QUANTIFYING LEG MOVEMENT ACTIVITY DURING SLEEP

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SYNOPSIS

Currently two sets of similar (but not identical) rules for recording and scoring PLMS and periodic leg movements (LMs) during wakefulness (PLMW) exist. The first set was published in 2006 by a task force of the International Restless Legs Syndrome Study Group, endorsed by the World Association of Sleep Medicine (WASM/IRLSSG) and the second in 2007, by the American Academy of Sleep Medicine (AASM). In this paper we review the basic recording methods, scoring rules, and computer-based automatic detection programs for LM activity during sleep with a focus on PLMS, the most frequent type of LM activity during sleep. However, also other, less frequent LM activities, such as Alternating Leg Muscle Activation, Hypnagogic Foot Tremor, High Frequency Leg Movements, and Excessive Fragmentary Myoclonus are briefly described.

INTRODUCTION

The recording and scoring of leg movement activity (LMA) during sleep is an essential component in the characterization of sleep and a required component in the assessment of periodic leg movements during sleep (PLMS). Besides characterizing PLMS, there are several other, mostly high frequency, leg movement patterns that can be identified during sleep such as alternating leg movement activity (ALMA), hypnagogic foot tremor (HFT) or high frequency leg movements (HF) (1).

Currently two sets of similar (but not identical) rules for recording and scoring PLMS and periodic leg movements (LMs) during wakefulness (PLMW) exist. These were partly informed by algorithms proposed for the automatic detection of LMs in polysomnographic recordings PSG (2) and include mathematically defined parameters such as thresholds, intervals, and amplitude (3;4). First, in 2006 a task force of the International Restless Legs Syndrome Study Group endorsed by the World Association of Sleep Medicine (WASM/IRLSSG) (5) introduced a major revision of the scoring rules which were then substantially (but not entirely) adopted by the American Academy of Sleep Medicine (AASM) in 2007 (6) and are being periodically updated (7). Scoring criteria for leg movements other than PLMS are specified in the AASM rules.

In the following we will review the basic recording methods, scoring rules, and computer-based automatic detection programs for LMA during sleep with a focus on PLMS, the most frequent type of LMA during sleep.

BASIC RECORDING METHODS

Electromyography

Surface electromyography (EMG) is the gold standard for recording leg muscle activity during sleep. It is acquired by means of silver-chloride electrodes attached to the inputs of a differential amplifier, in order to obtain a bipolar derivation. It is usually recommended that interelectrode impedance should be at least $<10\text{ K}\Omega$ (but better $<5\text{ K}\Omega$) (5); the skin preparation procedure, before electrode placement, is very important and may include the shaving any excess hair, cleaning the skin with alcohol pad, and light abrasion. For a better adhesion of the electrodes, the use of collodion is recommended because it is non-conductive, holds through hair (not only on the scalp), oils and perspiration, and provides high performance for long-term recordings. However, collodion is highly flammable and produces fumes; thus, appropriate air purifier, fume extractor, or ventilation systems should be used. Finally, a conductive paste for long-term recordings must be used to ensure a good electrical contact between the skin and the electrodes.

Surface EMG electrodes should be placed at 2–3 cm apart or 1/3 of the length of the anterior tibialis muscle, whichever is shorter. Electrodes must be located longitudinally on the muscles, symmetrically

around the middle. EMG signals must be obtained from both the right and the left leg and recording the two signals in one channel is strongly discouraged. Baseline resting EMG amplitude (i.e. in the relaxed muscle) should be $\pm 2\text{--}3\ \mu\text{V}$ ($4\text{--}6\ \mu\text{V}$ peak-to-peak; WASM/IRLSSG) (5) or $\leq 10\ \mu\text{V}$ (AASM) (7). The WASM/IRLSSG rules recommend that prior to the recording, a calibration should be carried out in order to obtain from the relaxed anterior tibialis muscles a non-rectified signal no greater than $\pm 5\ \mu\text{V}$ (or $10\ \mu\text{V}$ peak-to-peak, $5\ \mu\text{V}$ for rectified signals) for clinical purposes, and $\pm 3\ \mu\text{V}$ (or $6\ \mu\text{V}$ peak-to-peak, $3\ \mu\text{V}$ for rectified signals) (5).

