changes compared to the pre-movement baseline. The nocturnal sleep period was defined based on sleep diary. Sleep and wakefulness during the nocturnal sleep period were scored based on non-dominant wrist acceleration with a validated algorithm implemented in the GGIR open-source software.

Results: Segmental and lower-body regional movements were significantly greater fractions of total movements during nocturnal sleep than during nocturnal wakefulness, whereas the opposite occurred

for global movements. Segmental and regional movements were associated with mono- or bi-phasic changes in HR and PWA, with early increases in HR and decreases in PWA variably followed by later opposite changes. Global movements were associated with larger, monophasic increases in HR and decreases in PWA. The changes in HR and PWA started 2-4 s earlier than the onset of movement.

Conclusions: Our study indicates the feasibility of recording movement-related HR and PWA patterns during nocturnal sleep and wakefulness with a combination of wearable sensors. The motor fingerprint of nocturnal sleep and wakefulness and the sleep movement-related HR and PWA patterns have the potential to be developed into biomarkers of sleep and cardiovascular disorders.

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Multi-Night At-Home Evaluation of Oura Ring Against Dreem Headband in Free-Living Older Adults

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Introduction: Although sleep-tracking wearables are widely used, few validation studies have assessed their accuracy and night-to-night stability in older adults under free-living conditions. This study evaluated the Oura Ring against the Dreem headband across multiple nights, focusing on both measurement bias and intra-individual variability.

Materials and methods: Forty-five older adults [mean age $\pm$ SD: 74.4 $\pm$ 2.4 years; 23 females] concurrently wore the Oura Ring and Dreem headband at home. The Dreem headband served as a research-grade EEG reference to evaluate the performance of the Oura Ring in free-living older adults. We analysed 215 nights of paired data to compare nightly estimates of total sleep time (TST), sleep efficiency (SE), wake after sleep onset (WASO), sleep onset latency (SOL), and time spent in each sleep stage. Bias (Oura – Dreem) and the standard deviation (SD) of nightly bias were calculated for each subject to evaluate measurement stability. We also report epoch-by-epoch agreement metrics including accuracy, sensitivity, specificity, Cohen's kappa and prevalence-adjusted bias-adjusted kappa (PABAK).

Results: On average, Oura underestimated TST by 17.5 $\pm$ 42.3 minutes, SE by 3.5 $\pm$ 8.4%, and REM by 23.2 $\pm$ 36.9 minutes, and overestimated SOL by 11.5 $\pm$ 27.3 minutes, WASO by 6.0 $\pm$ 38.9 minutes, and light sleep by 7.8 $\pm$ 46.5 minutes. Deep sleep was slightly underestimated (-2.1 $\pm$ 32.2 minutes). Mixed models showed no significant effect of night on bias across any variable, supporting stability over time. The night-to-night variability (SD) of these biases was significantly lower in participants with higher SE; indicating greater measurement stability in more efficient sleepers. Accuracy, sensitivity, and specificity for sleep-wake classification were 85.6% ($\pm$ 6.7%), 88.4% ($\pm$ 7.5%), and 75.7% ($\pm$ 15.4%), respectively, with a Cohen's kappa of 0.58 ($\pm$ 15%) and PABAK of 0.71 ($\pm$ 13%).

Conclusions: In this multi-night validation study under free-living conditions in older adults, Oura Ring demonstrated reasonably accurate and stable multi-night sleep estimates when compared to the Dreem headband, with systematic but consistent biases across nights. Notably, higher sleep efficiency was associated with reduced night-to-night variability in Oura's measurement bias, suggesting a link between sleep fragmentation and device reliability. These findings support the use of Oura for longitudinal sleep monitoring under naturalistic conditions in older adults, with appropriate consideration of its limitations in subjects with lower sleep efficiency.

Non-Contact Supine Position Estimation Using a Sound-Based AI Model

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Introduction: In this study, we introduced sleep position prediction - specifically supine position detection - as an auxiliary task within a sound-based AI model for sleep analysis. Supine-predominant obstructive sleep apnea (OSA) is frequently observed, with supine sleep consistently associated with greater OSA severity in adults. However, the proportion of time spent in the supine position is often overrepresented during hospital-based polysomnography (PSG), potentially due to physical constraints imposed by the monitoring apparatus. These discrepancies between sleep positions recorded during PSG and those typically assumed at home may lead to inaccuracies in the apnea-hypopnea index (AHI) and its clinical interpretation. Home-based sleep position monitoring, conducted under natural conditions, could offer valuable complementary information to contextualize PSG findings - especially when enabled by contactless tools such as sound-based AI models.

Materials and methods:

The latest sound-based AI model processes 80 consecutive Mel spectrograms, each representing a 30-second epoch, and employs a feature extractor to capture breathing pattern characteristics, followed by classifiers to predict sleep stages, OSA events, and snoring. Maintaining this two-stage structure, we extended the model by adding a position classifier trained to distinguish supine epochs from non-supine epochs using PSG-derived labels. The training dataset included 2,973 nights comprising hospital PSG recordings (with PSG equipment audio or smartphone audio) and home PSG recordings (with smartphone audio). A separate evaluation set of 802 nights was used (mean age: 50.5 ± 15.4 years; male:female = 530:272; mean BMI: 25.5 ± 3.6 ; mean AHI: 21.2 ± 20.6). Supine position predictions were evaluated on an epoch-by-epoch basis, and predicted supine ratios (percentage of total sleep time spent in the supine position) were compared with PSG-derived references.

Results: For the supine class, the model achieved a sensitivity of 0.85, specificity of 0.72, and an F1 score of 0.85 across the entire evaluation dataset. The overall epoch-by-epoch accuracy for supine versus non-supine classification across the evaluation dataset was 81.44%, with a macro F1 score of 0.79. When evaluated on smartphone-recorded audio only (237 nights), supine-specific sensitivity, specificity, and F1 score were 0.80, 0.71, and 0.80, respectively. The overall accuracy and macro F1 score in this subset were 76.84% and 0.75. The mean supine ratio based on PSG labels was 66.19% (SD 21.32), while the model-predicted supine ratio was 66.17% (SD 25.02). Predicted supine ratios showed moderate correlation with PSG-derived values ($r = 0.67$), with a mean error of 0.02% (SD 19.03).

Conclusions: This study demonstrates the potential of a sound-based AI model as a contactless tool that aids interpretation of AHI measurements affected by sleep position. While the model showed moderate agreement at the group level, its accuracy in estimating individual supine ratios from single-night data remains limited. Further refinement in detecting position-specific acoustic features from Mel spectrograms may enhance prediction performance. Nonetheless, integrating non-contact sleep position monitoring with sleep staging and OSA detection strengthens the role of sound-based AI as a practical and scalable complement to conventional sleep diagnostics.

Optimizing PPG Sequence Length for Deep Learning-based Sleep Stage Classification

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Introduction: Photoplethysmography (PPG) is a non-invasive and cost-effective measurement for sleep monitoring, particularly suitable for wearable applications. Although electroencephalography (EEG) remains the gold standard for sleep staging, PPG-based approaches have gained attention for their potential in unobtrusive home monitoring. Deep learning-based sleep stage classification using PPG has shown promising results; however, the effect of input sequence length—especially considering temporal dependencies between sleep stages—remains underexplored. This study investigates how varying PPG sequence lengths affect the performance of a deep learning model in classifying sleep stages, aiming to identify an optimal trade-off between model accuracy and sequence length.

Materials and methods: We utilized the publicly available Multi-Ethnic Study of Atherosclerosis(MESA) dataset, which provides comprehensive overnight physiological recordings, including PPG signals. PPG data from 321 subjects were segmented into non-overlapping 30-second epochs and preprocessed using standard filtering and normalization procedures. Each epoch was originally annotated with one of five sleep stages—Wake, N1, N2, N3, and REM—according to the American Academy of Sleep Medicine(AASM) guidelines. For this study, the stages were relabeled into four categories by merging N1 and N2 into Light Sleep(LS), and designating N3 as Deep Sleep(DS). The dataset was then split into training, validation, and test sets in a 7:1:2 ratio through subject-level stratified partitioning, ensuring generalization to unseen subjects.

Sequences were constructed from consecutive 30-second PPG epochs, with durations ranging from 30 seconds to 10 hours(i.e., N=1 to 1200). A sequence-to-sequence classification framework was implemented by adapting TinySleepNet, originally developed for EEG-based sleep staging. Considering the distinct characteristics of PPG, we modified the architecture by replacing the LSTM layer with bidirectional GRU units to capture bidirectional temporal dependencies while maintaining computational efficiency.

Results: The length of PPG sequences significantly influenced the sleep stage classification performance. Short sequences(N=1–30, corresponding to ≤ 15 minutes) showed low classification accuracy, particularly for LS and REM stages, suggesting insufficient temporal context for reliable stage discrimination. As sequence length increased, classification performance progressively improved. The optimal balanced performance across all stages was observed at N=300(2.5 hours), achieving a DS accuracy of 54.6%, thereby highlighting improved detection of this minority class. Notably, extending the sequence length beyond N=600(5 hours) led to continued improvement in Wake and LS stage accuracy, but increased misclassification of DS, indicating that class imbalance and overfitting to dominant sleep stages may have negatively impacted overall stage discrimination.

Conclusions: This study demonstrates that PPG sequence length has a substantial influence on deep learning-based sleep stage classification. Sequences of 1.5–2.5 hours(N=180–300) achieved the most balanced performance, maintaining consistent classification accuracy across both majority and minority stages. In contrast, sequences longer than 5 hours led to higher misclassification for minority stages, likely due to class imbalance and overfitting to dominant classes. These results highlight that selecting optimal sequence length is important to maximize the performance of PPG-based sleep staging models, particularly in real-world monitoring environments.

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Participation in at-home obstructive sleep apnoea monitoring: Findings from six months of daily mobile-based check-ins

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Introduction: Multi-night monitoring of obstructive sleep apnoea (OSA) severity is important to understand individual disease characteristics. To fully capture OSA's impact on daily life, it is equally important to assess daytime functioning; however, traditional measures of sleep-related daytime impairment are difficult to employ longitudinally. Therefore, we investigated the feasibility of a smartphone-based 'check-in' for long-term daily monitoring of self-reported daytime functioning in an OSA sample.

Materials and methods: Participants were recruited from public and private outpatient sleep clinics in Adelaide, South Australia, after referral for suspected OSA. Over a 6-month period, participants responded daily to a brief (<1 minute) daytime functioning questionnaire using Hoap, a consumer-available 'check-in' smartphone application. Questionnaire items, derived from the validated Acute Recovery Stress Scale, relate to six domains: sleep, fatigue, motivation, mental capacity, physical capability, and emotional balance. The Withings Sleep Analyser, a validated and FDA-approved under-mattress sleep sensor, was used to derive the nightly apnoea-hypopnoea index (AHI; events/hr). The

feasibility of this naturalistic monitoring approach was assessed through descriptive statistics and non-linear mixed effect modelling (Generalised Additive Models) of (a) initial self-report uptake (≥ 8 self-reports within first fortnight), (b) time-dependent change in adequate self-report rate (≥ 4 reports per week), and (c) the probability of a self-report occurring on any given day, as a function of various sleep-related and demographic predictors.

Results: On average, participants ($n=68$; 54% female) were obese [mean $\pm$ SD] (BMI: 32 ± 8 kg/m²), middle-aged (53 ± 15 years), had moderately severe OSA (AHI: 16.6 ± 18.4 events/hr), and made a self-report 3.7 (± 2.4) times per week. The proportion of the sample who achieved an adequate self-report rate declined over time but remained above 70% for one month post recruitment. The probability of adequate initial uptake was highest for those aged ~ 40 years and declined with increasing age (e.g., 40-50% less probable for those aged ~ 70 years), $p = 0.012$. Adequate initial uptake was more probable for females (probability: 87%) than males (probability: 58%), $p = 0.011$. Baseline sleep variables, including OSA severity, did not predict adequate initial uptake (all $p > 0.05$). Time-dependent variation in adequate self-report rate differed by all baseline demographic and sleep-related predictors (smooth-by-factor interactions: $p < 0.001$), though effect sizes were minimal. Within-individuals, the probability of a self-report on a given day was 10% greater following a night of high OSA severity (75th percentile; AHI = 23.5) than a night of low OSA severity (25th percentile; AHI = 2.8); smooth terms $p < 0.0001$.

Conclusions: These novel data support the feasibility of app-based check-ins within a clinical OSA cohort, with self-reports every second day appearing achievable for many. Although future research is needed to identify factors that enhance initial uptake and sustained use, our findings have important implications for both sleep clinicians and researchers monitoring daytime functioning over extended periods. They also serve as a foundation for future decision-making about daily prompts and app utility for longitudinal studies in clinical sleep health contexts. Appropriate use of daily check-ins may also help to advance knowledge of temporal relationships between OSA severity and daytime functioning.

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Pediatric AHI Estimation Using a Sound-Based AI Model: Toward Non-Contact Sleep Apnea Screening at Home

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Introduction: This study evaluates the efficacy of a sound-based AI model for predicting the apnea-hypopnea index (AHI) in pediatric populations as a potential non-contact adjunct to traditional polysomnography (PSG). Diagnosis of obstructive sleep apnea (OSA) in children with sleep-disordered breathing (SDB) typically requires overnight, hospital-based level I PSG. However, PSG is often challenging in pediatric populations due to the discomfort and burden of physical contact from electrode and sensor placement. Given these barriers, a sound-based contactless approach could enable more accessible and child-friendly OSA monitoring at home.

Materials and methods:

The performance of a sound-based AI model for AHI prediction was evaluated using synchronized audio recordings from PSG equipment and corresponding PSG data collected over 195 nights from 191 pediatric patients who slept alone in a hospital setting. Participants had a mean age of 15.04 years (SD: 3.26; range: 2.7-18.9), a mean body mass index (BMI) of 22.66 (SD: 5.50), and a mean AHI of 7.65 (SD: 17.39). Based on PSG-derived AHI values, the dataset was categorized as follows: 91 nights with no OSA (AHI < 1), 59 nights with mild OSA ($1 \leq \text{AHI} < 5$), 13 nights with moderate OSA ($5 \leq \text{AHI} < 10$), and 32 nights with severe OSA (AHI ≥ 10). The AI model detects apnea and hypopnea events in 6-second sub-epoch intervals and estimates AHI based on the counts of predicted events and predicted sleep stages. The model was previously trained and validated in adults, achieving high accuracies (92%, 93%, 94%), sensitivities (0.94, 0.94, 0.93) and specificities (0.88, 0.91, 0.95) at AHI thresholds of 5, 15, and 30.

