PLMS and PLMW in Healthy Subjects as a Function of Age: Prevalence and Interval Distribution

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Study Objectives: Several studies have demonstrated a positive correlation between periodic leg movements during sleep (PLMS) and age in healthy subjects. However, little is known about periodic leg movements during wakefulness (PLMW) in this population. Although the definitions of PLMS and PLMW specify a typical intermovement interval of 20 to 40 seconds, scoring criteria allow an intermovement interval of 4 to 90 seconds. The aim of the present study was to look at the prevalence and interval distribution of PLMS and PLMW in relationship with age in a population of healthy subjects.

Design: Periodic leg movements were recorded during 1 night.

Setting: Sleep laboratory, Hôpital du Sacré-Coeur de Montréal.

Participants: Sixty-seven healthy subjects aged between 5 and 76 years (32 F, 35 M).

Interventions: N/A

Measurements and Results: The presence of PLMS was rare before the age of 40, but then the index increased dramatically. PLMW index was higher in younger subjects compared with middle-aged subjects. Interval histograms of PLMS did not revealed a clear peak in younger subjects. With advancing age, PLMS interval histograms show a peak around 15 to 35 seconds, which is not observed in younger subjects. On the other hand, despite high indexes, PLMW interval histograms do not show a clear peak for any age group.

Conclusion: These results illustrate that interval evaluation is an important feature of the calculation of periodic movements to discriminate spontaneous motor activity from PLMS or PLMW.

Keywords: PLMS, PLMW, age, interval

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INTRODUCTION

PERIODIC LEG MOVEMENTS DURING SLEEP (PLMS) ARE DESCRIBED AS EXTENSIONS OF THE BIG TOE AND DORSIFLEXIONS OF THE ANKLE WITH OCCASIONAL flexions of the knee and hip, occurring repetitively during sleep. These movements last 0.5 to 5 seconds and they typically show a frequency of about 20 to 40 seconds. PLMS were first described in patients with restless legs syndrome (RLS).[1] However, PLMS are also reported in other sleep disorders such as narcolepsy,[2-5] rapid eye movement sleep behavior disorder,[6] obstructive sleep apnea,[2,3,7,8] insomnia,[2,4] and hypersomnia.[2,4] Moreover, PLMS are also documented in patients without any sleep complaint.[4,9,10]

Several studies have shown that PLMS increase with age. The presence of PLMS is rare in children,[11] whereas it is common in middle and older age.[9,10,12-15]

Patients with RLS also present similar movements during wakefulness (periodic leg movements during wakefulness, PLMW).[16] It is possible that, in addition to the involuntary movement, a voluntary contraction occurs in order to better relieve the dysesthesia. This would thus produce longer movements when patients are awake. Therefore, a duration criterion of 0.5 to 10 seconds is used when scoring PLMW.[17] In patients with RLS, the PLMW index increases with age.[18] Little is known about PLMW in subjects without RLS. One study showed more PLMW in healthy teenagers, compared with healthy young adults.[19] However, the evolution of PLMW with age in nonclinical populations remains unclear.

Although the definitions of PLMS and PLMW specify a typical interval of 20 to 40 seconds, scoring criteria allow an intermovement interval (IMI) of 4 to 90 seconds.[20,21] We can thus wonder whether all PLMS or PLMW are truly periodic. If the IMI criteria are not sufficiently restrictive, nonperiodic motor activity can be identified wrongly as PLMS or PLMW.

The aim of the present study was to look at the prevalence and the interval distribution of PLMS and PLMW in relationship with age in a population of healthy subjects.