EMG signals are produced by the muscle situated under the skin and adipose tissue below the electrodes, which are able to record activity of superficial muscle. Muscle size and amount of adipose tissue significantly influence the amplitude of the surface recorded EMG signal. This is the reason why surface EMG signals are considered semi-quantitative and calibration of EMG activity is recommended (5). The amplitude of surface EMG potentials depends also on the distance between the recording electrodes and can range between $<20\ \mu\text{V}$ and up to several mV, depending on the factors listed above.

EMG signals are constituted of superimposed motor unit action potentials produced by several motor units, each with a typical repetition rate of firing of about 7–20 Hz. Surface EMG records the sum of this activity and produces a signal with a wide spectrum. Thus, the spectral content of the EMG signal requires high sampling rates that should never be lower than 200 Hz; 400 to 500 Hz are usually recommended (5;7). Band-pass filtering is usually applied with typical settings at approximately 10–100 Hz and with a notch filter at 50 or 60 Hz, depending on the power line frequency.

Actigraphy

Actigraphy refers to devices whose sensors integrate motion amplitude and speed and whose output is a signal with magnitude and duration depending on these motion features. This signal is appropriately amplified, filtered, and digitized to be stored in the device memory, most often in terms of movement counts per epoch. The length of the epoch is of crucial importance and can be fixed at 1 min or can be chosen by the user (from a fixed list of epoch lengths). Epoch length is very important because, in conjunction with the memory capacity of the device, it determines the maximum recording time. Data are stored essentially in three different ways by actigraphs and some of them allow the user to select the preferred mode while other do not. With the Time Above Threshold mode, the amount of time per epoch during which activity exceeds the set threshold is stored; the Zero Crossing mode assesses the number of times per epoch that the activity signal produced by the accelerometer crosses a threshold set around zero; finally, with the Proportional (or Digital) Integration mode, the area under the curve is stored for each epoch. Some devices allow the simultaneous use of multiple modes. There are no conclusive statements in the literature on which is the most accurate among these modes.

Actigraphy is typically worn at the wrist to monitor rest-activity cycles for several days or weeks but for the assessment of LMA, actigraphic monitoring of foot or leg movements (LMs) has been proposed (8;9). When used for the assessment of LMA, sampling rate of the actigraphy must be considerably higher, ≥ 10 Hz (5). Because it offers the possibility to record multiple nights in a home environment, it has been proposed as a tool to overcoming the problems caused by the relatively large night-to-night within-subject variability reported to occur for PLMS (10). However, actigraphy alone is unable to discriminate between PLMS and LMs occurring during wakefulness; moreover, arousal or other related events (apnea) cannot be detected. A recent review and meta-analysis on the use of actigraphy for the measurement of PLMS has demonstrated significant heterogeneity among the few studies available for type of actigraph, position of the sensors on the legs, and methods for counting PLMS (11). In particular, an important limitation was noted in the inability to reliably combine data from actigraphs placed on both limbs, in most devices. Thus, currently, actigraphy cannot substitute EMG recording within a nocturnal polysomnography for characterization of LMA during sleep.

Other methods

Several producers propose piezoelectric sensors for the recording of limb movements during sleep. These sensors, placed around the ankle or around the leg, transduce motion, vibration and tension into an electrical signal. They are very sensitive and there is no warranty that the signal produced corresponds exclusively to events generated by the limb. There are no convincing validation studies for the use of these sensors and they are not recommended by any guideline. The only advantage that they offer is that they do not need skin preparation; however, this is counterbalanced by a cost higher than that of silver chloride electrodes.

IDENTIFICATION OF LEG MOVEMENTS DURING SLEEP

The basis for the classification and scoring of LMA during sleep is the identification of single leg movement events. According to current standard rules, their onset is defined as an EMG increase of ≥ 8 μ V above the resting baseline, while the offset is marked at the point when the EMG amplitude decreases to < 2 μ V above the resting level and remains below that value for at least 0.5 s. An event can contain one or more periods with EMG amplitude below the offset level that last < 0.5 s each. The duration of the event is the time between its onset and offset; it must be at least 0.5 s and no longer than 10 s. Currently, all other LMA events not meeting these criteria are discarded and not considered any further, at least for the scoring of PLMS.