Results: In the pediatric dataset, epoch-by-epoch four-stage sleep staging accuracy was 72.66%, with a macro F1 score of 0.71. Three-class classification of respiratory events (normal, apnea, and hypopnea) in 6-second sub-epochs yielded an accuracy of 96.64% and a macro F1 score of 0.71. AHI estimation based on these predictions showed high correlation with PSG-derived AHI ($r = 0.94$) and a mean error of 0.17 events/hour (SD 5.80). At clinically relevant pediatric AHI thresholds (≥ 1 , ≥ 5 , and ≥ 10), the model achieved accuracies of 77%, 89%, and 94%; sensitivities of 0.66, 0.75, and 0.84; specificities of 0.91, 0.94, and 0.96; ROC AUC values of 0.84, 0.91, and 0.95, respectively. For four-category OSA severity classification, the model yielded 68.20% accuracy and a macro F1 score of 0.56. While sensitivity at lower AHI thresholds was reduced compared to adult data, model performance at the AHI ≥ 15 threshold remained comparable, with sensitivity of 0.92 and specificity of 0.97.

Conclusions:

This study demonstrates the potential of a sound-based AI model as a viable, non-contact approach for pediatric AHI monitoring. Limitations include the relatively low audio quality of PSG recordings and the small number of nights recorded from children under 10 years of age (only 17 nights). Nonetheless, the results support the feasibility of sound-based AI models for accurate and comfortable in-home pediatric OSA monitoring.

Pilot Study Objectively Identifies Veterans with PTSD and Nightmares from Polysomnograms Using a Chaos Theory Approach

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Introduction: Our Veterans suffer from a high prevalence of post-traumatic stress disorder (PTSD) that they experience uncontrollably during wake and sleep. PTSD is diagnosed using subjective history and questionnaires. PTSD is complex and heterogeneous; no single treatment is effective. Data supports an increase in sympathetic activity in some PTSD patients with nightmares; this may be a pathophysiological mechanism that increases their risk of cardiovascular disease. Prazosin crosses the blood brain barrier and blocks the response of norepinephrine and epinephrine in the brain. Challenge: A large VA study did not demonstrate efficacy of prazosin to decrease nightmares.

Hypothesis: Objective quantification of physiological sleep pattern using raw signals from the sleep study when Veterans are unconscious will identify which PTSD subtype will benefit from prazosin.

Objective: Use a chaos theory approach to identify PTSD during sleep using raw signals from the polysomnogram (PSG).

Materials and methods: Data: PSGs from Veterans at the Philadelphia VA.

Raw Signals: EEG leads and ECG lead was used to plot a trajectory for each Veteran.

HRA-based Dynamic Index: 5-minute intervals of sleep for a total of 120 minutes for each subject was used to calculate 112 metrics for each Veteran.

UMAP was used to visualize similarities and differences of their dynamic properties between subjects.

Results: Panel A Representative of a normal sleep pattern: a Veteran [subject 226] that does not have PTSD and does not have Obstructive Sleep Apnea (OSA).

Panel B Representative of a PTSD sleep pattern: a Veteran [subject 225] that does have PTSD but does not have OSA.

Panel C Representative of an OSA sleep pattern: a Veteran [subject 199] that does not have PTSD but does have OSA.

Panel D Table of characteristics of subjects including the Apnea-Hypopnea Index (AHI), PCL5 score (Questionnaire for diagnosing PTSD), PTSD diagnosis (taken from CPRS problem list), history of nightmares, traumatic brain injury (TBI) and hypertension (HTN). We calculated the Weighted Hypoxemia Index (WHI) and used the arousal index from the PSG to represent degree of sleep fragmentation (SF).

Panel E Box plot that demonstrates the HRA-based index for each of the subjects.

Panel F UMAP of all subjects to visualize the similarities and differences.

Panel G UMAP comparing Normal vs PTSD.

Panel H UMAP comparing Normal vs OSA.

Conclusions: 1. The sleep pattern is significantly different between a Veteran without PTSD (Panel A) and a Veteran with PTSD (Panel B) and a Veteran with OSA (Panel C).
2. The heterogeneity within Veterans with PTSD (Panel G) and OSA (Panel H) could be explained by age & medications.
3. Implication for the sleep field: This pilot study suggests that physiological raw signals from the PSG may identify a PTSD subtype that could benefit from prazosin.

Prospective real-world validation of a smartwatch-based OSA detection algorithm: A comparative study with polysomnography

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Introduction: Obstructive sleep apnea (OSA) is a significant health concern that requires accurate diagnosis and monitoring. While polysomnography (PSG) remains the gold standard for diagnosis, recent advancements in wearable technology offer potential alternatives for screening. In February 2024, the Galaxy Watch algorithm received de-Novo FDA approval for detecting signs of moderate to severe obstructive sleep apnea in adults aged 22 and older. This study aims to evaluate the accuracy of this device in estimating the Apnea-Hypopnea Index (AHI).

Materials and methods: We prospectively recruited adults aged 22 and older with suspected obstructive sleep apnea (OSA) from August 2023 to June 2024. All participants underwent simultaneous level 1 polysomnography while wearing the Galaxy Watch 6. We assessed the correlation between the estimated AHI (eAHI) from the Galaxy Watch algorithm and the AHI from polysomnography using Pearson's correlation analysis. Additionally, we performed a ROC curve analysis to determine the optimal eAHI cut-off value for diagnosing moderate to severe sleep apnea (AHI $\geq$ 15) and evaluated its accuracy.

Results: Data from 58 subjects were included in the analysis. The Pearson correlation coefficient between eAHI and AHI was 0.848 ($p < 0.001$), indicating a strong positive correlation. ROC curve analysis revealed that an eAHI cut-off value of 12.5 could differentiate moderate to severe sleep apnea (AHI $\geq$ 15) with 95% accuracy (sensitivity 90%, specificity 100%).

Conclusions: The AHI estimated by the Galaxy Watch algorithm shows a high correlation with the AHI from polysomnography and can accurately identify moderate to severe sleep apnea. These findings suggest that the Galaxy Watch is potentially valuable as a sleep apnea screening tool.

Protocol for creating a multimodal, free-living sleep and physical activity validation dataset for the human activity recognition and epidemiological communities

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Introduction: Wearable sensors offer a convenient and cost-effective alternative to polysomnography for large-scale sleep assessment. They are also less disruptive, therefore more likely to capture usual behaviour. However, they have limited ability to detect sleep, primarily because most validation studies have been conducted in small, homogenous samples under laboratory conditions. These studies often rely on a single modality (e.g., accelerometer only) collected over one night, without considering the full 24-hour activity cycle. Our aim is to collect a multimodal validation dataset capturing all 24-hour physical behaviours (i.e., sleep, sedentary behaviour, and physical activity) and to annotate wearable sensor data with gold-standard, ground-truth labelled data, for application to large-scale accelerometer datasets with linked health records.

Materials and methods: We will recruit 150 young adults aged 18-30 years from the general population. Data collection will take place over 4 nights and 3 days. During this period, participants will be asked to continuously wear five devices: a research-grade ActiGraph LEAP device on the dominant wrist, a consumer-grade Fitbit device on the non-dominant wrist, an Axivity AX6 device on the dominant thigh and ankle, and a chest-mounted wearable ECG patch (Bittium Faros 180). Participants

will also be asked to place a consumer-grade sleep sensor under their mattress (Withings). Ground-truth measures will be obtained from a standard at-home polysomnography (PSG) assessment on the first night for sleep, a wearable video camera for waking behaviours, and the ECG patch for heart rate. Additionally, we will collect information about participants' sleep quality (PSQI), insomnia symptoms (ISI), and mental health (GAD-7 and PHQ-9) to characterise the prevalence of sleep disturbances and depressive symptoms within our sample.

Results: Data collection is ongoing. This study will enable comparison of sleep estimates from wearables worn on different parts of the body and the under-mattress sleep sensor with the gold-standard PSG as reference. Additionally, it will allow for the validation of physical activity classifications using ground-truth video camera annotations and heart rate and heart rate variability from wrist-worn photoplethysmography (PPG) sensors against a ground-truth chest-worn ECG patch. Furthermore, combining different signals from PPG and accelerometry may improve the detection of physical behaviours. The final annotated dataset will be made publicly available upon completion.

Conclusions: This study will generate one of the largest multimodal validation datasets to date for 24-hour behavioural monitoring in free-living conditions. It will allow researchers to improve existing and develop new methods of sleep and physical activity measurement, ultimately improving our understanding of how these behaviours relate to health outcomes in large-scale wearable datasets such as the UK Biobank.

Real-Time Ventilation and Air Purification Improve Sleep Quality in Healthy Adults

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Introduction: Poor indoor air quality, particularly elevated levels of carbon dioxide (CO₂), particulate matter (PM₁₀), and fine particulate matter (PM_{2.5}), has increasingly been recognized as a disruptor of healthy sleep. In this study, we hypothesized that improving indoor air quality through a ventilation purification system capable of simultaneously reducing CO₂, PM₁₀, and PM_{2.5} levels could enhance sleep quality. To test this hypothesis, we evaluated objective sleep parameters under two operating modes of the system: a basic ventilation mode and an enhanced mode featuring real-time sensor-based automated control, to assess whether these interventions could meaningfully improve sleep architecture.

Materials and methods: In this prospective crossover study, 22 healthy adults underwent overnight polysomnography (PSG) under three distinct conditions: (1) no air quality intervention, (2) basic ventilation mode (Ventilation Mode 1), and (3) enhanced ventilation with real-time CO₂-driven automated control (Ventilation Mode 2). Mode 1 maintained levels at 1000 ppm, while Mode 2 increased ventilation airflow to sustain CO₂ concentrations at 700 ppm. The primary endpoint was sleep architecture measured by PSG.

Results: Air quality differed significantly across conditions. During the no-intervention nights, average CO₂ levels reached 2476 ppm, with PM₁₀ and PM_{2.5} concentrations at 13.7 and 9.2 µg/m³, respectively. Ventilation Mode 1 reduced CO₂ to 1035 ppm and nearly eliminated airborne particulates (PM₁₀: 0.97 µg/m³; PM_{2.5}: 0.30 µg/m³). Ventilation Mode 2 achieved even lower CO₂ concentrations (720 ppm), while maintaining particulate levels at similarly low ranges.

Ventilation Mode 1 resulted in significant improvements: sleep efficiency increased from 86.4% to 90.7% ($p = 0.045$), REM sleep time increased from 65.7 to 92.7 minutes ($p = 0.037$), and WASO decreased from 52.7 to 34.4 minutes ($p = 0.039$). Ventilation Mode 2 demonstrated broader and more pronounced benefits across multiple parameters: total sleep time increased from 374.0 to 402.9 minutes ($p = 0.002$), and sleep efficiency improved from 86.4% to 91.0% ($p = 0.007$). Additional gains were observed in REM sleep, which increased from 65.7 to 92.6 minutes ($p < 0.001$), and in WASO, which decreased from 52.7 to 28.9 minutes ($p = 0.005$). Although there was no statistically significant difference between Ventilation Mode 1 and Mode 2, the magnitude of improvement was greater with Mode 2.

Conclusions: Both ventilation strategies led to measurable improvements in sleep architecture when compared to no intervention, suggesting that even moderate control of indoor CO₂ can positively influence sleep quality. However, the advanced system used in Ventilation Mode 2, which offered tighter CO₂ control and continuous air quality optimization, produced greater improvements across a broader range of sleep outcomes. These findings underscore the clinical value of intelligent environmental regulation as a non-pharmacologic approach to enhancing sleep health.

Reliability of YASA for automated longitudinal sleep scoring in stroke and Parkinson's Disease

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Introduction: Sleep disturbances are common in both stroke and Parkinson's disease (PD). Characterizing and developing treatment strategies requires scalable, reliable sleep staging. Preferably, this should be accurate and feasible for longitudinal use in clinical and research contexts. Currently, sleep assessments often rely on single-night recordings, potentially missing transient features or subtle changes in sleep architecture.

Manual EEG scoring, while the gold standard, is time-consuming and subject to high intra- and inter-rater variability. Several automated algorithms have been developed and validated on large PSG datasets, including clinical populations such as PD. These include Z3Score (Patanaiik et al., 2018; ~90% accuracy in healthy adults, ~72% in Parkinson's), Stanford-stage (Stephansen et al., 2018; ~87%), SeqSleepNet (Phan et al., 2019; ~87%), and U-Sleep (Perslev et al., 2021; F1 ~0.79 in healthy adults, ~0.76 in sleep apnea). However, these methods are trained on full PSG data from controlled environments, and their performance on EEG from wearable devices in at-home settings remains unclear.

To address this, we evaluated the reliability of the open-source YASA (Vallat & Walker, 2021) algorithm using wearable EEG data from patients with stroke and PD. Establishing its accuracy is key to enabling large-scale sleep monitoring, including future assessments of night-to-night variability.

Materials and methods: This longitudinal study includes patients with stroke (S, n = 12) and Parkinson's disease (PD, n = 8), with ongoing recruitment. Each participant undergoes 15 nights of sleep monitoring using the Tosoo AXO wearable EEG device, which includes four dry electrodes placed on the forehead, bilateral temples, and the mastoid region. As of now, the dataset comprises over 300 nights of EEG recordings.

To validate YASA accuracy, a random subset of 20 nights (10 S, 10 PD) was manually scored by two trained scorers with experience in clinical EEG analysis using ScoringHero, producing a gold-standard reference. Automated scoring was then performed using YASA on the same data. Agreement between manual and automated annotations was assessed using Cohen's kappa and F1 scores for each sleep stage.

Results: Sleep stage distributions (epochs) were as follows:

S: Wake – 4123, N1 – 323, N2 – 2878, N3 – 2439, REM – 1524

P: Wake – 4556, N1 – 155, N2 – 3266, N3 – 1341, REM – 445

F1 scores were highest for Wake, N2, and N3: Wake – 0.889 (S), 0.927 (P); N2 – 0.682 (S), 0.791 (P); N3 – 0.753 (S), 0.727 (P). N1 performed poorly (0.248 in S, 0.173 in P), consistent with its rarity and fragmentation. REM agreement was moderate in stroke (0.611) but lower in PD (0.28), likely due to reduced and disrupted REM in PD patients. Mean Cohen's kappa was 0.639 (S) and 0.691 (P), indicating moderate overall agreement.

Conclusions: Limited performance for N1 and REM may be due their underrepresentation in these specific populations. Overall, YASA generalises remarkably well to neurological populations, demonstrating only minor penalties in accuracy of Wake, N2, N3 and facilitating large-scale use in clinical contexts.

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Self-operable Wearable Transcranial Photobiomodulation on the Sleep Symptoms of People Living with Major Depressive Disorder: A Secondary Analysis of a Randomised, Sham-controlled Clinical Trial

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Introduction: Major depressive disorder (MDD) is closely linked to sleep disturbances, and there is a two-way relationship between them. Near-infrared transcranial photobiomodulation (tPBM) is a safe neuromodulation technique with potential antidepressant and hypnotic effects. Our recently published study (Guu et al., 2025) has found an intriguingly sub-optimal mood-elevating effect, along with a significant sleep-enhancing effect using a patient-operable wearable tPBM device. In the present study, we conducted a secondary analysis to further explore the potential mechanisms contributing to this effect.

Materials and methods: Forty-eight outpatients with major depressive disorder (MDD) were randomized 1:1 to the wearable transcranial photobiomodulation (tPBM) or sham group. Participants used the intervention daily for at least 20 minutes, up to 8 weeks. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep symptoms from baseline to week 12. Data were analyzed using the Mann-Whitney U test and the Wilcoxon signed-rank test.