METHODS

Subjects

Sixty-seven healthy subjects who have participated in different research projects were randomly selected for this study. They were between 5 and 76 years old (mean age: 35.81 ± 20.56 years; 32 females, 35 males). All subjects were studied in the sleep laboratory between 1999 and 2005. None of the subjects had any medical, psychiatric, or sleep disorders. In the different proto-

Disclosure Statement

This is not an industry supported study. Dr. Petit has received research support from Orphan Medical, Sanofi-Synthelabo, Pharmacia/Pfizer; Aventis, and GlaxoSmithKline; and is a consultant for XenoPort. Dr. Pennestri has received support from Fonds de la recherche en santé du Québec (FRSQ). Dr. Whittom has received support from Fonds de la recherche en santé du Québec (FRSQ). Dr. Montplaisir has received research support from Aventis, Sanofi-Synthelabo, Orphan Medical, Pharmacia/Pfizer, and GlaxoSmithKline; is a consultant for Shire BioChem, Aventis, KappaSanté, and Pfizer; has participated in speaking engagements supported by Boehringer Ingelheim, Shire, and GlaxoSmithKline; and is an advisory board member of Boehringer Ingelheim. Drs. Adam and Carrier have indicated no financial conflicts of interest.

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Table 1—Sleep Characteristics in the 7 Age Groups[a]

	5-9	10-19	20-29	30-39	40-49	50-59	> 60
No.	7	9	13	10	9	8	11
Males/females	5/2	7/2	5/8	5/5	5/4	5/3	3/8
Sleep latency, min	18.9 ± 7.8	28.6 ± 21.3	15.9 ± 12.6	10.8 ± 9.2	19.5 ± 24.4	12.3 ± 4.8	13.4 ± 7.9
Total sleep time, min	543.4 ± 24.1	461.7 ± 31.0	431.3 ± 36.7	426.0 ± 29.7	392.2 ± 73.0	410.5 ± 53.8	413.9 ± 24.5
Sleep efficiency, %	96.8 ± 1.7	94.0 ± 3.7	93.0 ± 4.0	90.5 ± 6.3	91.4 ± 4.2	87.5 ± 5.8	86.7 ± 4.7
Total duration of wake, min	45.4 ± 17.7	54.4 ± 26.5	48.6 ± 24.0	57.2 ± 31.3	66.1 ± 38.9	72.9 ± 32.4	78.9 ± 26.9
Awakenings, no.	21.6 ± 8.1	21.7 ± 12.8	25.4 ± 10.2	29.5 ± 19.6	32.2 ±10.3	37.8 ± 20.9	41.6 ± 13.7
Sleep stage, % of total sleep time							
1	4.9 ± 1.4	7.8 ± 4.2	7.1 ± 4.1	9.6 ± 4.3	7.5 ± 4.2	11.5 ± 6.2	14.3 ± 8.0
2	61.2 ± 5.8	54.5 ± 8.5	61.2 ± 9.3	64.7 ± 5.2	65.6 ± 5.4	66.7 ± 5.9	67.7 ± 8.3
SWS	15.3 ± 4.0	20.5 ± 9.9	11.6 ± 10.2	4.1 ± 4.1	4.5 ± 4.2	0.8 ± 0.9	0.4 ± 0.9
REM	18.6 ± 3.0	17.2 ± 5.6	20.1 ± 4.7	21.6 ± 5.9	22.3 ± 5.2	21.1 ± 3.4	17.6 ± 4.4

[a]Age groups are in years. Data are presented as mean ± SD unless otherwise indicated. SWS refers to slow-wave sleep; REM, rapid eye movement sleep.

cols, subjects (except children aged 5 to 9 years) had to fill out a screening questionnaire in which they were asked about sleep problems. They were specifically asked whether they experience urges to move associated with unpleasant leg sensations. Subjects were excluded if they reported any sleep problems or if they answered positively to the RLS question, regardless of the presence of other diagnostic criteria. Subjects with an index of respiratory events (apneas + hypopneas) greater than 5 were excluded from the study. Subjects with a sleep efficiency lower than 80% were excluded (percentage of the time spent asleep over the recording time from sleep onset to the last awakening). No selection criteria concerning PLMS or PLMW index were applied. They were not taking any medication known to influence sleep or motor activity. All participants gave written informed consent before the beginning of their respective protocol.

