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MATPLM1, A MATLAB script for scoring of periodic limb movements: preliminary validation with visual scoring



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ABSTRACT

Background and Purpose: A Matrix Laboratory (MATLAB) script (MATPLM1) was developed to rigorously apply World Associations of Sleep Medicine (WASM) scoring criteria for periodic limb movements in sleep (PLMS) from bilateral electromyographic (EMG) leg recordings. This study compares MATPLM1 with both standard technician and expert detailed visual PLMS scoring.

Methods and Subjects: Validation was based on a 'macro' level by agreement for PLMS/h during a night recording and on a 'micro' level by agreement for the detection of each PLMS from a stratified random sample for each subject. Data available for these analyses were from 15 restless leg syndrome (RLS) (age: 61.5 ± 8.5 , 60% female) and nine control subjects (age: 61.4 ± 7.1 , 67% female) participating in another study. **Results:** In the 'micro' analysis, MATPLM1 and the visual detection of PLMS events agreed 87.7% for technician scoring and 94.4% for expert scoring. The technician and MATPLM1 scoring disagreements were checked for 36 randomly selected events, 97% involved clear technician-scoring error. In the 'macro' analysis, MATPLM1 rates of PLMS/h correlated highly with visual scoring by the technician ($r^2 = 0.97$) and the expert scorer ($r^2 = 0.99$), but the technician scoring was consistently less than MATPLM1: median (quartiles) difference: 10 (5, 23). There was little disagreement with expert scorer [median (quartile) difference: -0.3 ($-2.4, 0.3$)].

Conclusions: The MATPLM1 produces reliable scoring of PLMS that matches expert scoring. The standard visual scoring without careful measuring of events tends to significantly underscore PLMS. These preliminary results support the use of MATPLM1 as a preferred method of scoring PLMS for EMG recordings that are of a good quality and without significant sleep-disordered breathing events.

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1. Introduction

Periodic limb movements in sleep (PLMS) occur as a motor sign of the restless leg syndrome (RLS), also known as Willis–Ekbom disease (WED) [1], but they also occur in other conditions [2] and tend to become more prominent with age [3]. These events have been most precisely defined in the World Associations of Sleep Medicine (WASM) criteria [4]. They are measured from uncalibrated electromyographic (EMG) recordings from surface electrodes on bilateral anterior tibialis muscles. The events from each leg are

combined following rules specified in the WASM criteria. These events are commonly identified by human visual scoring. The scorer moves through a night's recording of sleep of the patient observing at 30–120-s epochs, marking each leg movement event (LM) that meets the criteria for a PLMS. This is often assisted by a scoring program (RemLogic) that is part of the systems used to collect the physiological data from sleep. These programs mark potential PLMS, but most are not validated; they do not use the WASM/International Restless Legs Syndrome Study Group (IRLSSG) standard scoring criteria, and generally they need considerable visual correction. The WASM standard requires careful and detailed measurements of the EMG for each potential periodic leg movement (PLM). It provides an explicit definition of the EMG signal for a PLM rather than relying on the judgment of a visual scorer. The tedious nature of measuring PLMS by the WASM criteria, however, produces situations likely to lead to scoring errors. For example, scoring fatigue may occur when care has to be taken to measure hundreds of moves, leading to events being missed. Conversely, when they are rare, false expectations can lead to failure to measure possible events. Moreover,

Abbreviations: EDF, European Data Format; EMG, Electromyography; IRB, Institutional Review Board; IMI, Inter-movement interval; IRLSSG scale, International Restless Legs Syndrome Study Group Severity Scale; LM, Leg Movement; PAM-RL, Physical Activity Monitor for Restless Legs; PLM, Periodic Leg Movements; PLMS, Periodic limb Movements of Sleep.

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the current visual scoring process focuses on the absolute number of events, and it does not closely assess start and stop times of events and thus usually does not provide a good measure of the durations and inter-movement intervals (IMIs) between the events. Recent studies have noted that the measurement of PLMS should include consideration of these other features that are not reliably produced by the usual visual scoring, particularly for IMIs and the periodicity index [5].

In this paper, we demonstrate the ability to score PLMS from the EMG component of patients' polysomnogram (PSG) using a program (MATPLM1) on Matrix Laboratory (MATLAB), and to validate its accuracy for the detection of events in comparison with the traditional visual scoring. The validation focuses on the detection of PLMS events independent of related factors such as electroencephalographic (EEG) arousal or respiratory events. Future versions of MATPLM1 will add script to mark the PLMS occurring with significant events. This validation study not only determines at the macro-level agreement for the total number of PLMS during a night recording, but also evaluates at the micro-level the basis for difference from a stratified random selection of specific PLM covering the full night's recording. This MATLAB program provides a general application for use on any EMG with sleep-stage scored data from sleep laboratories that can be converted to European Data Format (EDF). It also provides the periodicity index and descriptive statistics with arrays for PLM durations, amplitudes, sleep stages, time, and IMI for each PLMS. The script allows adjusting significant parameters, for example, sampling rate, filter densities, and minimum IMI, and it can be used for batch processing of a large set of data.