Results: Poor sleep (PSQI global score > 5) was common in both the tPBM group (mean = 10.58, SD = 3.05) and the control group (mean = 11.64, SD = 2.98) at baseline. A significant difference in the PSQI global score between the two groups was observed at week 8 ($z = -2.90$, $p = 0.004$), with the tPBM group showing a greater improvement. In the tPBM group, the PSQI global score significantly decreased at both week 8 ($z = -2.92$, $p = 0.004$) and week 12 ($z = -3.19$, $p = 0.001$), compared to baseline (week 0). Among all the sub-components, sleep latency significantly decreased at week 8 compared to baseline in the tPBM group ($z = -2.44$, $p = 0.02$), but not the control group ($z = -1.59$, $p = 0.11$). In contrast, sleep disturbances scores significantly increased from baseline at both week 8 and week 12 in both the tPBM and sham groups (tPBM week 8: $z = -3.12$, $p = 0.002$, week 12: $z = -2.97$, $p = 0.003$; sham week 8: $z = -3.36$, $p = 0.001$, week 12: $z = -2.31$, $p = 0.021$). Further analysis showed that participants with better sleep latency in the tPBM group (PSQI sleep latency score < 2) had a greater reduction in BDI scores from week 0 to week 8 ($M = 12.31$, $SD = 11.41$) compared to those with poorer sleep latency (score ≥ 2 ; $M = 7.64$, $SD = 12.07$), although the difference was not statistically significant ($z = -1.19$, $p = 0.25$).

Conclusions: Self-administered wearable tPBM might improve sleep symptoms in people living with MDD mainly through reducing the sleep latency. The discomfort of wearing the device at bedtime might contribute to the increased sleep disturbance score, which was offset by the sleep induction effect of tPBM, and therefore resulted in the overall sleep improvement only in the tPBM group. Based on this study, the sleep latency reduction effect of wearable tPBM might be further pursued in larger study to characterize its impact on the mood symptoms.

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Self-supervised learning of breathing-related patterns improves sleep staging from wrist accelerometry

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Introduction: Accurately measuring sleep architecture is critical for understanding how sleep influences mental, neurological, and physical health. Wrist-worn accelerometers offer a convenient, low-cost option for monitoring sleep at home, but most existing methods can only distinguish between sleep and wake. Detailed staging including identifying REM and deep sleep remains a challenge due to limited physiological information in the signal and small labeled datasets. However, small fluctuations during still periods may reflect breathing patterns, which could help resolve sleep stages. Here, we apply self-supervised learning to overcome the issue of limited dataset sizes and propose a task focused on extracting breathing information.

Materials and methods: We applied a self-supervised learning strategy recently proposed by the authors to leverage the large unlabeled UK Biobank dataset, containing ~700,000 days of wrist-worn accelerometer data from 109,000 subjects. A transformer masked autoencoder was pretrained using UK Biobank data by reconstructing the masked signal using the Log-Scale Mean Magnitude (LMM) loss and an adaptation termed Band-Amplification (BA) loss, in which the model reconstructs a signal with the 0.1–0.6 Hz band amplified 1,000-fold for input patches without movement. For downstream evaluation, we used data from 247 subjects with wrist accelerometry and sleep stage labels from concurrent polysomnography, grouping N1 and N2 stages into 'light sleep'. Outputs from the frozen encoders of the pretrained models were used to train linear classifiers. For comparison, we also trained the full model from scratch. All downstream evaluations were done in a 5-fold cross-validation setting with 80-20 train-validation split.

Results: The best overall performance came from the model pretrained with the respiration-enhancing loss, which achieved a macro F1 score of 0.415 ± 0.018 . The standard pretrained model followed with 0.406 ± 0.012 , while the model trained from scratch performed worst at 0.370 ± 0.010 . For the BA loss model, the stage-specific F1-scores were: 0.407 ± 0.02 for deep sleep, 0.34 ± 0.014 for light sleep, 0.294 ± 0.028 for REM sleep, and 0.619 ± 0.03 for wake.

Conclusions: We demonstrated that self-supervised pretraining is a viable strategy for improving deep learning-based sleep staging from wrist-worn accelerometry. Furthermore, this work showed that applying field knowledge to tailor the pretraining by focusing on the 0.1-0.6 Hz band, where we expect to find a breathing signal intermittently, can further improve performance, especially for REM sleep.

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Silicon Nanowire Field-Effect Transistor Biosensors for the Detection of Melatonin as Sleep Disorder Biomarker

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Introduction: With the increasing of the incidence of circadian rhythm sleep disorder (CRSD), developing continuous monitoring methods for CRSD becomes an important trend for assessing individual sleep quality and guiding treatment. Among that, melatonin is one of key biomarkers of CRSD, which concentration in physiological samples effectively reflects the status of an individual's circadian rhythm disorder at different times. However, current melatonin detection technology is still insufficient to meet the practical application requirements for immediate clinical diagnosis. In this study, we developed a simple and efficient method for melatonin detection using an aptamer-modified silicon nanowire field-effect transistor (SiNW FET) biosensor. This biosensor enables real-time, highly sensitive, and rapid detection of melatonin over a wide concentration range (15 fg/ml to 1.5 ng/ml), with a lower limit of detection reaching the fg/ml level. It is demonstrated that the melatonin detected by the SiNW FET biosensor shows good agreement with those detected by mass spectrometry, which is commonly used in clinical applications for melatonin detection. It is expected that modifying SiNW FET biosensors with aptamer monolayers can provide a promising method for examining melatonin in future CRSD treatments.

Materials and methods: Materials: the following chemicals were used: melatonin aptamer ; 3-aminopropyltriethoxysilane (APTES), anhydrous ethanol, acetone, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC, $\geq 98\%$), N-hydroxysuccinimide (NHS), bovine serum albumin (BSA, $\geq 98\%$) and phosphate buffer solution (PBS). All other chemicals used in this study were of reagent grade, and

deionized water was utilized for all experiments.

Methods: In our melatonin detection study, we utilized a Keysight B1500A semiconductor analyzer to apply a precise voltage to SiNWs-FET and accurately measure their current responses. To evaluate the performance of the SiNWs-FET, we initially established a baseline control using a 1×PBS.

Subsequently, a series of PBS solutions containing varying concentrations of melatonin were prepared and delivered precisely to the SiNWs surfaces via microfluidic technology for comprehensive performance testing.

Results: we prepared melatonin solutions with concentrations ranging from 15 fg/mL to 1.5 ng/mL. The SiNWs-FET biosensor possesses high specificity for detecting melatonin biomarkers. The binding of the aptamer to the target molecule near the silicon nanowire surface induces conformational changes, which enhance the carrier concentration in the channel and consequently produce a significant electrical signal.

Compared with conventional mass spectrometry methods used in clinical settings for detecting melatonin, using an aptamer-modified SiNWs-FET biosensor offers a significantly shorter detection time. Despite the promising results, further validation with a large number of actual saliva samples is necessary to ensure the stability and consistency of the detection outcomes before commercialization can be pursued.

Conclusions: we achieved highly sensitive detection of melatonin in solutions using SiNWs-FET biosensors surface-modified with aptamers. The detection limits ranged from 15 fg/mL to 1.5 ng/mL, and the current response exhibited a strong linear correlation with the logarithm of the melatonin concentration. It was confirmed that silicon nanowire SiNWs-FET modified with melatonin-specific aptamers demonstrated a specific response to melatonin. This approach facilitated highly sensitive and continuous monitoring of saliva collected at different times from patients with circadian rhythm sleep disorders.

Sleep Phenomics and Annotator: A Website Tool for Individual-Level Sleep Phenotype Quantification for Clinicians and Researchers

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Introduction: Polysomnography (PSG) signals contain rich phenotypic information, which is crucial for assessing sleep disorders and the pathology of various organ systems. Clinicians often generate hypotheses directly inspired by clinical practice and directly beneficial to patients, but they lack the ability to quantify and test them due to a lack of computational training in clinical education. This gap is widened by the rapid advancements in artificial intelligence (AI), when sleep medicine begins to incorporate AI-derived metrics. However, accessing AI metrics is again challenging for clinicians. For example, many clinicians implicitly consider the burden imposed by apneas. In this case, quantifying hypoxic burden would significantly enhance the precision of individual-level decision-making. Therefore, we urgently need an accessible tool to fill the gap and promote technical integration in sleep medicine.

Materials and methods: We introduce Sleep Phenomics and Annotator (SPA), a clinician-friendly web platform designed for the easy quantification of PSG-derived sleep phenotypes, as well as the viewing of PSG signals and spectrograms. After logging in, users can upload signal files in the European Data Format (EDF), which can be exported by many mainstream clinical PSG software. Then, the user is taken to a screen where they can map channels from their uploaded EDF file to a standardized list of channel names. SPA automatically calculates various sleep metrics and allows users to download the results as a tabular file. In the backend, we used several packages, such as: (1) Flask as a web framework; (2) MNE for neurophysiological data processing; (3) NumPy and SciPy for signal processing. In the frontend, the technologies include: (1) Plotly.js for an interactive EEG waveform visualization; (2) jQuery for a dynamic user interface. Users are responsible for ensuring data privacy, such as de-identifying the exported EDF, a function commonly provided in clinical PSG software. The backend will automatically delete all uploaded files once the analysis is complete.

Results: SPA displays the PSG plot along with three spectrograms for the frontal, central, and occipital regions of the brain, respectively, if available. SPA computes various sleep metrics in addition to the standard parameters in sleep report, including EEG band powers, sleep depth, sleep spindles, slow

oscillations (SOs), spindle-SO coupling, brain age, arousal burden, sleep atonia index, heart rate and variability, respiration rate, apnea/hypopnea self-similarity (loop gain), and oxygen saturation metrics (average SpO₂, hypoxic burden). Metrics are stratified by sleep stages as appropriate. The platform features a modular design, enabling the easy integration of new metrics in the future. We provide detailed explanations and normative ranges for each metric to support individual-level decision-making. SPA is being deployed in Beth Israel Deaconess Medical Center internally and will be publicly available after the internal phase.

Conclusions: SPA provides an intuitive and accessible interface tailored for clinicians and researchers, eliminating the need for coding and bridging the gap between clinical sleep medicine and quantitative sleep research. SPA supports individual-level sleep data analyses, which may potentially lead to a paradigm shift in sleep medicine.

Sleep physiology characteristics in patients with Obstructive Sleep Apnea from Vietnam

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Introduction: Obstructive sleep apnea (OSA) profoundly disrupts sleep architecture, respiratory patterns, and cardiovascular function. While OSA polysomnographic characteristics are well-documented in Western populations, comprehensive data from Southeast Asian populations remain limited. This study characterizes sleep physiological parameters across OSA severity levels in Vietnamese patients, providing essential normative data for this underrepresented population.

Materials and methods: We conducted a cross-sectional analysis of 374 patients diagnosed with OSA (AHI ≥ 5 events/hour) who underwent overnight polysomnography at a tertiary hospital in Ho Chi Minh City, Vietnam. Patients were stratified into mild ($5 \leq \text{AHI} < 15$), moderate ($15 \leq \text{AHI} < 30$), and severe ($\text{AHI} \geq 30$) OSA groups. Comprehensive polysomnographic parameters were analyzed, including sleep architecture (N1, N2, N3, and REM stages), sleep quality indices (total sleep time, sleep efficiency, REM latency, and wake after sleep onset), respiratory event distribution, and heart rate variations across sleep stages. Statistical comparisons were performed using ANOVA with significance set at $p < 0.05$.

Results: The cohort comprised 374 patients (mean age 50.74 ± 14.81 years, 79.68% male) with severe OSA predominating (52.94%), followed by moderate (25.67%) and mild OSA (21.39%). Mean AHI was 37.20 ± 23.80 events/hour.

Sleep architecture showed marked disruption: reduced total sleep time (5.55 ± 1.33 hours), poor sleep efficiency (69.99%), prolonged REM latency (2.24 ± 1.64 hours), and elevated wake after sleep onset (1.67 ± 1.04 hours). Sleep stage distribution revealed pathological changes: increased N1 (21.66% vs normal 5-10%), predominant N2 (63.69%), severely reduced N3 (3.14% vs normal 15-25%), and decreased REM sleep (11.18% vs normal 20-25%).

Respiratory events demonstrated distinct sleep stage preferences: 65.36% occurred during N1-N2, 12.46% during REM, and only 1.42% during N3 sleep. This distribution varied significantly according to OSA severity ($p < 0.001$). Interestingly, mild OSA showed higher NREM-AHI than REM-AHI (16.13 ± 15.59 vs. 8.13 ± 3.42 events/hour), while severe OSA affected both stages equally (NREM-AHI: 49.03 ± 23.90 , REM-AHI: 55.59 ± 18.17 events/hour).

Cardiovascular parameters were correlated with OSA severity. Mean heart rate increased progressively: 66.57 ± 9.71 (mild), 67.95 ± 10.11 (moderate), and 71.89 ± 13.23 beats/min (severe) ($p < 0.001$). Similar patterns were observed during N1-N2 and REM sleep ($p < 0.01$), whereas the N3 heart rate remained stable across severity groups ($p = 0.743$), suggesting preserved autonomic regulation during deep sleep.

Notably, traditional sleep continuity parameters (total sleep time, REM latency, sleep efficiency, and wake after sleep onset) showed no significant differences across severity groups (all $p > 0.05$), indicating that sleep fragmentation is a universal OSA feature, regardless of severity.

Conclusions: This study provides a comprehensive sleep physiology characterization in Vietnamese OSA patients, revealing profound sleep architecture disruption with increased light sleep, reduced restorative sleep, and differential respiratory event impact across sleep stages. The finding that mild OSA preferentially affects NREM sleep, whereas severe OSA equally affects all sleep stages, offers important pathophysiological insights. Preserved N3 cardiovascular stability despite respiratory disturbances highlights the protective nature of slow-wave sleep. Progressive cardiovascular activation

with increasing OSA severity underscores the systemic effects of this disorder. These normative data establish important baseline characteristics for OSA management and research in Southeast Asian populations, where genetic, anthropometric, and environmental factors may influence disease expression differently from Western cohorts.

