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Original article

Periodic limb movement counting in polysomnography: Effects of amplitude

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Abstract

Background and purpose: This study investigates the relationship between periodic limb movement (PLM) counts obtained with standard scoring criteria and PLM counts scored without amplitude criterion (AC).

Patients and methods: Twenty-four sleep laboratory patients with a PLM index (PLMI) >5 per hour of sleep in a previous polysomnography (PSG) underwent a full night of digital PSG. PLM were twice scored manually: first, according to standard criteria, and second, without AC.

Results: The overall PLMI for time in bed was 34.4 ± 30.7 with AC and 50.2 ± 36.4 without AC. The PLMI in non-rapid eye movement (NREM) sleep was 45.3 ± 40.1 versus 63.4 ± 47.6 ($P<0.001$), in REM sleep 11.5 ± 15.1 versus 25.7 ± 35.4 ($P=0.001$) and in wakefulness 29.0 ± 31.1 versus 46.0 ± 36.1 ($P<0.001$) with and without AC (Wilcoxon tests).

Conclusions: In comparison to PLM counts obtained with standard criteria, PLM counts obtained without consideration of amplitude are remarkably higher. Counting without AC increases the sensitivity to detect small PLM and probably allows for identification of PLM sequences which would not have fulfilled the periodicity criteria otherwise. PLM counts without AC might be more useful to investigate the periodicity of PLM and possible changes with treatment.

Keywords: Restless legs syndrome; Scoring; Sleep; Polysomnography; Actigraphy

1. Introduction

Periodic limb movements (PLM) are present in over 80% of patients with restless legs syndrome (RLS) [1,2], and an increased PLM index (PLMI) is considered as supportive of diagnosis of RLS [3]. PLM are also found in other sleep disorders, such as narcolepsy [4], REM sleep behavior disorder [5], sleep-disordered breathing [6,7] and in Parkinson's disease and multiple system atrophy [8–10]. In individuals without RLS, the presence of PLM plus daytime sleepiness or insomnia allows for classification as periodic limb movement disorder [11]. PLM were also reported in a polygraphic screening study in 45% of elderly subjects who were not specifically questioned for RLS, but some of whom reported leg jerks [12].

The first polysomnographic recordings of PLM were performed by Lugaresi in 1965 [13]. In 1982, Coleman defined criteria for scoring PLM in polysomnography (PSG) [14], which were later slightly modified and adapted by the American Sleep Disorders Association (ASDA) [15]. PLM are recorded and scored from tibial anterior (TA) surface electromyography (EMG). Standard criteria allow identification of a leg movement as a PLM if it has a duration between 0.5 and 5 s, and an inter-movement interval between 5 and 90 s (from onset to onset) and if it forms part of a series consisting of four or more leg movements. Additionally, the criteria require that tibial anterior EMG activation has an amplitude of at least 25% of the amplitude reached during biologic calibration.

In our daily sleep laboratory practice, we frequently noticed tibialis anterior EMG activation in PSG, which did not reach the amplitude criterion (AC) but otherwise would have fulfilled all criteria for PLM. As the threshold for the

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AC seems to be arbitrarily chosen, and its clinical significance is unknown, we wondered to which extent PLM counts are influenced by the AC.

Therefore, we investigated the relationship between PLM counts obtained with standard scoring criteria and PLM counts scored according to the same criteria except the AC in a mixed sleep disorder population.

2. Methods

2.1. Study design and patient collective

Twenty-four patients (mean age 57.5 ± 12.0 years) with a PLMI above 5 per hour of sleep in a previous PSG underwent a full night (8 h) of digital PSG recording with bilateral tibialis anterior surface EMG.

Patients were selected consecutively from the sleep laboratory based on the presence of PLM irrespective of their principal diagnosis.

2.2. Inclusion criteria

Patients were eligible, if their PLMI was higher than 5 per hour of sleep in a previous PSG or first night of recording (adaptation night in the sleep laboratory). Patients with untreated breathing disorders of sleep were excluded, because in this condition PLM cannot always be reliably separated from leg movements related to resolution of periodically recurring respiratory events. Patients on efficient nasal continuous positive airway pressure (CPAP) therapy could be included.