SCORING OF LEG MOVEMENTS DURING SLEEP

PERIODIC LIMB MOVEMENTS

The scoring of PLMS involves several sequential steps: After the identification of individual, monolateral LMs, these are combined to bilateral LMs if they occur near each other. LMs in the vicinity of sleep-disordered breathing events are identified and excluded and the remaining LMs are classified as periodic or non-periodic (isolated) based on their occurrence within a series of LMs characterized by their number and the interval between movements. Figure 1 shows, as an example, a PSG recording fragment with PLMS in a patient with RLS.

As mentioned above, there are currently two standard set of rules for the scoring of PLMS, the 2006 WASM/IRLSSG rules (5) and the continuously updated AASM rules, with the latest update published in 2016 (7). While the two sets are very similar, even today there remain several critical differences in the rules that are listed in Table 1.

Table 1. Critical differences between the WASM/IRLSSG (5) and the AASM (7) scoring rules for periodic leg movements.

	WASM/IRLSSG (5)	AASM (7)
Scoring of periodic leg movements		
Sleep/Wake	All LMs form PLM series For PLMS, only those during sleep are counted	Only LMs during sleep form PLM series, a PLMS series continues across intermittent wake periods < 90 s; in this case LMs during wake are ignored.
Bilateral leg movements	offset-to-onset <0.5 s	onset-to-onset <5 s
Respiratory-related leg movements (RRLM)	Excluded from PLM series	Excluded from PLM series
RRLM definition	Any leg movement occurring within: ± 0.5 s around the ending of an apnea/hypopnea event	Any leg movement occurring within: 0.5 s before the start to 0.5 s after the end of an apnea, hypopnea, respiratory effort related arousal or sleep-disordered breathing event

One of these differences concern the rule to combine monolateral LMs to bilateral LMs. The WASM/IRLSSG criteria consider LMs as bilateral if the offset of the first event is <0.5 s before the onset of the subsequent event. In contrast, the AASM rules consider LMs as bilateral if the onset of the first events is <5 s before the onset of the next event. Since LMs can be between 0.5 s and 10 s, the AASM rule also classifies some overlapping LMs as bilateral. None of the two sets of rules report a rationale for their choice of the specific criteria for bilateral movements. Despite these differences, a recent study has shown that in patients with

RLS in the overwhelming majority of events bilateral LMs are overlapping with each other and at the same time are correctly identified by both the current WASM/IRLSSG and AASM rules (4). Although the two set of rules differ considerably in their definition of bilateral LMs, they provided largely corresponding classifications in subjects with RLS and could be considered equivalent in a clinical context (4).

Both sets of rules exclude LMs that occur in the vicinity of sleep-disordered breathing events (i.e. respiratory related leg movements (RRLMs)), from the inclusion into PLMS series and these LMs have to be identified and excluded before proceeding to determine the PLMS index. For the WASM/IRLSSG rules, a LM must be excluded from the PLMS analysis when it is associated with the resumption of respiration at the end of an apnea/hypopnea event, defined as any part of the LM in the interval of ± 0.5 s around the end of the breathing event. Differently, for the AASM a LM should not be counted when it occurs during a period starting 0.5 s before the beginning of a sleep-disordered breathing event to 0.5 s after the end of this event. Sleep-disordered breathing events include apneas, hypopneas, and respiratory effort related arousals. None of these criteria were evidence based and a recent systematic evaluation has shown that both set of rules critically underestimate the number of LMs associated to respiratory events, which are systematically increased around the end of respiratory events, over a period significantly longer than specified in either set of rules (-2 s to $+10.25$ s) (12).

Both set of rules agree that, subsequently to combining monolateral LMs and excluding RRLMs, a periodic sequence is defined as a series of four or more LMs separated from each other by 5 to 90 s. A further crucial point at this step is the question of whether only LMs during sleep or also during wake are part of a PLM series and how intervening wakefulness affects a possible PLM series. Here, the WASM/IRLSSG rules (5) recommend that all LMs during sleep and wake can form part of a PLM series, and that for the computation of the PLMS index only those during sleep are counted. Periodic leg movements during wake are counted for the PLMW index. In contrast, the most recent AASM rules (7) state that if the intervening wakefulness is short (< 90 s) than any LM occurring during wake is ignored and the PLM series continues across the this period, provided that the distance between the last LM during sleep before the wakefulness and the first LM during sleep after wakefulness is less than 90 s. It is currently not known if this difference between the two sets of rules will result in significant differences in the corresponding PLMS indices and if these differences have a clinical meaning.