PROCEDURES

Subjects were recorded for 1 or 2 nights in the sleep laboratory. Only the first night was used for analyses. Sleep was recorded and scored by the standard method.[22] Sleep was monitored using 2 electroencephalogram leads (C3-A2 and O2-A1), right and left electrooculograms and chin electromyogram. Oral and nasal airflow were recorded with a thermistor, thoracic and/or abdominal respiratory movements were recorded with strain gauges, and oximetry was performed to detect apneas and hypopneas, although these sensors do not allow the exclusion of subjects with upper airway resistance syndrome. Respiratory events were not recorded in children. Surface electromyogram electrodes, placed 3 to 4 cm apart on the right and left anterior tibialis muscles, were used to record leg movements during sleep (PLMS) and during periods of nocturnal wakefulness, including the presleep onset period (PLMW). An electrocardiogram was recorded from a standard D1 lead.

PLMS were scored according to standard criteria.[20,21] Only movements lasting 0.5 to 5 seconds, separated by intervals of 4 to 90 seconds and occurring in series of at least 4 consecutive movements were counted. PLMW were scored following modified Coleman criteria, allowing for movement duration up to 10 seconds.[17] The amplitude criterion for detecting both types of movements was at least 25% of the amplitude of the voluntary movement performed at the beginning of the recording.

Statistical Analyses

Several PLMS and PLMW characteristics were measured: number, index, mean duration, and mean IMI. First, the relationship between age and movement parameters was assessed by Pearson product-moment correlations. Subjects were then divided into 7 age groups: 5 to 9 years, 10 to 19 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, and 60 years and older. Sleep characteristics for the 7 age groups are presented in Table 1. In addition, Kruskal-Wallis analyses of variance followed by multiple comparisons (by ranks) were performed on the PLMS and PLMW indexes. Finally, the mean of the individual distributions of PLMS and PLMW IMI durations was illustrated with histograms for each age group.

RESULTS

PLMS and PLMW Characteristics in Relationship With Age

Pearson correlation coefficients were calculated between age and both PLMS and PLMW characteristics. With advancing age, there was a significant increase in the PLMS index ($r = 0.50$; $p < .001$) and a significant decrease of the PLMS duration ($r = -0.28$; $p < 0.05$). The mean PLMS IMI was not correlated with age ($r = 0.18$; $p = .19$). However, during wakefulness, the PLMW index was negatively correlated with age ($r = -0.34$; $p = .005$). With advancing age, there was also a significant increase in the mean PLMW IMI ($r = 0.25$; $p < .05$), whereas the mean PLMW duration was not correlated with age ($r = -0.06$; $p = .64$).

The distribution of mean PLMS index values as a function of age is illustrated in Figure 1. The Kruskal-Wallis analysis of variance showed a significant between-age group difference ($H = 17.4$; $p = .008$). Multiple comparisons revealed a significantly higher PLMS index in the older age group (60 years and older) compared with the 30- to 39-years group. The distribution of the mean index (Figure 1) rather suggests that PLMS increase linearly with age.

The distribution of mean PLMW index values as a function of age is illustrated in Figure 2. The Kruskal-Wallis analysis of variance also revealed a significant between-age group difference ($H = 18.5$; $p = .005$). Multiple comparisons revealed a significantly higher PLMW index in the younger age group (5-9 years)