2.3. Polysomnography

Digital PSG (Schwarzer Brainlab for Windows Version 3.00; Munich, Germany) included electroencephalography (EEG) according to the 10–20-system [16] (C3-A2, C4-A1, O1-A2, O2-A1), horizontal and vertical electrooculogram (EOG), bipolar surface EMG of mental and submental muscles and bipolar surface EMG of both tibialis anterior muscles. Respiratory monitoring consisted of nasal and buccal airflow (thermocouple) and additional nasal pressure cannula in 10 of 24 patients, tracheal microphone, thoracic and abdominal respiratory effort (Piezo), finger oximetry and electrocardiogram (ECG). Infrared video was recorded during the whole night and digitally stored. Sleep stages were visually scored in 30-s epochs according to standard criteria [17].

2.4. PLM recording and scoring

For PLM recordings, bipolar surface EMG leads were placed on the belly of both tibial anterior muscles with a maximum distance of 4 cm between. EMG was recorded with the low frequency filter at 50 Hz, the high frequency filter at 300 Hz, a sampling rate of 500 Hz and amplification set at 100 μV/cm. Impedance of TA surface EMG electrodes had to be lower than 10 kΩ.

Biologic calibration of the EMG recordings was performed as indicated in the instructions of the ASDA Task Force: “While lying awake in bed patients are instructed to slowly dorsiflex and plantarflex the great toe of each foot to approximately 30° without resistance” [15].

PLM during sleep (PLMS) were manually scored according to standard criteria [15]. For PLM during wakefulness (PLMW) a maximum duration of 10 s was allowed in accordance with the longer duration of EMG activation found during wakefulness [18]. For epochs which were obscured by gross body movement artifacts, no PLM counting was performed.

PLMI were calculated for time in bed (TIB), non-rapid eye movement (NREM) sleep, REM sleep and for wakefulness (consisting of wakefulness before sleep and intersleep wakefulness).

An EMG activation in one tibial anterior muscle was scored as a single leg movement if it was separated from an EMG burst on the other side by less than 5 s (from leg movement onset to leg movement onset). If EMG activation on the right and left TA muscles was separated by more than 5 s, two leg movements were scored.

In a second step, after conventional PLM counting, PLM were counted again according to the same criteria, except for the AC in the same subjects and the same PSG recordings. PLM counts obtained with both methods were compared.

2.5. Study collective

Twenty-four patients were included. Twelve had RLS with PLM; 12 patients had periodic limb movement disorder (PLMD) without RLS [11]. Seven of them had additional sleep-disordered breathing (obstructive sleep apnea syndrome, $n=5$; upper airways resistance syndrome, $n=2$), but all were studied while on efficient nasal CPAP or bilevel positive airway pressure (BIPAP) therapy; one had additional nightmares. At the time of the PSG recording, seven patients were treated for RLS ($n=5$) or PLMD ($n=2$); the others were untreated. Treatment was levodopa/benserazide 100/25 mg/d ($n=5$), cabergoline 2 mg/d ($n=1$), pergolide 0.35 mg/d ($n=1$). Five patients were treated with a selective serotonin reuptake inhibitor (RLS, $n=2$; PLMD, $n=3$), two with amitriptyline (RLS, $n=1$; PLMD, $n=1$).

2.6. Statistics

All values are presented as means and standard deviation. The PLMI were not normally distributed; therefore, non-parametric Wilcoxon tests and Spearman’s correlation analysis were performed. *P*-values smaller than 0.05 were considered to indicate statistical significance. Multiple

comparisons for different sleep stages were accounted for using the Bonferroni correction. In this case, a *P*-value smaller than 0.0167 was considered to indicate statistical significance. SPSS® for Windows version 12.0 (SPSS, Inc., Chicago, USA) was used for data analysis.

3. Results

The overall periodic limb movement index (PLMI) obtained with the standard counting method was 34.4±30.7 PLM/h (h) for TIB (mean±standard deviation). In contrast, the PLM index was 50.2±36.4 PLM/h without the AC for TIB. This difference was statistically significant ($P<0.001$, Wilcoxon test). The PLM counts obtained with both methods showed a high correlation (Spearman's correlation rho=0.956, $P<0.001$), as illustrated in Fig. 1.