COMPUTER-BASED LM DETECTION

As described above, leg movements are defined by strictly quantitative parameters that make them a very prominent candidate for computer-based evaluation. In fact, automated approaches have been proposed in the literature starting from the 1990's and all of the methods were reported to perform quite well.

Kayed et al. (13) reported the performance of an undisclosed algorithm applied by a recording system commercially available at that time (1990) and now obsolete, which showed a sensitivity of 94% and a specificity of 85%. Further algorithms have been published by Tauchmann and Pollmächer in 1996 (14), Roessen et al. in 1998 (15), Wetter et al. (16) and Pittman et al. (17) in 2004.

In 2005, Ferri et al. (2) described a detection of leg movements performed by using two thresholds: one for the starting point and another to detect the end point of each leg movement; values of sensitivity and specificity $\geq 90\%$ were found in all recordings and sensitivity and false-positive rates were used to set-up amplitude cut-off values for the two thresholds. These values were subsequently adopted by both the current sets of internationally accepted criteria to detect PLMS.

Table 2. Overview of computer-based leg movement detection algorithms.

Study	Sample	Key features of the algorithm	Main results
Kayed et al. 1990 (13)	10 recordings of subjects with PLMS	not described in detail	PLM event count: Sensitivity 94% Specificity 85%
Tauchmann & Pollmächer 1996 (14)	10 recordings of 5 subjects with RLS	Threshold and bridge criteria	LM detection: Sensitivity 93% Specificity 89%-92%
Roessen et al. 1998 (15)	30 recordings of subjects with PLMD	Amplitude thresholding after various filter operations	No significant differences in %PLM/TIB and LMI/TIB; LMI/TST higher with the automatic scoring
Wetter et al. 2004 (16)	10 recordings of subjects with RLS	pattern recognition based on burst density, amplitude and duration	LM detection: Sensitivity 94%
Pittman et al. 2004 (17)	31 recordings of subjects with various sleep disorders	Adaptive segmentation based on relative energy of time-frequency features	PLM detection: Agreement 92%-93%
Ferri et al. 2005 (2)	Recordings of 15 RLS/PLMS and 15 control subjects	Amplitude thresholding after filtering and rectifying	LM detection: Sensitivity $\geq 90\%$ Specificity $\geq 90\%$
Moore et al. 2014 (18)	recordings of 78 subjects with various sleep disorders	adaptive noise cancellation and noise adjusted threshold detections	PLM detection: Sensitivity 73%-77% Specificity 99%-100%
Huang et al. 2015 (19)	recordings of 15 RLS and 9 control subjects	Amplitude thresholding after filtering	PLM detection: Sensitivity 96% Specificity 92%
Alvarez-Estevéz 2016 (20)	70 recordings of patients with various sleep disorders	Various filter operations and dynamic baseline determination	PLM detection: Average sensitivity 82% Specificity 100 %
Shokrollahi et al. 2016 (21)	65 patients with stroke, TIA or other diagnoses	Kernel sparse representation of K-nonnegative matrix factorization of the signal time-frequency matrices	PLM index ≥ 30 : Overall accuracy 97%
LM: leg movements; PLM: periodic leg movements; TIA: transient ischemic attack; TIB: time in bed; TST: total sleep time.			

There has been a recent renewed interest in LM or PLM detectors (Table 2). Moore et al. (18) have described another method characterized by adaptive noise cancelling of cardiac artifacts and noise-floor

adjustable detection thresholds with promising performance and have made the code public for use in personalized applications and modification. A further, interesting and promising algorithm has been published by Huang et al. (19) who have made a MATLAB[®] script publicly available and have underlined the need for a good reference human scoring when assessing the performance of automatic systems that might be adjusted better if an accurate and expert scoring is used. Alvarez-Estevéz (20) proposed a detection method based on various filter operation and the determination of an adjusted baseline. Finally, Shokrollahi et al. (21) have proposed an algorithm consisting of three main steps: 1) representing the signal using time-frequency matrices, 2) decomposing the TFM matrix into its significant components by applying the K-nonnegative matrix factorization technique, and 3) applying the kernel sparse representation to the decomposed signal for classification.