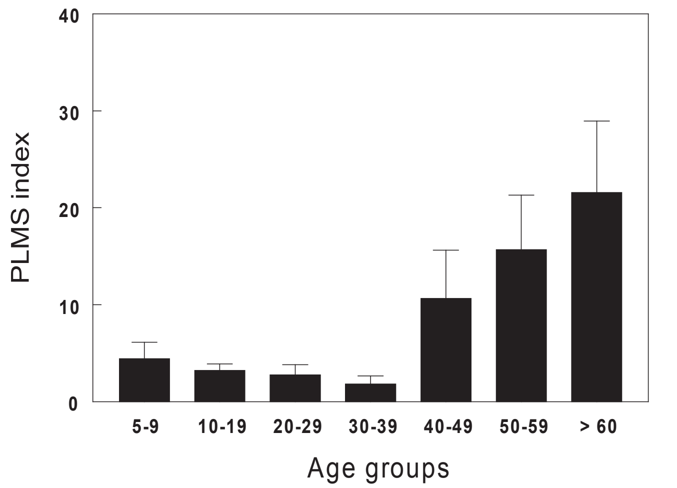

Figure 1—Mean periodic leg movements during sleep (PLMS) index for healthy subjects according to 7 age groups (5-9 y, 10-19 y, 20-29 y, 30-39 y, 40-49 y, 50-59 y, and 60 y and older). Vertical bars represent the SEM.

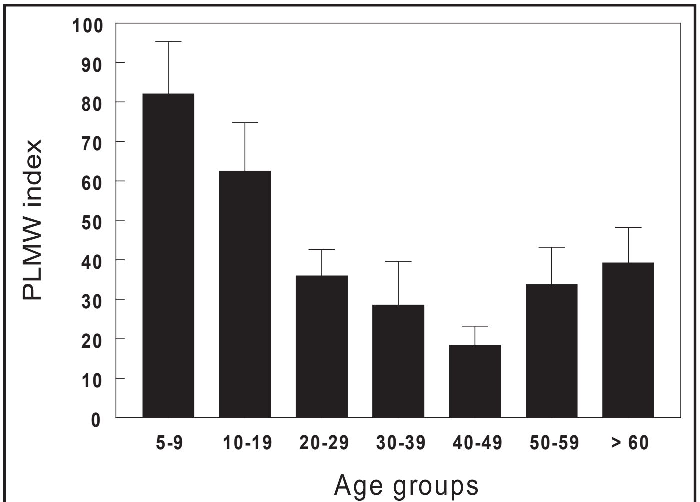

Figure 2—Mean periodic leg movements during wakefulness (PLMW) index for healthy subjects according to 7 age groups (5-9 y, 10-19 y, 20-29 y, 30-39 y, 40-49 y, 50-59 y, and 60 y and older). Vertical bars represent the SEM.

compared with both the "30 to 39 years" and "40 to 49 years" age groups. The age-related distribution of the mean PLMW index (Figure 2) yet suggests a U-curve evolution.

Movement Periodicity as a Function of Age

The distribution of IMI was influenced by age. Figure 3 illustrates the mean of the individual distributions of PLMS IMI duration per age group. With advancing age, the PLMS interval histograms show a peak between 15 and 35 seconds; no peak was observed in younger subjects. Figure 4 illustrates the mean of the individual distributions of PLMW IMI duration per age group. A pattern quite different from that of PLMS emerges. In fact, the PLMW interval histograms do not show a clear peak for any age group. The figure rather illustrates an important number of small IMI shorter than 15 seconds, especially in young subjects, which seems to reflect spontaneous motor activity rather than PLMW per se.

DISCUSSION

PLMS and PLMW Prevalence in Relationship With Age

Because the present study included a wide range of age groups, it allowed us to evaluate the evolution of PLMS from young children to older subjects. As expected, the PLMS index was significantly correlated with age. However, Figure 1 presents a more precise picture of PLMS evolution with age. In fact, the presence of PLMS was very rare before the age of 40, but then the index increased dramatically. These results are consistent with other studies reporting a low prevalence of PLMS in children and a high prevalence in middle-aged and older subjects. [9-15] This increase in prevalence is probably associated with the decrease of D_2 receptors, which is observed in healthy humans and animals with advancing age.[23-24] Wong and coworkers[23] have indeed demonstrated a decrease in human D_2 receptors more marked from about 35 to 40 years of age.