The PLMI in NREM sleep was 45.3±40.1 with AC and 63.4±47.6 without AC ($P<0.001$, Wilcoxon test; Spearman's correlation rho=0.965, $P<0.001$), in REM sleep 11.5±15.1 with AC and 25.7±35.4 without AC ($P=0.001$, Wilcoxon test; Spearman's correlation rho=0.925, $P<0.001$) and in wakefulness 29.0±31.1 with AC and 46.0±36.1 without AC ($P<0.001$, Wilcoxon test; Spearman's correlation rho=0.879, $P<0.001$). The differences were statistically significant even after Bonferroni correction (threshold for significance, 0.0167). The sleep state-specific PLMIs are graphically illustrated in Fig. 2.

An example of different PLM sequences is shown in Fig. 3. Fig. 3A shows an epoch recorded during biologic calibration of leg movements. Fig. 3B corresponds to an epoch obtained during stage 2 sleep in the same patient as Fig. 3A. Compared to biologic calibration, all leg movements in the sequence fulfill the AC, except one (arrow).

The other results of the PSG are shown in Table 1.

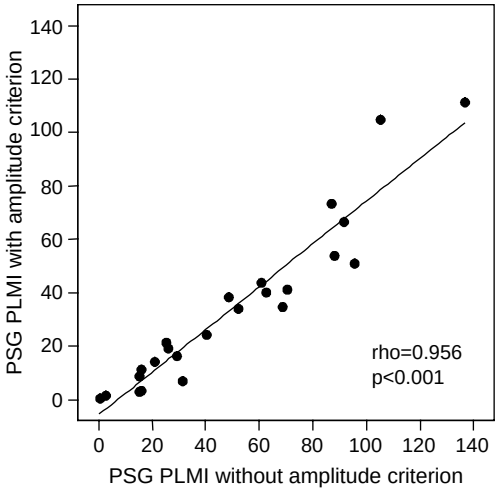

Fig. 1. Correlation analysis of PLM indices with and without amplitude criterion for time in bed. PLM indices scored without amplitude criterion (*x*-axis) versus PLM indices scored with amplitude criterion (*y*-axis) (Spearman's correlation).

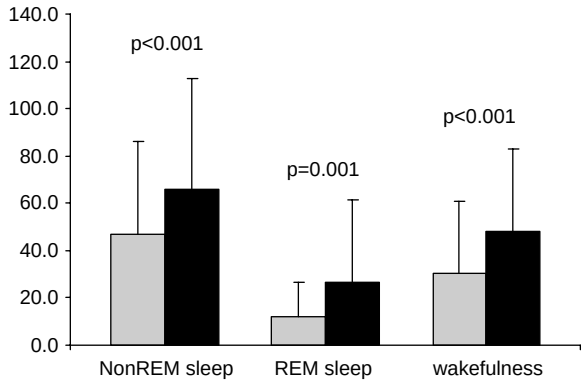

Fig. 2. State-specific PLM indices (PLMI) for NREM sleep, REM sleep and wakefulness counted with and without amplitude criterion (AC). Grey bars show values obtained with AC, black bars values counted without AC. Data are given as means±standard deviations and compared with Wilcoxon tests, significance level was set at 0.0167 after Bonferroni correction.

4. Discussion

This study demonstrates that the amplitude criterion (AC) has a statistically significant impact on PLM counts obtained from visual scoring in PSG. When the AC was strictly followed, PLM counts were significantly lower (34.4±30.7 PLM/h) than when the AC was left aside (50.2±36.4 PLM/h). This means that the sensitivity to detect PLM is higher when the AC is not considered.

The significant difference of PLM counts with and without AC may relate to several different factors. First, periodic tibial anterior muscle activation may occur in the absence of a certain amplitude but may be clearly visible in the PSG. Second, leaving aside the AC allows for counting more PLM sequences. The minimum number of leg movements in a PLM sequence is four. If one of these leg movements does not reach the AC, this may lead to the need to discard a whole PLM sequence, when periodicity criteria (maximum inter-movement interval 90 s) are no longer met after one of the PLM is removed due to low amplitude. Furthermore, low-amplitude leg movements can occur in the middle of a PLM sequence, adding exactly one leg movement count to the sequence, and, of course, there could be whole PLM sequences consisting of only low-amplitude leg movements.