SleepRes auto-adjusting positive airway pressure, with and without KPAP™, is equivalent to Philips-Respironics's for the treatment of obstructive sleep apnea

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Introduction: Auto-adjusting positive airway pressure (APAP) is the most commonly prescribed PAP modality for obstructive sleep apnea (OSA) treatment in the US. Kairos PAP™ (KPAP™) is a SleepRes proprietary feature that allows pressure to be decreased for better comfort during inspiration and much of expiration. Although KPAP™ showed equivalent efficacy to CPAP in a recent study, it has not been tested with APAP. Now, SleepRes has been developing their own APAP algorithm incorporating KPAP™. Therefore, in this study, we compared the efficacy of SleepRes APAP, with or without KPAP™, to that of a previously FDA-approved and widely-used APAP model (Philips-Respironics Omnilab) on OSA severity

Materials and methods: Thirty-five participants previously diagnosed with OSA (apnea-hypopnea index (AHI)>10 events/h) were randomized to receiving SleepRes or Philips-Respironics APAP in two separate, in-laboratory sleep studies, according to a randomized, crossover design. Additionally, a non-randomized third-night was conducted to test the efficacy of SleepRes APAP combined with KPAP™ vs. Philips-Respironics APAP. Sleep studies were all conducted within a six-week time frame. Both manufacturers' devices were set to their full pressure range (5-20 cmH₂O). Sleep studies were scored by a registered polysomnographic technician blinded to treatment allocation at a central scoring facility. The primary outcome of the study was the effect of the interventions on the AHI with 4% desaturations (AHI₄). Secondary outcomes were the AHI_{3a} (hypopneas scored with 3% desaturations or arousals), and the AHI in separate sleep stages. Study endpoints were assessed using linear mixed-models, adjusting for period, sequence, baseline AHI and percentage of sleep time spent supine.

Results: Of the randomized participants, thirty-three completed at least one treatment arm and were analyzed according to a modified-intention-to-treat approach. They were 54 ± 11 year old (mean ± SD), had a BMI of 34.2 ± 4.8 kg/m², and a baseline AHI of 34.7 ± 21.8 events/h. The majority of them was male (58%), white (55%; 33% black, 6% Asian) and non-hispanic (88%). Philips-Respironics APAP reduced AHI₄ and AHI_{3a} to 2.6 and 7.9 events/h, respectively. SleepRes APAP yielded an AHI₄ and AHI_{3a} similar to that of Philips-Respironics APAP's (mean difference [95%CI]: -0.2 [0.8, -0.4] events/h, P=0.451; -0.4 [-1.9, 1.4] events/h, P=0.669; respectively). Results were similar when KPAP™ was added (-0.1 [-1.2, 1.2] events/h, P=0.840; 1.1 [-1.9, 4.7] events/h, P=0.520; respectively, vs. Philips-Respironics). AHI₄ and AHI_{3a} were comparable with the primary outcome in non-rapid eye movement sleep (non-REM). This was also the case for AHI_{3a} in REM sleep. However, the REM AHI₄ was reduced slightly more only on SleepRes APAP vs. Philips-Respironics APAP (-1.5 [-2.7, 0] events/h, P=0.046). The same did not occur when comparing KPAP™ vs. Philips-Respironics APAP (i.e., AHI₄ was unchanged between interventions). A total of 29 participants completed all treatment arms of the study (N=1 dropped out for equipment intolerance, N=1 due to onset of central apnea, N=1 was lost to follow-up, N=3 for personal reasons).

Conclusions: SleepRes APAP and APAP plus KPAP are efficacious and comparable to Philips-Respironics APAP for the treatment of OSA despite a substantially lower pressure with KPAP™.

Sleep Stage Classification Using Cardiorespiratory Features from Smart Mattress Signals: A Case-Based Validation Study

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Introduction: Non-contact physiological signal-based sleep staging has recently gained attention as a potential alternative to polysomnography (PSG). High-resolution smart mattress systems with a sampling rate of 200 Hz can detect subtle vibrations associated with cardiac and respiratory activity. This study investigates the feasibility of predicting sleep stages by separating heartbeat and respiration signals through two case-based analyses. To evaluate the capability of a high-frequency smart mattress system to separate cardiac and respiratory components from raw pressure signals, and to classify sleep stages based on cardiorespiratory features.

Materials and methods: Raw data were sampled at 200 Hz with the smart mattress system (Huijia Health Life Corporation) for approximately 25,000 seconds, totaling about 5 million data points. Each 30-second segment (epoch), containing 6,000 samples, underwent signal processing: a band-pass filter was used to detect respiratory peaks, while a band-pass filter extracted R-peaks for calculating heart rate (HR) and root mean square of successive differences (RMSSD). Features extracted per epoch included HR, RMSSD, respiratory rate, and respiratory variability. These features were input into a personalized classification function to estimate sleep stage labels (Wake, N1, N2, N3, REM) in accordance with AASM 30-second epoch standards.

Results: Both case studies demonstrated the feasibility of sleep stage classification using the extracted features. Case A exhibited physiological transitions consistent with expected patterns across Wake, non-REM (N1–N3), and REM stages. In Case B, 66.4% of total sleep time was identified as N2 stage, with detectable transitions in heart rate variability and respiratory dynamics across different stages. The proposed method yielded stable staging performance without requiring BCG or EEG signals.

Conclusions: This study demonstrates the potential of high-frequency smart mattress signals for non-invasive, epoch-based sleep stage classification. By using basic signal processing and classification methods to identify heart rate and breathing patterns, we can accurately determine sleep stages, which sets the stage for future large-scale, contactless sleep monitoring.

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Sleep Stage Classification Using RGB-Fused Multimodal Images from Physiological Signals

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Introduction: This study proposes a novel approach for sleep stage classification by fusing three physiological signals, Heart Rate (HR), Photoplethysmogram (PPG), and Oxygen Saturation (SpO₂), into a single RGB image. Each signal is transformed into a 2D visual representation using methods suitable for its characteristics: Gramian Angular Field (GAF) for HR, Markov Transition Field (MTF) for PPG, and Recurrence Plot (RP) for SpO₂. These 2D representations are assigned to the red, green, and blue channels of a composite image. A convolutional neural network (CNN) is then employed to classify the fused image into one of sleep stages. Experimental results on the publicly available sleep dataset demonstrate the effectiveness of this multimodal visual fusion method.

Materials and methods: We utilized the MESA (Multi-Ethnic Study of Atherosclerosis) dataset with full-night signals recorded during polysomnography (PSG). Each subject's data is segmented into 30-second epochs, excluding segments with missing or zero values. Then the HR, PPG, and SpO₂ signals are transformed into a 2D representation tailored to its physiological properties using GAF, MTF, and RP, respectively. These modality-specific visualizations are mapped to RGB color channels, HR (red), PPG (green), and SpO₂ (blue), resulting in a single image. This fusion strategy not only preserves the temporal uniqueness of each signal but also encodes them into a coherent visual format suitable for deep CNNs. We employed a ResNet-based CNN and the model is trained with categorical cross-entropy loss and Adam optimizer using subject-wise splits (70% train, 15% validation, 15% test). To evaluate model performance under different class resolutions, we conducted experiments using three different label settings: 5-class (Wake, N1, N2, N3, REM), 4-class (Light Sleep merges N1 and N2), and

3-class (NREM merges N1~N3). This approach enables comprehensive assessment of model performance under various clinical and application-relevant scenarios.

Results: The performance of the proposed method is evaluated through experiments using multiple classification schemes. In the 5-class, the model achieved an overall accuracy of 38.3% and a Cohen's Kappa of 0.24, with reasonable performance in classifying Wake and REM stages but reduced precision for intermediate stages like N1 and N2. The 4-class scenario showed improved balance and yielded an accuracy of 44.0% (Kappa: 0.26). In the 3-class, the model reached the best performance with 63.0% accuracy (Kappa: 0.40). These results demonstrate that the proposed method is useful for sleep stage classification, even though the numerical score is modest compared to EEG-based systems, the distinct visualization strategy achieves this using only peripheral signals, which can be collected with a single wearable sensor, such as a fingertip pulse oximeter.

Conclusions: This study demonstrates the feasibility and effectiveness of RGB-fused multimodal signal visualization for sleep staging. The proposed pipeline provides a scalable solution for sleep analysis using minimally intrusive biosensors, and introduces a novel multimodal image fusion framework with strong potential for broader biosignal classification tasks.

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Sleep Stage is Visible: Non-contact Sleep Staging using Infrared Video

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Introduction: Sleep staging, the classification of sleep into Wake, N1, N2, N3, and REM stages, is essential for diagnosing sleep disorders and understanding sleep-related health outcomes. Polysomnography (PSG), the clinical gold standard, involves overnight monitoring with multiple wired sensors and manual scoring by experts. While accurate, it is costly, labor-intensive, and uncomfortable, often disrupting natural sleep patterns and making it impractical for everyday use. To overcome these limitations, we present a deep learning framework that directly classifies sleep stages from raw infrared video. This approach brings sleep monitoring closer to everyday settings by enabling fully non-contact, unobtrusive, and robust observation without requiring wearable devices or clinical supervision.

Materials and methods: We conducted experiments using a subset of the Korea Video Sleep Study (KVSS) dataset, consisting of 475 overnight infrared video recordings from a single hospital, including both healthy individuals and patients with sleep disorders. Each recording includes labels scored by experts and was captured at 640×480 resolution and 5 fps. To ensure subject independence, the data were split into 70 subjects for validation, 70 for testing, and the rest for training.

Our framework adopts a two-stage architecture designed to address the temporal characteristics of sleep video at multiple scales. Stage 1 utilizes a 3D convolutional neural network (MoViNet) to process short-term dynamics within each 30-second epoch, aiming to extract fine-grained motion features like breathing and subtle body movements. To further enhance sensitivity, we incorporate a pixel-wise temporal encoding module and apply an intra-subject discriminability loss during training. Stage 2 leverages a MAMBA-based sequence model to capture long-range temporal dependencies and model the global sleep architecture across the full night.

Results: Our model achieved 0.79 accuracy and 0.75 macro F1-score in the four-class setting, where N1 and N2 stages are merged into a single Light category, and 0.69 for both metrics in the five-class setting. We introduced three domain-specific techniques: pixel-wise temporal encoding, intra-subject discriminability loss, and long-range sequence modeling using Mamba. These components each contributed significant performance gains and worked together to address the challenges of video-based sleep staging. To interpret the model's behavior, we applied Video Eigen-CAM to activation maps in MoViNet. The resulting spatiotemporal saliency maps revealed that the model successfully captured rhythmic patterns in the chest region, as well as subtle body movements.

Conclusions: We propose the first deep learning framework that performs sleep staging directly from raw infrared video without relying on intermediate physiological signals. By incorporating strategies tailored to sleep video, the model achieves strong performance across diverse subjects including patients. The approach offers a fully non-contact alternative to traditional polysomnography, paving the way for scalable, at-home sleep monitoring using infrared video in everyday settings.

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SLEEPYLAND: Trust begins with fair evaluation of automatic sleep staging models

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Introduction: Despite the recent surge in deep-learning algorithms for automatic sleep staging, fair comparisons remain unfeasible, as models are rarely evaluated on the same set of data, and pre-trained model weights rarely released publicly. We present SLEEPYLAND, the first fully open-source tool that fairly benchmark state-of-the-art algorithms on the same harmonized corpus of **in-domain ~27'500** sleep recordings, i.e., **~220'000 hours**, drawn from **17 different cohorts** hosted in the National Sleep Research Resource (NSRR) repository. To leverage the complementary strengths of individual models, we introduce **SOMNUS** (Soft-voting Over Multiple Networks for Unified Sleep-staging), an ensemble that aggregates probabilistic outputs across different models and channel configurations.

Materials and methods: U-Sleep [1], DeepResNet [2] and SleepTransformer [3] models have been re-implemented in a unified framework, and re-trained on NSRR recordings (single- and multi-channel EEG/EOG setup) with consistent preprocessing and sleep-segments sampling, as described in [4]. Pre-trained models weights openly released in [5]. The generalization of SOMNUS was quantified on additional **7 out-of-domain datasets**, i.e., **~84'000 hours** sleep recordings, mainly including the large Bern Sleep-Wake Registry (BSWR), with 8'410 recordings from patients and healthy subjects aged 0-91 years, and the Dreem Open Datasets (DOD-H, DOD-O), with 80 recordings, each scored by five independent physicians. Per-recording macro-F1 (MF1) and Cohen's κ were computed, and soft-consensus hypnoidensity similarity was assessed by average cosine similarity (ACS) [6]. Performance and clinical-marker estimation consistency among architectures were modelled with GAMLSS [7-8], conditioning MF1 and stage-specific errors on age, gender, apnoea-hypopnoea index (AHI) and periodic-limb-movement index (PLMI).

Results: On in-domain test sets, SOMNUS achieved a median MF1 of 78 % (range: 69–87%), exceeding the best single-model in 90% of cases/recordings ($p < 0.001$). On the large out-of-domain BSWR, SOMNUS reached a median MF1 of 72%, showing robustness, but only a modest +1% gain over top individual models. On multi-scored data, SOMNUS outperformed the best human scorer, i.e., MF1 85.2% vs 80.8% on DOD-H, and 80.2% vs 75.9% on DOD-O, better reproducing the scorer consensus than any individual expert ($\kappa = 0.89/0.85$ and $ACS = 0.95/0.94$ for healthy/OSA cohorts). The analyses revealed consistent patterns of demographic and clinical bias across all models, including SOMNUS. Performance (MF1) and clinical-marker estimation errors were systematically modulated by age, AHI, and PLMI, with variations exceeding ± 5 percentage points across the 5th–95th percentiles. While SOMNUS improved robustness overall, it did not reduce or compensate for bias.

Conclusions: SLEEPYLAND provides the largest, most transparent benchmark to date for sleep-staging research, releasing reproducible pre-trained models and an extensible evaluation framework. **The SOMNUS ensemble consistently outperforms individual deep-learning models across 24 datasets, even exceeding expert-level agreement on multi-scorer data**, demonstrating strong generalization and alignment with consensus scorers. SOMNUS does not mitigate demographic or clinical bias, with all models exhibiting systematic performance variation across age, AHI and PLMI. SLEEPYLAND sets a new standard for fair benchmarking and paves the way for clinically robust sleep automatic systems.

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- [1] <https://doi.org/10.1038/s41746-021-00440-5>
- [2] <https://doi.org/10.1093/sleep/zsaa161>
- [3] <https://doi.org/10.1109/TBME.2022.3147187>
- [4] <https://doi.org/10.1038/s41746-023-00784-0>
- [5] <https://hub.docker.com/r/bspsupsi/sleepyland>
- [6] <https://doi.org/10.1093/sleep/zsad028>
- [7] <https://doi.org/10.21203/rs.3.rs-6278214/v1>
- [8] <https://doi.org/10.1109/SDS60720.2024.00045>

Resources: <https://github.com/biomedical-signal-processing/sleepyland>

Snoring Sound Detection: An Explorative Study on Use of TensorFlow.js for Sleep Quality Monitoring

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Introduction: This study presents the development and evaluation of a browser-based snoring detection application leveraging TensorFlow.js. The application was designed to perform real-time monitoring and analysis of snoring patterns as a non-invasive method for assessing sleep quality and conducting preliminary screening for potential sleep apnea.

Materials and methods: The model was trained on a dataset comprising 500 seconds of snoring audio (300 seconds from publicly available sources and 200 seconds of researcher-generated samples) and 500 seconds of background noise recordings. Testing was conducted over a cumulative duration of 200 seconds in various acoustic environments. All audio files were processed using Google's Teachable Machine platform, which segments input into 1-second intervals. No manual preprocessing or noise reduction techniques were applied. Model training was conducted using the Teachable Machine's built-in binary classification system powered by the TensorFlow framework, for 100 epochs using default hyperparameters. Model performance was evaluated based on sensitivity and specificity using a separate test split of the dataset.

