

RESTLESS LEGS SYNDROME AND PERIODIC LEG MOVEMENTS OF SLEEP: EVIDENCE FOR CONSIDERATION AS A SAME DISORDER

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Periodic Leg Movements (PLM) are repetitive, stereotyped flexor- withdrawal- like movements of the legs which occur during sleep and are thus called Periodic Limb Movements of Sleep (PLMS). PLM can also occur during wakefulness (Periodic Limb Movements of Wake or PLMW) especially in patients with Restless Legs Syndrome (RLS)^{1,2}. Formerly, PLMS were called nocturnal myoclonus³ due to their occasional myoclonic jerk character. With the purpose of emphasizing their repetitive periodicity and the fact that most PLM did not reach the speed of a myoclonic phenomenon, the term Periodic Limb Movements in Sleep (PMS) was later introduced.

Periodic limb movements disorder (PLMD) is defined as the presence of an abnormal number of PLM in polysomnographic studies with the simultaneous presence of insomnia (difficulties in initiating and/or maintaining sleep) and/or, occasionally, daytime fatigue or sleepiness, and with the exclusion of other causes of sleep disturbances⁴.

PLMs are defined by their electromyographic characteristics during polysomnographic recordings. Recording of PLM involves EMG surface electrodes placed in one or both anterior tibialis muscles. PLMS are scored only when they occur in series of four or more consecutive movements with a duration of each EMG burst for 0.5 to 5 seconds. These movements consist of dorsiflexion of the foot, extension of the big toe, and frequently also flexion of the knee and hip. Thus, Periodic Leg Movements of Sleep closely resemble the spinal- flexor reflex⁵. Therefore, PLMS have been compared to the triple withdrawal reflex^{6,7}. Nevertheless, some recent studies based on surface EMG findings^{8,9} have not confirmed this point.

The first descriptions of PLMS were performed on inpatients diagnosed with (Restless Legs Syndrome) RLS^{10,11}. In fact, 70-87% of the patients with RLS studied by PSG have a significant number of PLMS (5 per hour of sleep or more)^{12,13} and RLS is the most common condition associated with PLMS¹⁴. In RLS, the mean PLMS index increases with age. Furthermore, independently of the age factor, PLMS index increases with RLS severity¹⁵.

PLMS are a habitual finding in other primary sleep disorders, most frequently narcolepsy, REM Sleep Behavior Disorder (RBD) and narcolepsy. However, PLMS are also frequent in normal subjects without sleep disorders complaints, especially in the elderly¹⁶⁻¹⁹.

Despite the fact that PLMS are not specific to RLS, several facts suggest that both disorders share a common pathophysiological and clinical basis: First, recent genetic studies showed an association between a sequent variant in chromosome 6p and the presence of PLMs in icelandic RLS patients and their families. The association was strongest among relatives with PLMS without RLS, and disappeared in those RLS without PLMS²⁰. A simultaneous study performed in Germany and Canada has confirmed this association²¹. Thus, PLMS can be serving as an endophenotype for RLS, with characteristic genetic determination. Second, both RLS and PLMS share common risk factors, such as reduced serum ferritin indexes, gender, age, and European ancestry. From the point of view of the longitudinal course, PLMS can predate the onset of sensory disturbance. Furthermore, PLMS are more common in asymptomatic relatives of RLS patients than in the general population. Finally, PLMS and the sensorial disturbance of RLS might share a common pathophysiology and respond to both dopaminergic agents¹³ and to iron replacement. In fact, treatment of PLMS with dopaminergic medication might precipitate a full blown sensorial RLS-like disorder in previously asymptomatic patients with PLMS²². In summary, several pieces of evidence suggest that PLMS might constitute a phenotype of RLS characterized by specific motor disturbance. Such clinical forms might eventually, under given genetic and/or environmental circumstances, develop into developed Restless Legs Syndrome.

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