The key question is whether PLM counts with or PLM counts without AC are a better measure for PLM. One could argue in favor of the traditional criteria that the AC is probably a protection against false positive PLM and that very low-amplitude PLM might be less relevant regarding arousals or clinical consequence such as sleep disturbance or daytime sleepiness. On the other hand, the per definition arbitrary nature of the AC, and the fact that not amplitude but periodicity is the essential feature of PLM speaks against the AC.

Our study did not consider arousals or microarousals possibly associated with PLM. Highly divergent data exist on the percentage of PLM association with arousals [19,20]

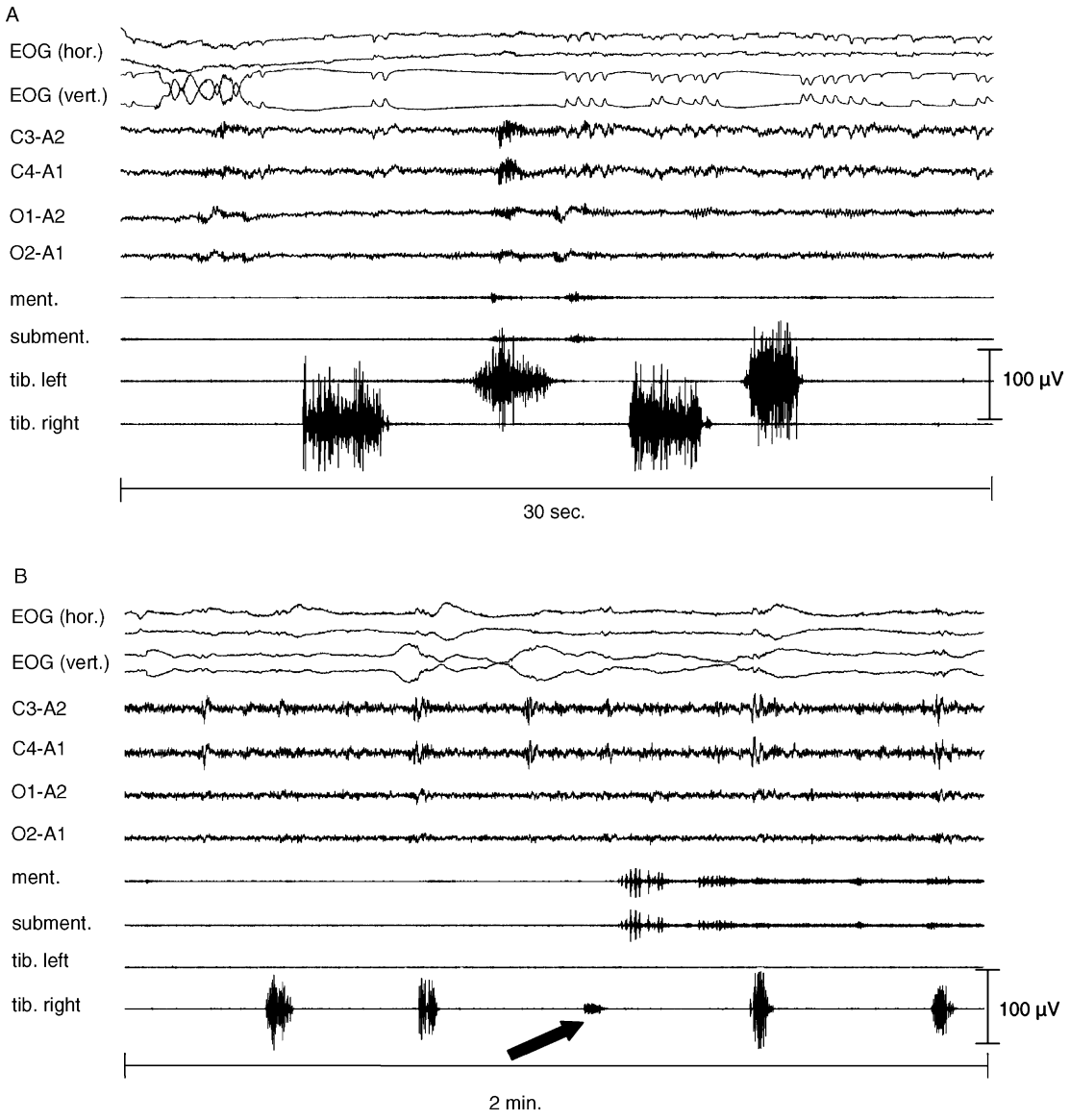

Fig. 3. (A) Shows an example of leg movements during biologic calibration. The patient is awake. (B) Shows five PLM during sleep in the same patient. Referring to biologic calibration all leg movements except the one marked with the arrow reach the amplitude criterion. Note the different time windows (30 s above, 2 min below).

and a low inter-rater reliability for PLM arousal scoring has been demonstrated (at least prior to a formal uniform definition of arousal) [21,22]. Moreover, EEG arousals accompanying PLM are often not visible to the human eye, but even then systematic changes in the EEG are present in spectral analysis [23].