Results: Performance evaluation revealed a high overall accuracy of 94.12%, supported by a sensitivity of 95.00%, specificity of 93.22%, precision of 93.44%, and an F1-score of 94.71%. These findings indicate the system's strong ability to reliably detect snoring events while minimizing false positives from ambient background noise. The model maintained consistent performance across varying acoustic environments without requiring manual preprocessing or noise filtering, underscoring the robustness of the browser-based approach. Additionally, the application was able to generate session-level statistics, such as snoring duration, frequency, and proportion, which enhance its utility for practical sleep quality monitoring.

Conclusions: The solution offers several advantages, including requiring no specialized hardware beyond a standard microphone, functioning entirely within a web browser without installation, ensuring privacy by processing all audio data locally, and providing detailed session statistics such as snoring duration, count, and percentage. This work demonstrates the potential of leveraging modern web technologies for accessible sleep monitoring solutions. It shows a high level of accuracy in distinguishing snoring sounds from ambient noise and provides relevant statistical information for sleep quality assessment. This approach opens new opportunities for creating user-friendly and widely accessible sleep monitoring technologies. Future research involving larger-scale studies with diverse user characteristics and environmental conditions is recommended to validate the system's external applicability and robustness in real-world settings. Furthermore, its web-based design enables potential integration with other health platforms or wearable devices for broader sleep monitoring applications.

Acknowledgments: This study was made possible through the collaborative efforts of the development team, insightful feedback from academic peers, and the utilization of open-source resources, complemented by AI-assisted grammatical correction, which collectively supported the training and evaluation of the snoring detection system.

Sound-Based AI Sleep Staging in Pediatric Patients

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Introduction: This study evaluates the efficacy of a sound-based AI model for pediatric sleep staging as a non-contact adjunct to traditional polysomnography (PSG). Sleep disturbances are prevalent in children and can significantly affect development, behavior, and quality of life. PSG remains the gold standard for evaluating these conditions. However, PSG presents significant challenges in pediatric populations due to the physical contact required for electrode and sensor placement. Previous studies report that one-third of parents consider their child's sleep during PSG to be atypical compared to home sleep. Even home-based PSG systems face limitations, notably due to young children removing monitoring leads. These challenges highlight the need for contactless technologies as a practical alternative, particularly in pediatric home settings.

Materials and methods: We evaluated the performance of a sound-based AI sleep staging model using synchronized audio recordings from PSG equipment and corresponding PSG data from 195 nights, obtained from 191 pediatric patients sleeping alone in a hospital setting. Participants had a mean age of 15.04 years (SD: 3.26; range: 2.7–18.9), a mean body mass index (BMI) of 22.66 (SD: 5.50), and a mean apnea-hypopnea index (AHI) of 7.65 (SD: 17.39). The sound-based AI model used in this study was previously validated in adults with an accuracy of 80.01% and a macro F1 score of 0.76 for four-stage classification. Epoch-by-epoch accuracy was evaluated, and macro F1 scores calculated per night were analyzed for correlations with age.

Results: Across the pediatric dataset, epoch-by-epoch sleep staging accuracy was 72.66%, with a macro F1 score of 0.71, indicating a modest reduction from adult performance by approximately 7% in accuracy and 0.05 in macro F1. Stage-specific performance analyses showed consistent reductions compared to adults for Wake, Light, and REM stages, each decreasing by approximately 0.08 in F1 scores. In contrast, the F1 score for the Deep sleep stage increased by about 0.06, primarily due to a significant improvement in precision. When examining macro F1 scores of individual nights by age, a positive correlation coefficient of 0.33 was observed between age and model performance. Linear regression analysis indicated that performance improved proportionally with age, with a slope of 0.02 and an intercept of 0.36, resulting in near-adult macro F1 scores of approximately 0.74 by age 19.

Conclusions:

This study demonstrates the potential of a sound-based AI model as a non-contact adjunct to PSG for pediatric sleep staging, particularly beneficial for children sensitive to conventional PSG procedures. Limitations include the relatively poor audio quality of PSG recordings and the scarcity of data from younger children, with only 17 nights recorded from children under 10 years old. Nonetheless, these findings suggest that incorporating additional younger pediatric data into model training could further enhance performance, ultimately supporting the practical application of sound-based AI models for accurate and comfortable pediatric sleep monitoring.

Submental Ultrasonography versus Drug-Induced Sleep Endoscopy for Upper Airway Assessment in Obstructive Sleep Apnea Patients

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Introduction: To compare submental ultrasonography (SMUS) with drug-induced sleep endoscopy (DISE) for assessing upper airway configuration in obstructive sleep apnea (OSA).

Materials and methods: In this cross-sectional study, adult OSA patients scheduled for DISE underwent SMUS beforehand to assess airway collapse at four anatomical levels using the VOTE classification. Agreement between SMUS and DISE findings was analyzed with Cohen's weighted kappa coefficient. Additionally, accuracy of artificial intelligence (AI)-derived apnea-hypopnea index (AHI) from SMUS compared with polysomnography (PSG)-derived AHI was assessed.

Results: Thirty-five patients (mean age 44.5 ± 12.3 years, 74% male) completed the study. Agreement between SMUS and DISE was low across all sites, with kappa values from -0.116 to 0.028 (velum: -0.009 to -0.106 ; oropharynx: -0.012 ; tongue base: 0.028 ; epiglottis: -0.116 to -0.030). AI-predicted AHI had limited accuracy: correct predictions occurred in 28.6% of cases, with underestimation in 48.6% and overestimation in 22.9%. AI-predicted AHI demonstrated limited accuracy: correct predictions occurred in 28.6% of cases, while 48.6% were underestimated and 22.9% overestimated. Underestimation was most pronounced in severe OSA, with a mean difference of 27.4 events/h compared to correct predictions ($p < 0.001$). Overestimation showed a smaller, borderline significant difference (14.2 events/h; $p = 0.052$)

Conclusions: SMUS demonstrated limited agreement with DISE for upper airway collapse assessment and limited accuracy in AI-derived AHI prediction. While SMUS cannot replace DISE for detailed evaluation, its non-invasive nature suggests potential as a supplementary tool when DISE is unavailable. Larger studies with refined protocols and improved AI algorithms are warranted to validate its clinical applicability.

Success of the Newly Instigated Certification in Sleep Science Credential: An Initiative of the Australia New Zealand Sleep Science Association

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Introduction: While international examinations of sleep physiologist knowledge exist, these do not always align with the specific context of sleep science in Australian and New Zealand. Thus, the Australian and New Zealand Sleep Science Association Certification Exam (ACE) providing the Certification in Sleep Science (CSS) credential was developed to cater for a more locally relevant credential and introduced in March 2024. The ACE represents a significant advancement in the recognition and standardisation of professional competency in sleep science across Australia and New Zealand. Aimed at recognising and supporting the professional development of sleep physiologists and scientists, the ACE builds on the former New Zealand Sleep Certification Examination (NZSCE), required for Clinical Physiologist registration in New Zealand.

Materials and methods: A multidisciplinary panel of subject-matter experts developed and govern the ACE. The assessment covers six core domains covering the comprehensive knowledge base expected of professionals working in sleep science. Questions underwent iterative development: drafted and reviewed by subject-matter experts. Individual exams are drawn at random from a large, vetted question bank: piloted by panel members and subjected to post-sitting review and difficulty analysis to inform ongoing calibration. The exam is delivered online under secure, proctored conditions, ensuring accessibility for candidates in metropolitan, regional, and remote locations while preserving integrity.

Results: Sixty candidates have participated across three exam sittings so far, yielding a 57 percent pass rate, demonstrating the exam's ability to discriminate competency levels. To date, 61 individuals hold the CSS credential, which includes those who have sat the exam, as well as 21 practitioners grandfathered via previous NZSCE success, and six members of the exam development committee.

Conclusions: The ACE exam represents a rigorous, adaptive assessment of sleep-science competency. Bi-annual exam sittings are planned to increase the cohort of CSS-credentialled professionals. Other goals include embedding the CSS into accreditation standards and achieving wider recognition by employers. Moreover, insights derived from exam performance data will inform ANZSSA's professional

education strategy, thereby enhancing the quality, consistency and impact of sleep-science practice across Australia and New Zealand.

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Telemedicine/Telemonitoring in Sleep Laboratories - a Game Changer for Resource Efficiency Without Compromising Patient Care?

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Introduction:

Obstructive sleep-related breathing disorders have significant individual and socioeconomic implications due to their increasing prevalence in terms of impairing performance at work, road safety, quality of life, and their impact on the cardiovascular and metabolic system. Positive-airway pressure (PAP) therapy is widely considered to be the gold standard in treating severe sleep-related breathing disorders, but therapy success is only achieved through sufficient adherence. However, the increasing number of patients needing PAP treatment is straining the capacities of sleep labs in terms of available sleep lab positions for diagnosis and adjustment to PAP therapy, as well as the individual long-term care of PAP patients.

The aim of this study was to investigate the use and contribution of telemedicine/telemonitoring in relieving inpatient resources in sleep labs and to determine the practical benefits of telemonitoring in clinical practice.

Materials and methods: In a prospective observational study, 2394 continuous PAP (CPAP) patients were telemedically monitored over a period of 91 weeks in a sleep lab setting. 1814 patients, who had been using CPAP therapy for 3 months, have been included into this study. Of those, 1650 patients agreed to be telemedically monitored. After CPAP adjustment, therapy data is first assessed via telemonitoring after 2-4 weeks to determine if the therapy is proceeding effectively or if interventions were necessary. The study examined therapy dropout rate, time to first intervention, type of intervention, resource situation, willingness to participate, and age distribution compared to the group of patients who rejected telemonitoring in the same period.

Results: The use of telemedicine/telemonitoring led to a significant reduction in dropout rate in the "TM yes" group (5.21%) compared to the "TM no" group (10.3%). The average age was similar in both groups. The willingness to participate in telemonitoring was 91.95%. The period between CPAP adjustment and initial information regarding therapy efficiency was 37 days in the "TM yes" group compared to 204 days in the "TM no" group. The most successful intervention was online pressure adjustment, which significantly improved compliance after 3 months. An increase in CPAP settings by 57% and PSGs by 26%, as well as a reduction in on-site checks at the sleep lab by 30.7%, were noted.

Conclusions: The implementation of telemedicine/ telemonitoring in clinical practice is an effective measure to relieve capacities in the sleep lab, by reducing waiting times for diagnostic nights and enable time-sensitive adjustments of PAP treatments, which allow for early intervention in case of therapy problems, improve the quality of long-term care, and reduce dropout rates

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The Effect of Different Auditory Stimulation Modalities on Sleep Slow Wave Activity and Cognitive Performance

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Introduction: Insufficiently restorative sleep is a significant public health concern, impacting health and daytime function. Evidence suggests that the benefits of sleep, including sleep quality, are associated with sleep EEG slow waves. Enhancing slow-wave activity (SWA) during sleep with auditory tones is a

promising non-pharmacological approach to improving restorative sleep. This study explores the effect of auditory stimulation modalities on SWA enhancement and the impact on daytime cognitive performance.

Materials and methods: Twenty-seven healthy subjects (16F; M_{age} : 38.1 ± 5.7 years) with regular sleep schedules. Participants used a closed-loop stimulation device (SmartSleep) at home, which recorded EEG data over multiple nights.

Four conditions were tested: SHAM (no stimulation), ITI (continuous 1-second fixed inter-tone interval (ITI) stimulation), PHASE (stimulation timed to a slow wave up-state), and BLOCK (15 tones-ON/15 tones-OFF with 1-second inter-tone interval stimulation). Each condition lasted 10 nights over two weeks. The three stimulation conditions were presented in randomized order separated by two SHAM weeks.

Cognitive assessments were conducted using the Cognition battery, which consists of 10 assays of accuracy and speed on major cognitive domains, including executive functions, episodic memory, and complex cognitive processing.

EEG data were automatically scored into four stages (Wake, Light NREM, Deep NREM, REM) using a validated deep neural network. SWA was calculated for each NREM epoch as power in the 0.5–4 Hz band. SWA enhancement for each stimulation condition was defined as the average SWA increase relative to SHAM.

Cognitive performance data were corrected for practice and stimulus set effects and z-transformed to facilitate comparisons across cognitive domains. Sleep architecture, SWA, and cognitive performance were analyzed using linear mixed-effects models. We adjusted the statistical significance values for multiple comparisons using the Benjamini-Hochberg procedure.

Results: Sleep architecture revealed that ITI increased Wake-After-Sleep-Onset (+2.8 min ; $p=0.049$), and BLOCK increased time-in-bed (+7.5 min; $p=0.045$). SWA did not differ among conditions, but the number of responders ($\geq 5\%$ SWA enhancement) was higher in BLOCK (14/27) than PHASE (10/27) or ITI (11/27) conditions.

Higher SWA in BLOCK was associated with better vigilance ($r: 0.64$; $p < 1e-4$) on the Psychomotor Vigilance Task and reduced risk-taking ($r: -0.49$; $p=0.012$) on the Balloon Analog Risk Task.

Conclusions: These findings suggest that block stimulation during sleep improves alertness the next day and may enhance slow wave activity.

The Impact of a Sleep Stage-Based Personalized Environmental Control Algorithm ("HeySleep") on Sleep Quality

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Introduction: Sleep quality plays a vital role in various aspects of physical and mental health, including immune function, cognition, and cardiovascular health. However, modern living environments often compromise sleep due to uncontrolled environmental factors such as light, temperature, ventilation, and noise. Previous studies have examined these factors individually in fixed, non-responsive settings. This study aims to evaluate the effectiveness of a real-time, closed-loop environmental control system ("HeySleep") that adjusts ambient conditions, including lighting, temperature, ventilation, and oxygen, according to polysomnography (PSG)-determined sleep stages, in order to improve both objective and subjective sleep quality.

Materials and methods: To minimize potential bias from the first night effect, 12 healthy participants were randomly assigned in a 1:1 ratio to one of two sequences: (1) control condition followed by HeySleep intervention, or (2) HeySleep intervention followed by control. Each participant completed two overnight PSG sessions in a controlled sleep clinic setting. Under the HeySleep condition, the system dynamically adjusted the ambient environment in real time based on detected sleep stages. At the onset of the sleep trial, room lighting was gradually dimmed over a 30-minute period to facilitate endogenous melatonin secretion and support circadian alignment. Once asleep, room temperature was

adjusted via the air conditioner - raised by 1°C during light sleep (N1-N2) and 2°C during deep sleep (N3) - to enhance thermal comfort. During REM sleep, temperature was held constant to accommodate the body's diminished thermoregulatory capacity. Air quality was managed through an automated ventilation system that maintained carbon dioxide (CO₂) levels below 700 ppm and actively filtered airborne particles. Additionally, an oxygen concentrator was deployed during sleep to ensure adequate oxygen delivery. Objective sleep parameters including sleep latency, total sleep time (TST), sleep efficiency (SE), and sleep architecture (light sleep, deep sleep, REM, and WASO) were assessed via PSG.