Several studies excluded healthy subjects presenting a PLMS index higher than 5 or 10. In the present study, the mean PLMS index was higher than 10 for the "40 to 49 years", "50 to 59 years" and "60 years and older" groups. We can thus wonder if it would be more appropriate to determine different criteria based on the subjects' age, especially because PLMS are not considered to influence polysomnographic sleep parameters in healthy subjects[3,10,25,26] although this issue still remains controversial.[27-29]

During wakefulness, the PLMW index seems to be negatively correlated with age. However, when the mean index is plotted for each age group, a quite different pattern appears. The PLMW index was higher in younger subjects, lower in middle-aged subjects, and slightly increased again (although it failed to reach statistical significance) in older subjects. This is consistent with 1 study published in an abstract form, reporting a higher PLMW index in healthy children than in teenagers.[19] It should be noted, however, that PLMW were not studied very often in healthy subjects. On the other hand, a study conducted in RLS patients reported an increase of the PLMW index with age.[18] It is possible that the evolution of PLMW with aging is different in healthy and RLS subjects. However, discrepancy may also result from differences in samples. The mean age of RLS patients in that study was 51 ± 10.8 years; consequently, there were probably no children, teenagers, or young adults in that sample. In the present study, the PLMW index was actually higher in older age groups. In fact, if only subjects older than 30 years are considered, the PLMW index would be found to increase significantly with age ($r = 0.50$; $p = .003$).

IMI as a Function of Age

If we consider the IMI histograms, it is quite clear that PLMS do not show a preferential interval in younger groups. A clear peak in IMI becomes obvious only for the last 3 age groups, namely: 40 to 49 years, 50 to 59 years, and 60 years and older. These are the same groups presenting a mean PLMS index higher than 10, which is consistent with the conclusion that younger subjects do not present typical PLMS. In younger subjects, an important number of small IMI during sleep can be observed, which are not as apparent in older groups. It probably means that children and young adults move more often in their sleep. In addition, results of the present study show that movement duration during sleep decreases with age. Taken together, these results suggest that young healthy subjects present longer movements with small