Although the tibial anterior muscle is the most frequently activated muscle in PSG [24], and PLM initiate most frequently from the tibial anterior muscle [24], Provini and co-workers have shown that the muscle recruitment pattern in PLM is highly variable even in an individual patient [25]. Other leg muscles were frequently involved, upper limb muscles sometimes, and trunk muscles rarely, and sometimes even co-activation of antagonist muscles was observed. It has also been suggested that a stereotyped pattern generator at the level of the spinal cord is involved in PLM [26], which is periodically activated and disinhibited by a cyclic fluctuation of arousal [27,28]. In fact, there have been studies demonstrating an ongoing cyclic alternating pattern (CAP) activity even in the absence of PLM [29].

We suggest that the AC induces false negative PLM counting. If PLM reflect the activity of a central rhythmic pattern generator, this pattern generator may activate variable muscle groups [25] and be active even in the absence of PLM activity visible in the TA EMG output.

Another disadvantage of the AC is that it demands an exact percentage of a response to a mainly qualitative instruction in the biologic calibration ("…slowly dorsiflex and plantarflex the great toe… to approximately 30° without resistance") [15]. The patient's compliance and the intensity

Table 1
Sleep variables in the study sample ($n=24$)

	Mean ± standard deviation
Time in bed (TIB) (min)	483.3 ± 12.0
Total sleep time (TST) (min)	367.2 ± 67.3
Sleep efficiency[a] (SE) (%)	75.9 ± 14.4
Wakefulness (% TIB)	18.1 ± 14.1
Stage 1 (% TIB)	16.7 ± 8.1
Stage 2 (% TIB)	42.8 ± 10.4
Stage 3 + 4 (% TIB)	6.7 ± 8.0
REM (% TIB)	14.4 ± 5.2
Sleep latency[b] (min)	27.4 ± 24.0
REM latency (min)	109.2 ± 61.0

[a] Sleep efficiency: ratio of total sleep time to time in bed expressed in percent.
[b] Sleep latency: first epoch of stage 2 (or three consecutive epochs of stage 1).

of movement during biologic calibration as well as small deviations in electrode placement greatly influence the PLM size reached during calibration and, therefore, the minimum amplitude required for subsequent PLM counting.

The gap between PLM counts obtained with and without the AC was significant for wakefulness, NREM and REM sleep, but it differed between states. The gap was smallest in NREM sleep, where leaving out the AC led to an increase of 40.0%. In wakefulness, leaving out the AC increased the PLM in the amount of 58.6%. In REM sleep, the increase was over 100%, but variability of PLM counts was particularly high expressed in the large standard deviation. The fact that the influence of the AC on PLM counts is different in NREM, REM and wake states is not astonishing, because PLM according to the criteria mostly occur in NREM sleep. PLM in wakefulness show distinct characteristics (specifically larger duration) [18], and PLM in REM sleep may show typical or abortive forms due to underlying muscle atonia [30].

It should be mentioned that the clinical significance of PLM (with or without AC) is still insufficiently understood and requires further research. Because this was an exploratory study, broad inclusion criteria were selected. Further studies will have to be done in more selective patient groups.

To summarize, in comparison to PLM counts obtained with strict application of standard criteria, PLM counts obtained without consideration of the AC are remarkably higher. This may relate to the fact that counting without AC increases the sensitivity to detect a single leg movement, and allows for identification of PLM sequences, which would not have fulfilled the periodicity criteria otherwise. The strict application of the AC is difficult as instructions are mainly qualitative. Moreover, the AC, as other established criteria for counting PLM, is an arbitrary variable and its clinical significance is uncertain. Detection of PLM without AC might also facilitate calculation of inter-movement intervals and periodicity in computerized PLM analysis.

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