Periodic legs movements in sleep: pathophysiology and clinical significance

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Target Muscle for PLM
Two surface electrodes longitudinally on Tibialis Anterior

1) Sampling rate: 200 - 500 Hz
2) Distance ≈ 2-3 cm
3) Impedence < 5-10 KΩ
4) Filters between 10 e 100 Hz

Periodic leg movements during sleep (PLMS) are electromyographic activations recorded from the anterior tibialis muscles, lasting between 0.5 an 10 seconds\(^1\-^3\)

A PLMS series\(^1\-^3\) is defined as:
1. minimum number of consecutive LM events is 4
2. period length between LMs (time between onsets of consecutive LMs) 5-90 s
3. leg movements separated by less than 5 seconds are counted as a single leg movement

The PLMS Index reflects the number of leg movements included in PLMS series per hour of sleep\(^1\-^3\)

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PERIODIC LEGS MOVEMENT

30 sec

PERIODIC LEGS MOVEMENT

240 sec
EEG, ECG, BP PLM-related activations

Example of a leg activity meter
PERIODIC LEGS MOVEMENT

PLMS have been indicated to closely resemble the triple flexion reflex, which consists of dorsiflexion of the ankle and flexion of the knee and hip, obtained with the contraction-relaxation of several muscles. Such a small EMG activation was thought to recall the crossed extensor reflex, which is a withdrawal reflex occurring when a person steps on a painful object and the leg that is stepping on the object pulls away. These findings were interpreted as an effect of a probable impaired supraspinal dopaminergic control of gait.
More than 80% of RLS patients show a clear peak of variable amplitude, usually with a maximum at around 20-30 s, and extending approximately between 10 and 40 s.
The Periodicity Index indicates the ratio between the true periodic movements and the total amount of movements during sleep. Theoretically, it can range between 0 (no periodic movements) and 1 (all movements are periodic).

The time distribution of PLMS throughout the night shows a typically decreasing course in RLS/WED patients while it is bell-shaped in controls.¹

PLMS show a high night-to-night variability in RLS (Hornyak et al., SLEEP 2005;28:331-335.)

RLS patients (n=42)  Non-RLS patients (n=73)
Brief Communication:

Night-to-night variability of periodic leg movement in sleep Medicine 14 (2013) 293–296

legs syndrome and periodic limb movement disorder: Comparison between the periodicity index and the PLMS index

Raffaele Forini, Stephen Fishbain, Massimo Mancori, Ildegi Hildi, Laura Ehrenasz,

Ennio Ongari-Manzoni, Maria Pazzini
PLMS index before and after treatment in the three different groups of patients

Distribution curve of the inter-LM intervals before and after treatment, in the three groups of patients

Abstract

Background: PLMS index is a common sleep disorder in patients with restless leg syndrome (RLS). The aim of this study was to investigate the effect of bromocriptine on PLMS index in patients with RLS. Twenty patients with RLS were randomly divided into three groups: bromocriptine, placebo, and no treatment. The PLMS index was measured before and after treatment. The results showed that the PLMS index was significantly reduced after treatment in the bromocriptine group, whereas no change was observed in the placebo and no treatment groups. The difference between the groups was statistically significant (p<0.004).

R1. Comparison between the PLMS change index obtained in the three groups of subjects; values are shown as mean and SD ( whisker).

R2. Distribution curve of inter-LM intervals before and after treatment, in the three groups of patients.
CONCLUSION

• PRA is significantly more effective than BRO in reducing PLMS in patients with a high level of PLMS index at baseline.
  – In patients with a PLMS index over 80, PRA suppressed more than 80% of events, while BRO decreased up to 50%.
  – After PRA treatment, the PLMS index decreased in all patients, while after BRO an increase of PLMS index was observed in 2 patients out of 15.

• Considering the distribution of inter-LM intervals, treatment with PRA completely abolished the dopaminergic peak, which persist after BRO.
• The results presented in this clinical study focus on the D3 receptor subtype as a possible preferential target of DA in RLS
• The involvement of other possible dopaminergic or non-dopaminergic neuronal circuits cannot be excluded.

The Periodicity Index indicates the ratio between the true periodic movements and the total amount of movements during sleep. Theoretically, it can range between 0 (no periodic movements) and 1 (all movements are periodic)^1

The time distribution of PLMS throughout the night shows a typically decreasing course in RLS/WED patients, while it is bell-shaped in controls^1

Increased PLMS Index has been reported in a very wide range of conditions

PLMS Index alone has a very low specificity for RLS

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R1  RFerri, 5/29/2011
The combination of number of PLMS, their periodicity (interval distribution graph), and night time distribution reveals disease specific patterns with RLS/WED and PLMD showing the highest periodicity together with the most evident decreasing slope of PLMS during the night.


Increased CAP RATE = increased SYMPATHETIC TONE


PLMS Are Accompanied Very Frequently by EEG and Heart Rate Changes and Are Embedded in the Cyclic Alternating Pattern (a Marker of Sleep Instability)

They are believed to cause arousals (PLMS/arousal index)²³

LMs during sleep are accompanied by evident changes in HR and EEG spectral power. Not only heart rate and EEG changes accompany PLMS, but also significant rises in diastolic and systolic blood pressure. Cardiac activation is significantly greater when the termination of respiratory events is associated with leg movements compared to those without leg movements.

Relationship between PLMS and Hypertension, Cardiovascular Disease, and Cerebrovascular Disease

The mechanisms mediating these relationships are probably multiple and complex. Causality is far from being established.
PLMS can be pharmacologically dissociated from arousals: a benzodiazepine decreases arousals only while a dopamine agonist decreases only PLMS.1

Example of polysomnographic recording of one of the subjects treated with pramipexole at baseline, with the presence of CAP accompanied by PLMS and after treatment, with CAP not accompanied by PLMS.
The BTBD9 and Meis1 gene variants conferring risk for RLS, in fact, are more robust predictors of PLMS in individuals who experience symptoms atypical of RLS, or none at all.
Conclusion: The time structure of leg movements occurring in conjunction with respiratory events exhibit features of periodic leg movements in sleep occurring alone, only with a different and longer period. This brings into question the validity, both biologic and clinical, of scoring conventions with their a priori exclusion from consideration as periodic leg movements in sleep.

Only OSAS patients with genuine PLMS not associated with apnea events had also respiratory-related leg movements.
Conclusion: Our data do not seem to support the hypothesis that PLMS are particularly frequent in PD but seem to indicate an interaction between PD pathophysiology and genetic pre-disposition for PLMS, producing a slightly increased number of patients with this sleep motor phenomenon, when compared to controls.