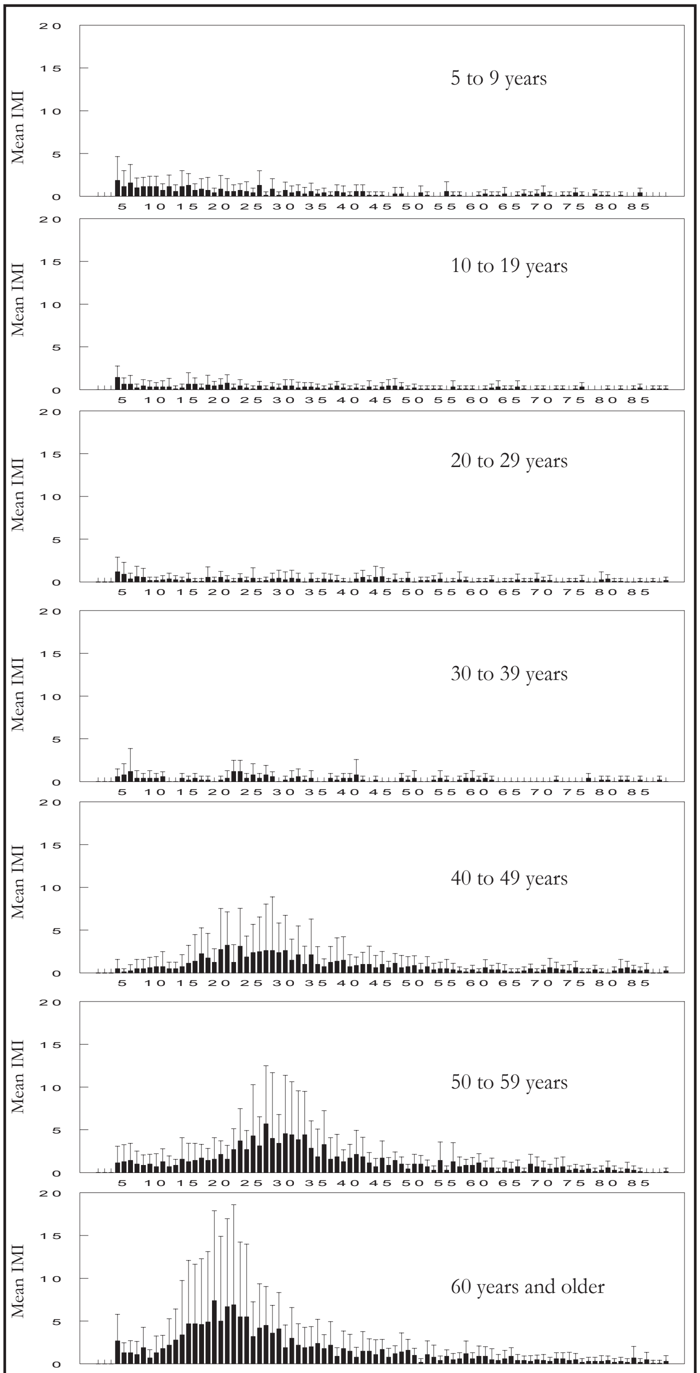

Figure 3—Duration of mean periodic leg movements during sleep (PLMS) intermovement intervals (IMI) among 7 age groups (5-9 y, 10-19 y, 20-29 y, 30-39 y, 40-49 y, 50-59 y, and 60 y and older). The distribution of IMI duration is calculated using a 1 second bin-width. Vertical bars represent the SD.