All these studies seem to indicate that PLMS can be detected reliably by means of computer-based automatic approaches. All of these approaches, however, suffer from the unknown precision of the human gold standard as all algorithm have been validated against a limited number of human scorers with varying degrees of experience and always within a single sleep center. It is currently unknown, what is the inter-center agreement of manual leg movement scorings which will be the limiting factors for any validation of automatic detection algorithms

OTHER LEG MOTOR ACTIVITIES DURING SLEEP

This section includes other phenomena of small motor activations of the feet (and legs) occurring at sleep onset, usually in trains, with short lasting bilateral alternating or unilateral (agonist/ antagonist) activations. According to current knowledge they are all considered benign movement phenomena.

Alternating Leg Muscle Activation

The term “alternating leg muscle activation” (ALMA) during sleep indicates a quickly alternating pattern of anterior tibialis activations occurring at a frequency from 0.5 Hz to 3 Hz. The usual duration of a single leg muscle activation within an ALMA pattern is 100 – 500 msec, and at least 4 alternating activations are needed to form an ALMA series. The phenomenon was reported to occur in all sleep stages but particularly during arousals (22;23). It is not clear yet if ALMA represents the PSG manifestation of a separate nosological entity or if it belongs to the wide spectrum of nocturnal motor activities of RLS. Figure 2 shows, as an example, two consecutive ALMA episodes during sleep in the patient reported by (23).

Hypnagogic Foot Tremor

Hypnagogic foot tremor (HFT), first described by Broughton in 1988 and later by others (24;25), is a clinical condition that has several similarities to ALMA; subjects exhibit repetitive foot movements occurring at the

transition between wake and sleep or during light sleep. PSG recordings show the presence of recurrent EMG potentials (at least 4) or foot movements typically at 1 to 2 Hz (range 0.3-4 Hz) in one or both feet. The EMG bursts are longer than those of myoclonus (250 – 1000 ms), and are organized in trains of variable length.

High Frequency Leg Movements

The term high frequency leg movements (HFLM) was recently proposed for a similar phenomenon (26). HFLM was defined as four or more discrete leg movements occurring at a frequency of 0.3-4 Hz, unilaterally, but sometimes with a bilateral pattern. Two thirds of the HFLM are observed during waking and approximately one third during sleep. However, the criteria to score this phenomenon have not been established yet and additional studies and reports are needed also to define their eventual relationship with RLS and their clinical relevance.

Excessive fragmentary myoclonus

Excessive fragmentary myoclonus (FM) is characterized by an abundance (> 20 minutes) of very short EMG bursts, which are usually less than 150 msec. EFM is a very common phenomenon even in healthy sleepers (27).

SUMMARY AND OUTLOOK

The recording and scoring of leg movement activity during sleep is well established and has been standardized according to international guidelines. Digital recording of leg muscle EMG during a nocturnal polysomnography represents the gold standard. At the same time, scoring criteria are the results of a dynamic process that reflects the progress in clinical sleep medicine and research and several elements of the current rules lack an empirical foundation. It is therefore expected that scoring rules will undergo further changes as new evidence emerges.

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Figure legends

Fig. 1. Periodic leg movements in a patient with restless legs syndrome.

Fig. 2. Two consecutive ALMA episodes during sleep in the patient reported by (23).

Key Points

- The recording and scoring of limb movement activity (LMA) during sleep is an essential component in the characterization of periodic leg movements during sleep (PLMS).
- Currently two sets of similar (but not identical) rules for recording and scoring periodic leg movements during wakefulness and sleep exist.
- Periodic limb movements are the most frequent type of activity during sleep. However, also other, less frequent LM activities can be recorded.
- Digital recording of leg muscle EMG during a nocturnal polysomnography represents the gold standard method.
- Several elements of the current rules lack an empirical foundation and recent data-driven studies are expected to give the basis for new and improved rules.

Key Words

Periodic leg movements during sleep, periodic leg movements during wakefulness, Alternating Leg Muscle Activation, Hypnagogic Foot Tremor, High Frequency Leg Movements, Excessive Fragmentary Myoclonus