2. Methods

2.1. MATPLM1 scoring algorithm

The MATPLM1 program reads the sampling rate from the EDF file. It applies the MATLAB implementation of a Butterworth filter with a low pass set at 225 Hz and a high pass set at 20 Hz to the EMG data, and then it rectifies the signal. The filter settings are parameters in the program set for the rectified signal and sampling rate for the data used in this study. They can be easily adjusted as appropriate. A separate text array specifies the sleep stage for each 30-s epoch of the night's sleep along with start and stop points for sleep scoring on the EMG. The WASM/IRLSSG criteria [4] are fully implemented in MATPLM1. These criteria suffice for the identification of PLMS without any visual review except for determining the resting EMG threshold. MATPLM1 also includes an algorithm to identify the resting EMG. MATPLM1 provides the results for combining both legs following the WASM criteria, but it can provide results for each leg separately if desired.

2.2. MATPLM1 algorithm for resting EMG level

The MATPLM1 algorithm determines the resting EMG level in two steps. First, it searches from the start of the record for the first consecutive 10-s interval where the patient has a stable EMG. A stable rectified EMG signal is defined by the maximum EMG signal $<20 \mu\text{V}$ and also less than five standard deviations (SDs) above the average for a 10-s period. This process effectively ensures that the stable EMG interval does not include a significant EMG movement event, such as a PLM. The resting EMG is defined as the median of the largest EMG reading from the first five 10-s intervals with stable EMG signal. In extreme cases, where five stable 10-s intervals are not found in the entire record, the program arbitrarily sets resting EMG at $18 \mu\text{V}$ (low threshold for movement end then is $20 \mu\text{V}$). Such a case only occurred in this study for one very severe RLS patient who had an exceptionally high number of LMs and no 10-s interval without some portion of a movement in the entire tracing. The

two thresholds for significant LM detection according to the WASM criteria are set as 2 and $8 \mu\text{V}$ above the resting EMG level for movement end and start, respectively.

2.3. Visual scoring

The validation was planned for two comparisons of MATLAB1 with visual scoring of PLMS. The first compared MATLAB1 to the usual sleep-laboratory technician scoring of the PLMS on all available records ($n = 24$) at the time of this study. The second compared MATLAB1 to an expert scorer on a subset ($n = 9$) of all the records that had the larger differences between the technician and MATLAB1 scoring. Experienced certified sleep technicians visually scored the records for the first comparison as they would for any clinical service. The PLMS were first identified and marked on the PSG tracing by the recording system (RemLogic-3). The sleep technicians visually inspected the PSG tracing, and based on the WASM/IRLSSG criteria they corrected the PLMS identifications. Major clinical and research centers normally use this evaluation process, which is considered standard for sleep medicine practice. This was part of the technicians' routine service provided for both clinical and research laboratories, and the technicians were unaware of the planned comparison with MATPLM1.

There is obvious concern that scorer fatigue for some PSGs, which could contain hundreds of PLMS, and low-rate expectancy for PSGs with few PLMS would lead to errors in carefully applying MATLAB scoring criteria. Therefore, the second comparison provided a check on the technician visual scoring accuracy. The expert scorer had been highly trained, and he had 5 years of experience scoring PLMS for research studies. He was instructed to take as much time as needed to carefully evaluate and measure each of the PLMS events using expanded displays where appropriate. He rigorously applied the WASM/IRLSSG criteria for PLMS. The subset of nine records selected for expert analyses included one record of the two records from severe RLS patients with PLMS/h >200 and all other records with a difference between the technician visual scoring and MATPLM1 that was >15 per hour and $>15\%$ of the technician score. The expert scoring generally required about 2–4 h per record for this detailed visual scoring of only the PLMS. The technician and expert visual scoring were done without the knowledge of the PLMS scores from MATPLM1 or from the other visual scorer.

2.4. Subjects

The data from the second of two consecutive nights of PSG recordings were available for all analyses from 15 RLS (average age \pm SD: 61.5 ± 8.5 , 60% female) and nine control subjects (average age \pm SD: 61.4 ± 7.1 , 67% female) who were participating in an ongoing RLS study. All subjects gave Johns Hopkins institutional review board (IRB)-approved informed consent for the sleep study and any analyses of the de-identified data used in this study. The RLS patients were off all RLS medications for at least 12 days, and at that time they had an average IRLS of 26.2 ± 5.5 (range 16–35). This provides a patient sample covering the full range of moderate (usual low score for clinical trials is 15) to very severe (maximum IRLS score is 40) RLS. Ten of the 15 RLS patients had been on dopamine agonists, three on an $\alpha 2\delta$, and one on an opioid. The RLS patients had been screened to include only those with an average PLMS >15 per hour over five days of recording at home starting when off medication for at least five days. This recording used the Physical Activity Monitor for Restless Legs (PAM-RL) (Phillips Respironics) that has been validated for use with RLS patients [6–8]. The controls were included only if they had an average of PLMS <10 per hour for five consecutive days of similar recording at home. Controls and RLS patients were clinically screened to exclude those with significant sleep or mental health disorder aside from RLS. In particular, we excluded

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