Results:

Compared to the control night, HeySleep led to significant improvements in several objective sleep parameters. SL decreased from 9.4 to 4.7 minutes ($p = 0.044$), TST increased from 347.5 to 446.1 minutes ($p = 0.012$), and SE improved from 82.1% to 91.8% ($p = 0.017$). WASO was reduced from 126.6 to 35.4 minutes ($p = 0.022$).

In terms of sleep architecture, deep sleep increased from 12.4% to 18.4% ($p = 0.027$), and REM sleep from 15.4% to 23.0% ($p = 0.007$). Wake time during the sleep period also decreased from 26.5% to 7.4% ($p = 0.020$). No significant changes were observed in light sleep, REM latency, respiratory disturbance index (RDI), or snoring metrics.

Conclusions: The implementation of HeySleep, a real-time, sleep-stage-responsive environmental control system, significantly enhanced key objective sleep parameters, including SL, TST, SE, and WASO. Notably, it also increased deep and REM sleep durations, two stages critical for physical and cognitive recovery while reducing wakefulness during the night. These findings suggest that personalized, closed-loop environmental control tailored to physiological sleep stages may offer a promising approach to improving sleep architecture and overall sleep quality in healthy adults.

Towards Digital Twins with Wearables: A Fully Data-driven Causal Analysis of Lifestyle Effects on Sleep Biomarkers

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Introduction: Over the past decade, mobile and wearable devices have seamlessly integrated into daily life, offering researchers unprecedented opportunities to analyze lifestyle habits. Continuous unobtrusive monitoring with wearables, combined with user input and contextual information collected over time, enables the exploration of complex relationships in multi-source data. These new data streams offer valuable insights into how lifestyle factors, such as alcohol intake and stress, interact with sleep. While previous studies have established associations, causal relationships remain unclear. To identify modifiable risk factors and guide effective interventions for improving sleep quality, it is essential to uncover the underlying causal mechanisms. In this work, we apply data-driven causal inference methods to estimate the effects of lifestyle factors on sleep, laying the groundwork for personalized digital twin prototypes that support lifestyle simulations and intervention design.

Materials and methods: Data collected over 30 days by 294 participants with wearables were aggregated daily, combined with contextual information from questionnaires and weather data, resulting in an analytical sample of 277 individuals. The wearable-derived metrics included active time, average stress, heart rate, and sleep-related measures such as resting heart rate, proportions of sleep stages, sleep score, and other sleep-derived biomarkers. We used causal discovery algorithms to construct a Maximal Partially Directed Acyclic Graph (MPDAG), initialized with a temporally ordered PC algorithm and refined with the Structural Expectation-Maximization algorithm. Bootstrapping ensured stability, while background knowledge on temporal ordering and exogeneity was incorporated. Adjustment sets for each research question were derived through the Intervention with DAG Absent

(IDA), which identifies valid local adjustment sets for causal effect estimation. Causal effects were then estimated using linear mixed-effects models to account for inter-individual variability.

Results: Causal discovery on the data from 80% of the participants yielded a lifestyle structure consistent with literature. Estimated causal effects (95% CI) on the hold-out set of 56 participants showed that alcohol intake decreased REM sleep percentage by either -4.76 (-6.02 ; -3.49) or -4.17 (-5.45 ; -2.90), corresponding to the two valid IDA-derived adjustment sets compatible with the MPDAG. Daily stress reduced REM percentage by -0.22 (-0.25 ; -0.18), and total sleep time increased the sleep score by 4.85 (4.25 ; 5.45). Random intercepts indicated significant inter-individual variability, highlighting personal differences across participants.

Conclusions: In this work, we showed that causal discovery methods can be exploited with longitudinal lifestyle data, enabling the identification of meaningful mechanisms. Further analysis aiming to understand individual-level effects revealed differences between participants, underscoring the value of personalization. Learned causal effects represent a foundation for constructing digital twins - personalized, computational representations of individuals that evolve with data. By enabling counterfactual reasoning (e.g., "What if I slept more?"), these models can simulate the impact of lifestyle changes before interventions are implemented and help inform patients and healthcare professionals. This supports the development of adaptive systems for behavioral coaching and health optimization, with the possibility of incorporating also reinforcement learning enhanced personalization. Future work will focus on extending the presented methodology with longer observation periods to uncover personalised behavioral insights.

Towards in-cabin contactless sleep prediction

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Introduction: Drowsy driving is a major cause of fatal vehicle crashes, contributing to 10–30% of all road traffic incidents. Driver monitoring systems are designed to detect drowsiness and are categorized into four main approaches: vehicular-, behavioral-, physiological-, and hybrid-based. Physiological systems are the most accurate, already providing great results exploiting cardiac parameters extracted with contact-based solutions; however, these systems are intrusive and costly.

This work proposes a physiology-based, non-contact method for sleep prediction by analyzing Respiration Rate (RR), acquired on-the-fly using a short-range, 60 GHz, automotive, standalone radar in a driving-seat-mockup and driving-simulator environments. Sleep events were, for the first time in this context, robustly validated by a sleep expert medical doctor using the American Academy of Sleep Medicine (AASM) guidelines for the Maintenance of Wakefulness Tests (MWT) scoring, with a special focus on microsleep events. Therefore, a preliminary solution for sleep prediction in drivers, using RR acquired by radar, was successfully developed and validated.

Materials and methods: The radar detects chest and abdominal motion to estimate RR at 1 Hz. Data are processed offline to simulate real-time operation. A classification algorithm labels each second as ALARM or NOT-ALARM, predicting a potential sleep event.

Participants wore a Polysomnographic (PSG) setup. Data were collected during a modified-MWT conducted in two settings:

- Driving-seat-mockup: 13 subjects (mean age: 39 ± 10 , 5 female) sat in a cockpit simulator and followed repetitive driving instructions on a tablet for 40 minutes.
- Driving-simulator: 13 subjects (mean age: 40 ± 20 , 4 female) sat in a Maserati Ghibli dynamic cockpit simulator and completed a 45-minute low-stimulus driving session with dim lighting and minimal external input.

Participants were instructed to resist sleep. The PSG data have been scored by a sleep expert medical doctor following the guidelines of AASM. The scored sleep events (Microsleep, NREM1, NREM2, NREM3, REM, Awake) are the Ground Truth labels.

Ground truth was compared against algorithm predictions using a confusion matrix.

Results: Evaluation was based on the timing between the ALARM and the sleep event scored by the medical doctor:

- True Positive (TP): ALARM occurred before the first sleep event.
- False Negative (FN): ALARM occurred after (or concurrently) the sleep event or was not triggered at all.
- False Positive (FP): ALARM was triggered, but no sleep event occurred.
- True Negative (TN): Neither ALARM nor a sleep event occurred.

Therefore, the overall accuracy was evaluated as follows.

- Prediction of the 1st sleep event:

Driving-seat-mockup: 69% (TP=9, TN=0, FP=3, FN=1)

Driving-simulator: 85% (TP=1, TN=10, FP=1, FN=1)

- Prediction of all sleep events:

Driving-seat-mockup 94% (TP=79, TN=0, FP=4, FN=1)

Driving-simulator 80% (TP=2, TN=10, FP=1, FN=2)

Conclusions: This study is a preliminary step towards assessing the feasibility of using RR acquired by an automotive-grade radar in a highly challenging environment for sleep prediction in drivers. Despite the unbalanced and limited sample size of the datasets, the results are promising. More investigations are needed, on the one hand to extend the dataset, on the other to test the radar capabilities in natural driving sessions where motion artifacts can play a significant role in degrading signal quality.

Transdiagnostic comparison of sleep measures across chronic physical and mental health disorders using FitBit data in the All of Us dataset

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Introduction: The association between sleep and chronic diseases is well established. However, most studies have examined individual disease groups separately, with few exploring sleep patterns transdiagnostically across multiple physical and mental health conditions. This study first compares sleep measures across groups of individuals with sleep disorders, mental health disorders, and cardiovascular disease, and subsequently evaluates the predictive ability of these measures for classifying disorders.

Materials and methods: Participants from the All of Us Research Program with more than 21 days of continuous sleep data collected prior to the prescription of sleep-affecting devices or medications were included. Sub-cohorts were identified using ICD-9 and ICD-10 codes mapped via the PheWAS package in R, comprising obstructive sleep apnea (OSA, N = 2,233), insomnia (N = 1,449), major depressive disorder (MDD, N = 2,370), anxiety (N = 3,128), bipolar disorder (N = 725), PTSD (N = 577), cardiovascular disease (CVD, N = 2,075), and controls (N = 3,954). Minute-level sleep-stage data (wake, light, deep, REM) were used to derive nightly sleep metrics including sleep efficiency, fragmentation, stage-transition dynamics, sleep onset latency, napping behaviour, and wake after sleep onset (WASO). These nightly metrics were summarised across each participant's longest continuous recording period by calculating statistical features such as the mean, coefficient of variation (CV), and entropy. Features were compared within sub-cohorts and against controls. An XGBoost binary classifier was fitted for each disorder versus controls using all sleep features, adjusting for age, sex, race, ethnicity, BMI, waist, and hip circumference. Model performance was assessed against a baseline model (without sleep features) and a model using sleep features only.

Results: Certain sleep measures showed marked differences between disorder cohorts and controls. For example, the CVD cohort had the highest WASO (SMD = 0.3), lowest sleep efficiency (SMD = -0.3), lowest percentage of deep and REM sleep (SMD = -0.5), and highest variability in the percentage of light, deep, and REM sleep stages (SMD = 0.6). While higher frequency and duration of morning naps were common across disorders, these measures were especially elevated in PTSD (SMD ≈ 0.5–0.6). The PTSD cohort also showed the highest variability in sleep onset times (SMD = 0.5), followed by MDD and bipolar disorder (SMD = 0.3), and anxiety, OSA, and insomnia (SMD = 0.2). XGBoost models achieved ROC AUC scores ranging from 0.69 (anxiety) to 0.78 (CVD) and 0.80 (OSA). Incorporating

sleep features improved classification metrics across all conditions, notably an improvement in ROC AUC score in classifying MDD (+0.07), PTSD (+0.06), bipolar (+0.06), and anxiety (+0.05), whereas the improvement in classifying CVD (+0.01), OSA (+0.03) and Insomnia (+0.03) are less pronounced. Models using only sleep features also demonstrated ROC scores >0.63 for all disease areas, confirming the predictive relevance of sleep patterns.

Conclusions: Our study highlights different patterns in sleep characteristics across diverse chronic health disorders. However, simple statistical summaries alone may lack sufficient granularity for accurate disease classification. Future extraction of higher-resolution sleep features could further distinguish these patterns, potentially enabling more accurate disease classification and prediction.

Transformer-Based Reconstruction of Thoracic Movement from Infrared Sleep Video for Non-contact Respiratory Monitoring

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Introduction: Thoracic movement patterns during sleep provide valuable biomarkers for both sleep stage classification and the diagnosis and severity assessment of obstructive sleep apnea (OSA). While conventional in-laboratory polysomnography (PSG) with thoracic belts remains the gold standard, its dependence on skin-contact sensors and vulnerability to motion artifacts limit its utility for long-term, home-based monitoring. In this study, we propose a non-contact infrared camera-based approach that reconstructs thoracic movement signal from de-identified video data.

Materials and methods: We utilized the Korea Video Sleep Study (KVSS) dataset, which comprises 475 infrared sleep video recordings synchronized with PSG data, totaling over 3,000 hours of footage collected in clinical settings. Participants (n = 475; 26% female) had a mean age of 53.4 ± 14.5 years and a mean BMI of 26.5 ± 4.2 kg/m². OSA severity was classified as follows: Normal (9.3%), Mild (21.5%), Moderate (25.9%), Severe (43.3%). To ensure anonymity, patient faces in the videos were de-identified. Video resolution was 640×480 pixels at 5 Hz frame rate. Using 60-second windows, we extracted motion-based features. These features were fed into a modified transformer architecture to reconstruct the thoracic signal. We measured thoracic movement-derived respiratory rate (TRR), defined as the number of breathing cycles per minute from both the PSG-derived thoracic movement signal and reconstructed thoracic signal using a power spectral density peak method in the 0.1–0.5 Hz frequency band.

Results: Our model achieved a mean absolute error (MAE) of 0.87 TRR, a root mean squared error of 2.58 TRR, and a mean absolute percentage error of 8.39%. In the frequency domain, the Pearson correlation coefficient was 0.911, and the concordance correlation coefficient was 0.803. Notably, our MAE of 0.87 TRR (≈ 0.87 breaths/min) is well below the ± 3 breaths/min clinical acceptability threshold reported in prior wearable vital sign studies.

Conclusions: Our proposed methodology offers non-contact, de-identified thoracic movement monitoring, minimizing patient discomfort and facilitating continuous tracking in environments such as homes, hospitals, and sleep clinics. We believe that it has the potential to replace traditional belt-based measurements in OSA diagnosis and sleep stage classification.

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Unobtrusive skin temperature estimation during sleep on a smart bed

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Introduction: The transition from wakefulness to sleep is associated with a decrease (of about 1 °C) in core body temperature which is facilitated by an increase in cutaneous blood flow that helps dissipate internal heat into the microenvironment surrounding the sleeper's body. The rise in cutaneous blood flow causes the skin temperature at distal (hands and feet) and proximal (near the abdomen) sites to increase by about 1 °C and 0.5 °C respectively.

Understanding the association between the dynamics of skin temperature, sleep onset and maintenance may inform strategies to optimize the in-bed microenvironment to enhance sleep quality. Characterizing the dynamics of skin temperature variations across sleep phases on a large scale requires an unobtrusive, longitudinal method for estimating skin temperature, ideally under ecologically valid (real-world) conditions.

Materials and methods: Leveraging the data from a temperature sensor strip (TSS) with five individual temperature sensors (separated from each other by 14 cm) embedded near the surface of a smart bed's mattress, we have developed an algorithm to estimate the distal skin temperature with a minute-long temporal resolution.

The TSS is transversally oriented with respect to the sleeper's body, spans a 67-cm-wide region, and is located 61-cm from the top of the bed.

The data from 18 participants (9M/9F; 44.4 [SD: 6.9] years-old) who recorded TSS and ground-truth skin temperature data from sleep during 14 nights at home and 2 nights in a lab were used to develop a regression model that uses a two-stage architecture (gradient boosted tree followed by a random forest) to estimate the distal skin temperature.

Using the in-home data, a five-fold cross-validation procedure was applied to train and validate the model such that the data from a participant could only be either in the training or validation set but not in both. The algorithm verification was performed with the in-lab data.

Results: The regression model can estimate the distal skin temperature at a minute-level resolution, with accuracy characterized by a mean bias of -0.002 °C, mean limits of agreement [-0.79 to +0.79 °C] and mean coefficient of determination $R^2=0.87$.

Thus, 95% of absolute approximation errors are below 0.8 °C and almost 90% of the variability in skin temperature can be explained by the regression model.