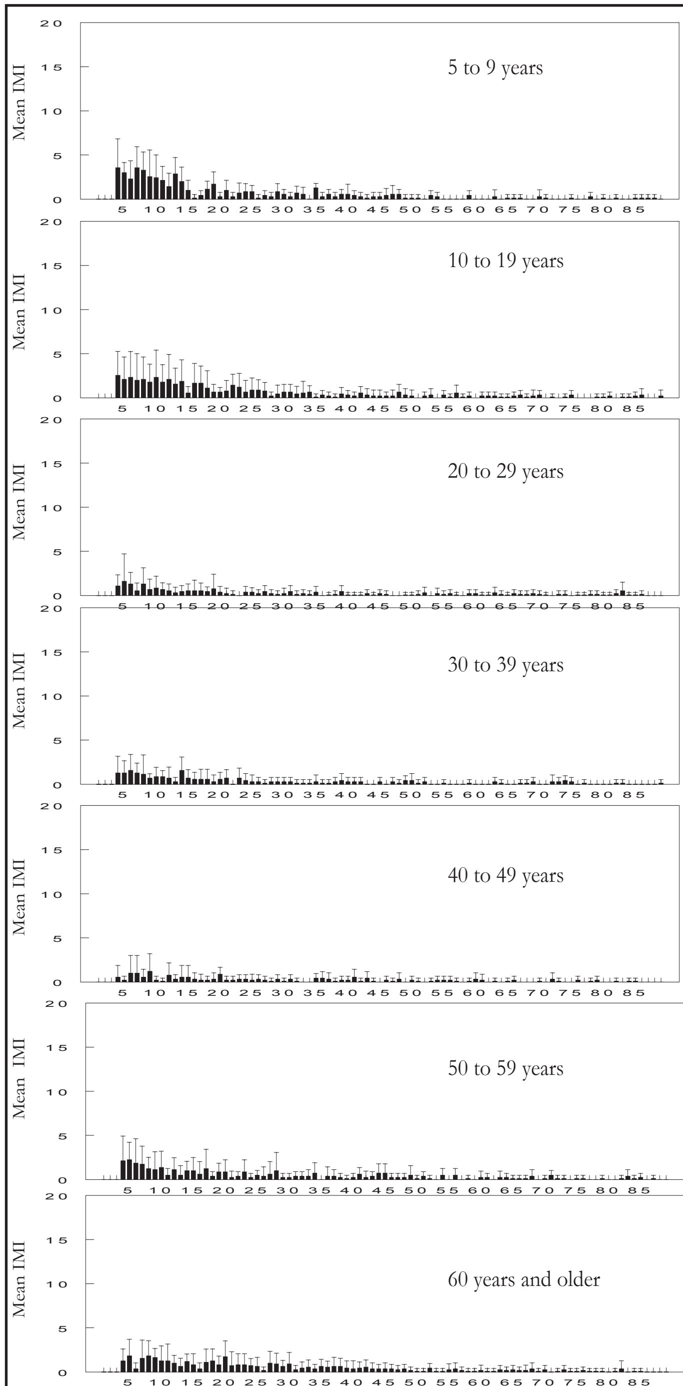

Figure 4—Duration of mean periodic leg movements during wakefulness (PLMW) intermovement intervals (IMI) among 7 age groups (5-9 y, 10-19 y, 20-29 y, 30-39 y, 40-49 y, 50-59 y, and 60 y and older). The distribution of IMI duration is calculated using a 1 second bin-width. Vertical bars represent the SD.

intervals during sleep, which are not PLMS. As they get older, subjects present less general motor activity during sleep, and the prevalence of typical PLMS increases.

The high PLMW index found in children and teenagers probably simply reflects spontaneous motor activity during wakefulness. Again, it is possible that these subjects move often when they are awake during the night, which is illustrated again with the important number of small intervals in young subjects. Moreover, the correlation between age and PLMW IMI shows that the mean interval increases with age, which suggests that older subjects move less often. The fact that we found elevated PLMW indexes in a healthy population presenting movements without a clear preferential IMI highlights the possibility that the periodicity criterion used for PLMW is not sufficiently restrictive. Results of the present study show that almost every movement occurring during wakefulness is probably considered as PLMW because an IMI between 4 and 90 seconds is used. One study illustrated the IMI histograms for PLMW in a RLS population, which yielded a different picture.[18] In that study, the histogram presented a clear peak in PLMW IMI, which suggests that the movements were truly periodic. It is thus possible that PLMW are a specific feature of RLS. PLMW evaluation in healthy subjects might reflect mostly motor activity.

Sensitivity of PLMS and PLMW Index in the Diagnosis of RLS

Taken together, the results of this study demonstrate that a high PLMS index is not a specific diagnostic tool for RLS in older subjects, as even healthy subjects present a PLMS index higher than 10. However, for children, teenagers, and young adults, a high PLMS index is quite rare and could be used as a strong supportive feature for a diagnosis of RLS. On the other hand, the PLMW index alone seems less useful as a tool for diagnosing RLS. In the present study, high PLMW indexes were observed in all age groups, in the absence of typical IMI.

Limitations and Conclusion

The present study has a few limitations that are important to mention. First, the number of subjects per age group is modest. Increasing the number of subjects would allow more robust statistical analyses and trend analyses. Second, the uneven men-to-women ratios between the youngest and oldest age group could potentially influence the data. Adjusting for a similar men-to-women ratio per age group would also allow sex-specific analyses. Finally, the present study assessed preferential intermovement intervals of PLMS and PLMW rather than periodicity per se. In order to rigorously study PLM periodicity, a different study design (e.g., autocorrelation, entropy) with only subjects with high PLMS or PLMW indexes should be used. Since the first objective of the paper was to investigate the prevalence of PLMS and PLMW in normal subjects of different age groups, subjects with few or no periodic leg movements were included in the present study.

In conclusion, it becomes clear that the periodicity evaluation is an important feature of periodic-movement calculation during sleep and wakefulness. In fact, if only the index is taken into account, important information is missing, and it becomes difficult to discriminate spontaneous motor activity from periodic movements. Finally, it could be appropriate to define different periodicity criteria in different age groups in order to better identify movements that are truly PLMS and PLMW.

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