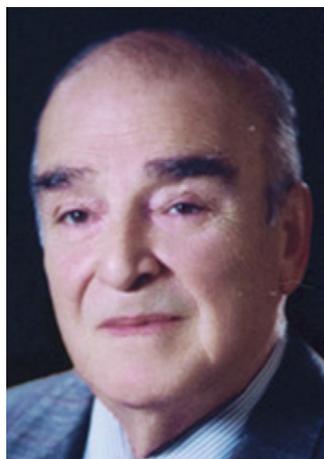




## In Memoriam: Şevket Akpınar, M.D. 1929–2010



Dr. Şevket Akpınar was born in İstanbul in 1929 and died May 27, 2010. Graduating from University of Ankara, School of Medicine in 1953, he completed specialization qualifications for neuropsychiatry in 1961 and later received fellowship training in neurophysiology, electroencephalography, psychopharmacology and sleep at the University of Missouri between 1969 and 1971.

When he returned to Turkey, he continued his work with treating sleep disorders, particularly insomnia, with special attention to difficulty in falling asleep.

During the early years of his sleep medicine work in Turkey (from 1975 to 1977) he indentified a set of patients with insomnia who also complained of a feeling of restlessness, especially in their legs. He observed that if sedatives, especially antipsychotics, were taken the complaints became worse. His review of the literature uncovered a generally negelected paper by Dr. Karl Ekbom [1] describing similar cases and identifying this condition as “restless legs.”

One of Akpınar’s patients with sleep problems and restlessness of the legs had opioid treatment after surgery; this patient claimed that not only had he not slept so well in years but also that he had no restlessness feeling for a short period after the surgery. Dr. Akpınar then focused his attention on the relationship between opioids and falling asleep.

He recognized that while opioids (which are indirectly related to the dopaminergic system) decreased restless legs, antipsychotics (which are dopamine antagonists) worsened symptoms. These

observations indicated a new approach. Based on the perspective that dopamine activity might play a role in the dysfunction leading to restless legs syndrome (RLS), Dr. Akpınar began prescribing levodopa and dopamine agonists to his patients presenting RLS symptoms. The dramatic benefits seen in the aforementioned patient were reported as a case study in 1978 [2]. This was the first report of dopaminergic treatment of RLS. He then described more cases in a presentation at the World Congress of Biological Psychiatry in 1981, but his seminal work, “Treatment of restless legs syndrome with levodopa plus benserazide,” was published in *Archives of Neurology* in 1982 [3]. It is rare in the history of modern medicine for a letter to the editor to totally revolutionize a field, but such was the impact of this publication. In this letter Dr. Akpınar studied five patients with RLS. Four subjects were given 200 mg of levodopa and 5 mg of benserazide one hour prior to going to sleep, and in the remaining subject the total dosage of levodopa was 500–700 mg. All patients exhibited complete disappearance of RLS. Bromocriptine mesylate, a dopamine agonist, gave similar results in the three cases in which it was used. A whole raft of open-label [4] and then double-blind studies of dopaminergic agents in RLS followed, culminating in large scale pharmaceutical trials of dopaminergic agents in RLS with resultant FDA and European counterpart approval of dopaminergic agents such as ropinirole and pramipexole for the treatment of RLS.

During his later years Dr. Akpınar worked on defining the dopaminergic system and electrophysiological indicators. Three articles

in particular, published during 2003–2009 put forth original and creative hypotheses for the pathogenesis of RLS [5–7]. Dr. Akpınar was the first to suggest that hypofunction of the diencephalospinal dopaminergic system in RLS might impact upon muscle spindles, ultimately resulting in the abnormal sensations of RLS [5], a hypothesis he presented as a special guest lecturer at the annual meeting of the International RLS Study Group (IRLSSG) in June of 2001 (which was later developed independently and more fully by Clemens, Rye and Hochman [8]). Akpınar's hypothesis of an abnormal EEG profile generated by the thalamus primarily responsible for RLS leading to the dopaminergic hypofunction [5–7] is a bold and distinct theory. He was also the first to make a serious attempt to analyze the possible role of GABA and glutamate in the pathogenesis of RLS from a detailed anatomical and neurophysiological point of view [6]. In addition, he postulated that dopaminergic hypofunction might result in a temporary accentuation of flexor pathways over extensor pathways leading to Periodic Limb Movements in Sleep (PLMS) [7]. While many of these theories have yet to be proven, they remain important guideposts for future research.

A PubMed search indicates that Dr. Akpınar published 91 peer reviewed articles in the literature, amongst which five were dedicated to RLS [3–7]. Although he contributed only a minority of his time to the study of RLS/PLMS, the impact of these few works has been enormous, and we in the field appreciate his important contributions. Dr. Akpınar will be sorely missed by his family, friends, colleagues, and younger generations he inspired.

References can be found in online supplementary material.

#### **Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.sleep.2010.09.001](https://doi.org/10.1016/j.sleep.2010.09.001).

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