The verification with the in-lab data showed agreement with the ground-truth distal skin temperature characterized by a coefficient of determination of 0.90.

Conclusions: The temperature sensing approach and regression model proposed in this study may enable accurate, unobtrusive, longitudinal and ecologically valid collection of distal skin temperature values during sleep. To the best of our knowledge, this is the first study reporting on the feasibility of unobtrusively estimating skin temperature while lying in bed. Additional research is needed to confirm these encouraging results in a larger cohort.

User-friendly and inter-operable software for automatic quantification of muscle activity during sleep

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Introduction: Although several algorithms for the analysis of muscle activity during sleep have been developed and validated, the lack of user-friendly interfaces and inter-operability across different polysomnography (PSG) software limits their use. We aimed to develop "Sleep Open-source Muscle Activity Analysis System" (SOMAS), the first user-friendly and inter-operable software for automatic quantification of muscle activity during sleep.

Materials and methods: We developed SOMAS as a stand-alone executable based on freely available MATLAB (The Mathworks, Inc.) Runtime shared libraries. SOMAS operates on data files in inter-operable European Data Format+ (EDF+) on local computers without any data sharing online. SOMAS quantifies muscular activity during sleep with two previously validated algorithms: the atonia index (AI) and the distribution of normalized electromyogram (EMG) values (DNE). Both algorithms provide metrics of muscle activity during all sleep stages and wakefulness. In addition, SOMAS calculates leg

movement (LM) indices according to the 2016 World Association of Sleep Medicine (WASM) criteria. Through several user-friendly interfaces, the user is asked to specify the desired analyses, to define annotations defining the hypnogram, to specify the electromyographic signals, and to define any other relevant annotation (e.g. artifacts to be excluded from analysis, annotations of LM). To confirm the validity of SOMAS, we considered sleep recordings of eight patients with isolated rapid eye movement (REM) sleep behavior disorder (iRBD), five with restless legs syndrome (RLS), seven with sleep breathing disorders and five clinical controls. For all subjects and sleep stages, the AI and LM indices calculated by SOMAS in the chin, upper and lower extremities were compared to the ones derived by Hypnolab (a previously proposed software) by means of Spearman correlations. In addition, the AI and DNE in REM sleep calculated in the chin, upper and lower extremities obtained by SOMAS were used to discriminate patients with iRBD from the remaining subjects by means of area under the curve (AUC). Finally, the periodic leg movement index and periodicity index calculated by SOMAS were compared between patients with RLS and clinical controls, and the AUC was used to assess the ability to discriminate between the two groups.

Results: The AI derived by SOMAS and Hypnolab showed high agreement across all muscles and sleep stages (Spearman $r > 0.97$ in 24 out of 25 comparisons). Similarly, all LM indices had excellent agreements (Spearman $r > 0.99$ in all comparisons). The AI and DNE in REM sleep also showed excellent discrimination abilities in differentiating patients with iRBD from the remaining subjects (AUC in the range 0.890-1.000). Finally, patients with RLS had higher PLMS index than controls ($30.31/h \pm 39.1/h$ vs $4.21/h \pm 5.52/h$) as well as higher periodicity index in sleep (0.509 ± 0.328 vs 0.254 ± 0.251). These two indices discriminated patients with RLS from controls with AUC of 0.750 and 0.714, respectively.

Conclusions: The high correlations between SOMAS and Hypnolab as well as the expected discriminations of patients with iRBD and RLS support the validity of the algorithms' implementation. SOMAS will help researchers by providing automatic, standardized and reliable methods for quantification of muscular activity during sleep.

Using Machine Learning to Identify Patient-Ventilator Asynchrony during Non-Invasive Ventilation in Patients with Motor Neurone Disease

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Introduction: Motor Neurone Disease (MND) is a rare and fatal neurodegenerative disorder. It progressively destroys the motor neurones responsible for voluntary muscle contraction, with symptoms worsening until the ability to speak, swallow, move, and even breathe unassisted are lost. For people living with MND, this onset of respiratory failure is often the final and most devastating stage of their illness. Non-invasive ventilation (NIV) is the most effective intervention currently available, extending survival times threefold compared to the best available medication. Yet despite this, NIV remains underutilised and poorly adhered to, with challenges to both uptake and usage. A key contributor to poor adherence is patient-ventilator asynchrony (PVA). PVA is a mismatch between a person's breathing effort and the mechanical assistance provided by their ventilator. This mismatch undermines their treatment by reducing comfort, disrupting sleep, lowering adherence, accelerating decline, and eventually hastening their demise. Identifying PVA currently requires labour-intensive manual review of polysomnography (PSG) recordings by skilled clinicians, a process that is difficult to scale. Acquiring these PSG recordings also involves an overnight titration study in a sleep lab, which poses significant logistical hurdles for patients and their families and is impractical to repeat frequently, particularly in this patient population. This project aims to address this therapeutic gap by developing a machine learning (ML) model that automates the detection and classification of PVA events. This program of work ultimately aims to bring automated real-time ventilator re-synchronisation to the bedside.

Materials and methods: A curated dataset of 30 PSG recordings with >9,000 clinician-scored PVA events acquired during a prior randomised controlled trial was used to train and validate a machine-learning algorithm. Multivariate time-series models were used to detect and classify two common and

distinct forms of PVA from PSG data – namely, Ineffective Effort and Double Trigger. Validation was then performed against clinician annotation to assess accuracy.

Results: 85% of Ineffective Effort events were concordant between clinician and ML scoring, with the remainder comprising 10% that were clinician-scored only and 5% being ML-scored only. In contrast, 51% of Double Trigger events were concordant between clinician and ML scoring, with 7% that were clinician-scored only and 42% being ML-scored only. The model achieved an F1 score of 0.92 for Ineffective Effort and 0.68 for Double Trigger. The reduced specificity observed in Double Trigger is likely heavily influenced by the substantially lower number of Double Trigger events in comparison to Ineffective Effort within both the training and validation data sets.

Conclusions: This project delivers a translational step toward automated PVA identification and correction for people with MND. Future research will determine if reducing reliance on manual clinician analysis will allow timelier and more effective NIV optimisation. We hope to deliver meaningful survival and quality-of-life gains for a population with very limited therapeutic options, sooner and more reliably than any pharmacological advance currently on the horizon.

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Validation of an Under-Mattress Monitoring Device Against Polysomnography for Heart Rate (HR) and Heart Rate Variability (HRV) Accuracy Assessment

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Introduction: Heart rate variability (HRV) is a widely used physiological marker for assessing autonomic nervous system function and overall sleep health. While electrocardiogram (ECG)-based HRV measurements obtained during polysomnography (PSG) are considered the gold standard, their complexity limits accessibility for routine or home-based monitoring. Advances in artificial intelligence have enabled the development of contactless, non-invasive sleep monitoring devices such as the Sleeptracker-AI, which utilizes multiple piezoelectric sensors placed under the mattress to detect heartbeats, respiration, and movement via ballistocardiography (BCG). This study aims to validate the accuracy of Sleeptracker-AI's heart rate and HRV metrics, specifically HR, Standard Deviation of Normal-to-Normal intervals (SDNN), and Root Mean Square of Successive Differences (RMSSD), by comparing them to simultaneous PSG-derived values.

Materials and methods: The study was performed on 102 adults (55% men and 45% women; mean age 40.6 ± 13.7 years; BMI 26.8 ± 5.8 kg/m²) who underwent a one-night unattended study and were simultaneously monitored using standard PSG and Sleeptracker-AI. HR and HRV metrics were compared between the two devices by analyzing both 5-minute windows and full-study averages. Data were evaluated across all ECG beats and matching beats (ECG beats within 500ms of a detected Sleeptracker-AI beat) during all sleep stages and periods of wakefulness while the participant was in bed. Agreement was assessed using Bland-Altman plots and Pearson correlation coefficients. Mean absolute error (MAE), root mean square error (RMSE), median absolute error, and robust RMSE were also calculated to quantify accuracy and variability for matching and non-matching beat conditions.

Results: The Sleeptracker-AI showed strong agreement with PSG across key cardiac metrics. RR interval analysis using matching beats demonstrated a small bias of -0.5 ms, with limits of agreement from -15.0 to $+14.9$ ms. HR analysis over the entire study duration showed excellent agreement with PSG, with high correlation coefficients ($r = 1.00$ for matching beats; $r = 0.99$ for all beats) and low median absolute errors (0.10 bpm for matching beats; 0.48 bpm for all beats). Analysis of the time-domain HRV components SDNN and RMSSD also demonstrated strong performance. SDNN showed strong correlations when based on matching ECG beats ($r = 0.98$) and declined when all beats were included ($r = 0.90$), further decreasing during wakefulness. Corresponding median absolute error increased from 2.34 ms (matching beats) to 16.18 ms (all beats), reflecting SDNN's high sensitivity to beat exclusion, particularly during motion. RMSSD showed a similar, but less pronounced pattern ($r = 0.96$ with matching beats; $r = 0.93$ with all beats), with values lowest during wake, and an increase in median absolute error (from 3.84 ms to 4.74 ms).

Conclusions: These findings indicate that the Sleeptracker-AI system provides reliable, long-term HR and HRV monitoring, particularly when beat detection coverage is high. Its non-invasive, contactless design makes it a practical tool for tracking cardiac autonomic dynamics and sleep health in real-world settings, supporting its utility for both research and clinical applications.

Validation of Automatic Sleep Stage Classification and Sleep Quality Assessment Using Smartwatch Technology

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Introduction: Polysomnography (PSG) is costly and impractical for evaluating widespread problems of insomnia and poor sleep quality. Despite consumer wearables are being alternatively used in sleep research, the validity of the devices and their resulting sleep measures remains a source for concern. To validate the automatic sleep stage classifier algorithm based on 3D-accelerometer (3D-ACC) and photoplethysmogram (PPG) signals derived from the Huawei® Watch against PSG. Additionally, we seek to establish a predictive model linking objective sleep parameters to subjective sleep parameters.

Materials and methods: The developed smartwatch technology was successfully applied to overnight recordings of 108 healthy subjects, with simultaneous one-night PSG measurements, and subjective sleep questionnaire were records manually by the subjects. We extracted objective sleep parameters, including total sleep time (TST), light sleep (% TST), slow wave sleep (% TST), and rapid eye movement sleep (REM, % TST) from smartwatch-based sleep staging, and subjective sleep quality index from subjective sleep questionnaire. The 9-fold cross-validation was used to evaluate the concordance between manual PSG scoring and smartwatch-based sleep staging. A nonlinear regression model was used to explore the relationship between objective and subjective sleep parameters, and we finally generate estimates of the overall sleep quality index.

Results: In this study, participants aged 18 years or older, of whom 53.70% were male. The mean[SD] of TST, light sleep time, slow wave sleep time and REM sleep time calculated by the smartwatch technology were 413.16[75.66] min, 269.74[60.92] min, 75.61[34.57] min and 67.81[32.41] min, respectively. Compared to the PSG, the accuracy of total sleep duration was 95.38%. The automatic sleep stage classification demonstrated moderate accuracy and kappa coefficient, which was 74.50% and 0.52, respectively. The objective sleep parameters explained an R-squared value of 31.2% for the subjective sleep quality index, with a mean absolute error of 3.1.

Conclusions: The smartwatch technology demonstrated moderate-to-high accuracy in automatic sleep stage classification when compared with PSG, supporting its potential as a practical tool for consumer-level sleep health assessment. Additionally, the moderate association between objective sleep parameters and subjective sleep quality suggests the feasibility of using wearable-derived data to infer subjective sleep quality, though further refinement of modeling approaches is warranted.

Visualizing Temporal Patterns in Sleep Tracker Accuracy: A Novel Approach to Validating Consumer Sleep Technologies

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Introduction: Consumer-grade sleep trackers such as Fitbit are widely used to monitor sleep in daily life, but concerns remain regarding their data accuracy—especially in detecting sleep stages. While prior validation studies often evaluate overall agreement with gold-standard methods, they typically treat device accuracy as a static property, overlooking the inherent temporal dynamics of human sleep. In particular, deep sleep tends to dominate early in the night, while REM sleep increases toward morning. This raises an important question: does the accuracy of sleep trackers vary across the night in relation to these temporal sleep patterns? This study proposes a novel, visually-driven validation approach to explore how sleep tracker accuracy fluctuates across sleep cycles. Instead of conventional methods

such as Bland–Altman plots or global accuracy scores, our method highlights time-dependent variation in sleep staging performance.

Materials and methods: We collected concurrent sleep data from 22 healthy adults (mean age 24.8 ± 4.4 years, 8 women) using both a Fitbit Charge 2 and a medical-grade single-channel EEG device during one night of at-home sleep. Epoch-level sleep staging from the EEG device was reviewed by an expert scorer. Fitbit data were extracted at 1-second resolution and aggregated into 30-second epochs, yielding a total of 18,759 epochs. To capture temporal trends, we segmented each participant's hypnogram into approximate sleep cycles (200 epochs per segment, based on average cycle length). Using R (ggplot2), we visualized epoch-by-epoch agreement across cycles to generate color-coded spectrums of classification accuracy for each stage.

Results: Visual analysis revealed clear temporal patterns in Fitbit-derived sleep staging. Accuracy for deep sleep was highest during the first two sleep cycles, while accuracy for REM sleep improved significantly in the latter half of the night. In contrast, accuracy for light sleep and wake stages remained relatively stable across cycles. These findings indicate that device performance is not uniform across the night and may align with physiological shifts in sleep architecture.

Conclusions: This is the first study to apply data visualization as a complementary validation method for sleep tracker accuracy across sleep cycles. Our approach uncovers temporal fluctuations in classification performance, providing new insights into how consumer devices behave across different sleep stages and times of night. Future algorithm development and validation efforts should incorporate temporal context (e.g., through segmented modeling) to improve the reliability of wearable sleep technologies.

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Wearable-derived Sleep Digital Biomarkers and Well-being: Preliminary Insights from Longitudinal Observational Study

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Introduction: Wearables and mobile health applications are increasingly used across diverse populations, enabling the continuous collection of behavioral and physiological data. By combining wearable-derived metrics with daily and clinically validated questionnaires, we can gain deeper insights into daily lifestyle habits and their relationship with health outcomes. In this preliminary analysis, we investigate how wearable-derived sleep digital biomarkers relate to next-day user-reported mood and whether mood and lifestyle factors, in turn, influence sleep architecture.

Materials and methods: We collected data from 21 participants over at least one month using Labfront, integrating longitudinal wearable data, daily self-reports, monthly validated questionnaires, and demographics. Participants also completed the PSQI, SF-12, and Bernese Sleep Health Questionnaire at baseline and monthly. Wearable-derived lifestyle and sleep-related digital biomarkers were aggregated on a daily basis. Repeated-measurement correlation analyses and Bayesian mixed-effects models were used to assess associations between mood and sleep measures. For all model coefficients, the probability of direction (PoD) was calculated.

Results: The cohort consisted of 6 (29%) female participants, and the average (sd) age was 31 (8) and BMI was 24 (3). All participants had university-level education. Sleep difficulties were mainly attributed to external or acute respiratory factors, with only one participant reporting use of sleep medication. Correlation analyses showed that higher mood was associated with more frequent social interaction ($r=0.11$, $pval<0.001$), while working hours were negatively associated with higher mood ($r=-0.095$, $pval=0.003$). No correlation was found between mood and cognitive load. Two Bayesian mixed-effects models provided additional insights on the effects directions and their PoD. Firstly, we examined association between wearable-derived sleep digital biomarkers on the next day's mood. Better mood was positively associated with total sleep time (94.1%) and deep sleep percentage (84.4%), but negatively associated with REM% (82.4%) and the number of nocturnal awakenings (99.8%). This indicates that long sleep with more of a deep sleep percentage was linked to improved next-day mood,

whereas fragmentation and REM-heavy sleep were associated with worse mood. Secondly, we investigated how mood and lifestyle factors influenced REM%. Here, REM% decreased with higher mood (53.7%), alcohol consumption (100%) and average daily stress (100%), but increased with greater cognitive load (95.4%). However, the too low PoD for mood suggests that mood does not predict subsequent REM%. Significant random intercepts in both models suggest inter-individual variability.

Conclusions: This study demonstrates the feasibility of combining wearable-derived digital biomarkers with self-reported measures to monitor sleep and well-being. Our findings suggest that specific sleep characteristics, such as longer total sleep time and greater deep sleep percentage, may predict better next-day mood, while fragmented or REM-heavy sleep is linked to lower mood. In contrast, mood showed limited predictive value for subsequent REM percentage, indicating that the relationship between mood and sleep may be more unidirectional. These preliminary results highlight the potential of integrating wearable and self-report data for real-time mental health and sleep monitoring. Future studies with larger cohorts and longer follow-up periods are needed to validate these associations and explore causal mechanisms.

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Wearable EEG Acquisition during IVF demonstrates High Feasibility and Acceptability

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Introduction: Advances in portable EEG technology can greatly expand both clinical and research capabilities for multi-night recordings in the home environment. However, the usability and feasibility of this technology over extended periods is largely unknown. The Compumedics Somfit, an adhesive wireless EEG monitoring system, worn on the forehead, was evaluated for its acceptability in a pilot study involving women undergoing in vitro fertilization (IVF) for up to 16 days.

Materials and methods: Participants were recruited as part of an ongoing study examining the relationship between sleep slow-wave activity and assisted reproductive treatment outcomes. The present preliminary sample included 5 women, aged 25-35, who underwent IVF for fertility treatment. Each participant wore the Somfit for 2 nights (adaptation, baseline) before and 8-14 nights during ovarian stimulation in their own homes. Outcome metrics on acceptability were collected from a survey administered upon completion of the study in 3 areas: sleep disturbance (difficulty falling asleep, difficulty staying asleep), difficulty with the device technology (associated mobile application, starting the recording, completing the recording), and physical disturbance (tightness, irritation, itching, headache). Participants were asked to rate these 9 items on a 3-point Likert scale (1 = None of the time, 2 = Some of the time, 3 = All of the time).

Results: All five women enrolled, completed the study. The mean difficulty score was 1.4 (SD = 0.5) for sleep disturbance and 1.5 (SD = 0.5) for device technology, indicating general satisfaction with regard to ability to use and sleep with the device. The mean difficulty score for physical disturbance was slightly higher, at 1.6 (SD = 0.6), with skin irritation as the item with the highest difficulty score.

Conclusions: In this preliminary analysis, the Somfit device proved to be well-tolerated, with minimal disruption to daily life. Participant feedback emphasized the comfort and convenience of the device, with most reporting no interference with their typical routines. While the IVF population provides a critical and under-explored context for wearable EEG technology, the findings also suggest that this approach can be extended to other clinical and health research settings where multi-night in-lab study is ill-advised, including in those with chronic conditions, mental health disorders, and aging-related changes.

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Weighted Hypoxia Index, a Translational Quantitative Metric, Predicts All-Cause Mortality

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Introduction: Oxygen saturation, measured by pulse oximetry, is widely utilized in clinical settings, however a method to quantify hypoxemia severity from basic science to clinical scenarios is lacking.

Materials and methods: We developed the Weighted Hypoxemia Index (WHI) to be adapted to different clinical settings by applying 5 steps to the S_pO_2 curve: (1) Identify desaturation/resaturation event by setting the upper threshold; (2) Exclude events as artifact by setting a lower threshold; (3) Calculate weighted area for each as X; (4) Calculate a normalization factor for each subject; (5) Calculate WHI as the summation of all weighted areas multiplied by . We assessed the WHI's predictive value for all-cause mortality and cardiovascular mortality using the Sleep Heart Health Study (enrollment 1995-1998, 11.1 years mean follow-up).

Results: We set varying upper thresholds at 92%, 90%, 88%, and 86%, a lower threshold of 50%, calculated area under the curve (AUC) and area above the curve (AAC), with and without a linear weighted factor (duration of each event), and used the same normalization factor of total sleep time <90% divided by total sleep time. After excluding subjects with missing data, we analyzed 4,509 participants (Alive: N=3,769; All-cause mortality: N=1,071; CVD mortality: N=330). Since WHI-AUC90 had the best results in predicting all-cause mortality, we then compared it to the Apnea-Hypopnea Index and Total Sleep Time <90%. WHI-AUC90 showed statistical significance across quintiles for all-cause mortality, but not cardiovascular mortality, in adjusted Cox regression models.

Conclusions: The WHI offers a versatile and clinically relevant method for quantifying hypoxemia severity, with potential applications to evaluate mechanisms and outcomes across various patient populations.

What are the optimal bedroom temperatures for sleep?

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Introduction: Adequate high-quality sleep is essential for optimizing physical, mental, and cognitive health. The bedroom temperature affects sleep quantity and quality. However, the optimal temperatures for sleep are unknown. Existing building standards define acceptable indoor temperature ranges, but these mostly apply to general living spaces rather than bedrooms. It remains unclear whether these prescribed conditions are generalizable to sleep. The purpose of this study is to review the evidence of optimal temperatures for sleep under steady-state temperature conditions.

Materials and methods: We conducted a literature search on Web of Science using the keywords "bedroom" AND "temperature" AND "sleep." Only peer-reviewed journal articles in English of laboratory experimental studies on the effects of room temperature on sleep were included. We excluded observational or lab studies involving personal comfort devices or dynamic temperature changes, as their focus extended beyond steady-state room conditions. We also reviewed dominant international standards and guidelines related to indoor thermal environments, with a specific focus on recommendations for sleeping environments.

Results: Eleven peer-reviewed studies met the inclusion criteria. Of these, three were conducted in the cooling season, four in the heating season, one in both seasons, and two did not specify the season. One study reported no significant changes in both objectively monitored and subjectively reported sleep quality across a broad temperature range (10–32.2 °C). In the remaining ten studies that found significant impacts of room temperatures on both objectively measured and subjectively rated sleep quality, the optimal temperature for sleep appeared to depend on the need to have heating or cooling. In cooling, the highest sleep quality was observed at temperatures between 24–29 °C across experimental ranges of 21–37 °C. In heating, sleep quality was highest at temperatures between 16–23 °C across experimental ranges of 10–23 °C. Variations in optimal temperature between the reviewed studies are mainly attributed to differences in the insulation of bedding and clothing (0.8 to 4.66 clo). A review of international standards and guidelines found general recommendations for residential indoor temperatures but no specific guidance for bedrooms. For instance, the WHO Housing and Health Guidelines (2018) suggests an indoor temperature range of 18–24 °C. CIBSE Guide A (2021) recommends 23–25 °C in summer and 17–19 °C in winter, while EN 16798 (2019) suggests 25.5–28 °C for summer and 16–21 °C for winter. ASHRAE standard 55 (2017) does not specify temperature ranges for sleeping people.

Overall, recommended temperatures generally align with experimental optima, though WHO and CIBSE advise cooler-than-evidenced levels for the cooling season.

Conclusions: The optimal bedroom temperatures for sleep appear to be 24–29 °C in the cooling season and 16–23 °C in the heating season. While current standards on temperature requirements are broadly consistent with experimental findings, revisions may be needed to address sleep comfort amid energy goals and warming nights.

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When deep learning models align: matching human consensus in sleep staging

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Introduction: Deep learning has led to rapid progress in automatic sleep scoring, with increasingly accurate models rivaling expert-level performance. However, the evaluation of such models must account for the well-known variability among trained sleep technologists [1]. Given that medical consensus consistently yields higher accuracy than individual expert assessments [2], models should strive to align with consensus-based scoring rather than emulate any single scorer's decisions. In this work, leveraging multi-scored datasets [3], we investigate consensus-aligned behavior by ensembling state-of-the-art deep learning models pre-trained on over 27'000 polysomnographic recordings under a unified, large-scale benchmarking protocol [4].

Materials and methods: We leveraged the out-of-domain DREAM Open Datasets [3], comprising 80 full-night polysomnographic recordings - 25 from healthy individuals (DOD-H) and 55 from patients with obstructive sleep apnea (DOD-O) - each independently annotated by five experienced sleep technologists. To investigate consensus-aligned performance, we aggregated predictions, without any additional fine-tuning on DOD, from pre-trained U-Sleep [5], DeepResNet [6], and SleepTransformer [7] models into an average-based ensemble, SOMNUS. Predictions were evaluated against those of individual human experts, their aggregated consensus, and against an in-domain benchmark model trained directly on the consensus itself. Performance was assessed using macro F1 score (MF1), Cohen's *kappa*, and per-stage F1 scores. To capture agreement with probabilistic consensus, we compared model-generated and consensus-derived hypnogram profiles exploiting the averaged cosine similarity (ACS) metric [8], quantifying the similarity between predicted and reference sleep stage probability distributions over time. Finally, we examined whether ensemble-derived

uncertainty, quantified by Shannon entropy and pairwise disagreement among the constituent models of SOMNUS, could identify epochs characterized by disagreement in the human consensus.

Results: Across both healthy (DOD-H) and OSA cohorts (DOD-O), SOMNUS consistently outperformed all individual human experts and the in-domain benchmark model (MF1_{DOD-H}: +4.4% and +2.8%; MF1_{DOD-O}: +4.3% and +2.6%). Ensemble predictions aligned more closely with the consensus than with any single scorer, both in discrete labels ($\kappa_{\text{DOD-H}}$: 88.9, $\kappa_{\text{DOD-O}}$: 85.4) and hypnosity profiles (ACS_{DOD-H}: 0.947, ACS_{DOD-O}: 0.939). Individual models within the ensemble also exhibited this consensus-oriented behavior. Ensemble disagreement was shown to track human scoring ambiguity: ensemble entropy and pairwise model divergence predicted regions of scorer disagreement with ROC AUCs up to 0.828.

Conclusions: Our findings demonstrate that training on heterogeneous datasets and diverse scoring styles enables deep learning models to generalize robustly to new data without further adaptation, achieving consensus-level performance, consistently outperforming individual human scorers and reducing the impact of inter-scorer variability. Alignment with consensus can be further enhanced by aggregating predictions from complementary models spanning different architectures and input configurations, as realized in SOMNUS. In addition, ensemble-derived uncertainty provides a robust signal of scoring ambiguity, offering a principled route to automated uncertainty quantification that can aid in flagging ambiguous epochs for potential review. Together, these results advocate for the use of ensemble-based approaches, pre-trained on large, diverse datasets, as effective consensus approximators and uncertainty-aware tools for automated sleep staging.

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[2] <https://doi:10.1001/jamanetworkopen.2019.0096>

[3] <https://10.1109/TNSRE.2020.3011181>

[4] <https://doi.org/10.48550/arXiv.2506.08574>

[5] <https://doi.org/10.1038/s41746-021-00440-5>

[6] <https://doi.org/10.1093/sleep/zsaa161>

[7] <https://doi.org/10.1109/TBME.2022.3147187>

[8] <https://doi.org/10.1093/sleep/zsad028>

Z4IP – Comprehensive Sleep and Activity Phenotyping Through Multifactor Mobile Data Integration

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Introduction: The ubiquity of smartphones offers unprecedented opportunities for scalable, real-time data collection over extended periods in naturalistic settings. We developed a proprietary mobile app (Z4IP; iOS and Android compatible) to collect multi-stream objective and subjective data for building a comprehensive profile of individual sleep, activity and wellbeing. Each of six functional modules, cognitive tests, questionnaires, audio diaries, time-use diaries, movement patterns and wearable integration, can be customized to satisfy different protocol requirements, and has been field-tested in studies involving community-dwelling, lab-based and hybrid monitoring. Here we assessed the feasibility of long-term monitoring via sleep and activity diaries across different age groups and study contexts: 1) freshmen monitored over their first semester in college (20 weeks); 2) junior doctors undergoing shifts during residential training (8 weeks); 3) older adults past statutory retirement age (10 days).

Materials and methods: Z4IP provides three modes of assessment: 1) ecological momentary assessments (EMA) within study-specific time windows (cognitive tests, questionnaires, audio diaries); 2) self-reports at participant's convenience (time-use diaries); and 3) continuous passive smartphone-derived metrics (movement patterns) and wearable-based behavioural phenotyping (Oura Ring). To foster sustained engagement, the platform incorporates a task completion and reward system, providing personalized feedback through participants' smartphones and enabling large-scale backend monitoring for researchers.

Compliance rates for the two components which demand the most active effort from participants – daily EMA incorporating a sleep diary, and time-use diary – were evaluated across the three aforementioned studies to assess the app's feasibility for long-term monitoring across different age groups.

Results: In Study 1 involving college freshmen (N=638; 51.7% female; mean age [SD]=20.4 [1.3]), the compliance rate of daily EMA questionnaires changed by -1.6% (linear fit) per week (80.1% in week 1 to 45.2% in week 20, end of study). Time-use diaries were completed for three separate fortnights: weeks 1–2, 84.0%; weeks 7–8, 66.2%; and weeks 15–16, 52.6%.

In Study 2, daily EMA compliance rates for medical interns (N=96; 59.4% female; mean age [SD]=24.7 [1.1]) changed by -3.8% (linear-fit) per week (77.1% in week 1 to 52.4% in week 8, end of participation). Time-use diary completion rate averaged 65.2% across the study.

The 10-day compliance rate in Study 3 involving older adults (N=411; 49.6% female; mean age [SD] = 74.2 [2.7]) was 92.3% for EMA questionnaires and 96.0% for time-use diaries.

Conclusions: The EMA sleep diaries effectively complemented wearable-derived objective sleep measures to provide comprehensive and sustainable sleep assessment, demonstrating Z4IP's robust utility for long-term monitoring. Although a gradual decline in compliance was observed over time – as is typical in longitudinal studies – engagement remained notably high. Over half of the freshmen completed EMA and time-use diaries through their examinations (week 16). Despite demanding internship shift schedules, most medical interns maintained daily reporting. High adherence among older adults further underscores the app's accessibility and user-friendliness. These results highlight Z4IP's potential as a scalable and adaptable tool for sustained digital phenotyping in real-world settings.

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