Brief Communication

# Diagnostic accuracy of the standard and alternative periodic leg movement during sleep indices for restless legs syndrome

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of the standard periodic leg movement during sleep (PLMS) index, a recently introduced alternative one, and the periodicity index (PI) for restless legs syndrome (RLS).
Subjects and methods: A total of 107 patients with RLS were retrospectively identified and included (47 males and 60 females, mean age 56.9 years), along with 48 normal controls (24 males and 24 females, mean age 52.0 years). The standard PLMS index, the alternative PLMS index, and the PI were calculated from polysomnographic recordings. In order to establish the best performing threshold for the diagnosis of RLS, sensitivity and specificity were calculated with a series of threshold values ranging from 5 to 20/hour for the two PLMS indices, and from 0.2 to 0.9 for the PI.
Results: The optimal threshold was found to be between 15 and 16/hour for the standard PLMS index, close to 13/hour for the alternative index, and around 0.5 for the periodicity index. With these thresholds, all methods showed high values of sensitivity and specificity, with corresponding high positive and negative predictive values and accuracy; the receiver operating characteristic (ROC) curve areas were similar, and the Kappa coefficient of agreement indicated a 'very good' agreement between the PLMS indices.
Conclusions: This study assessed the cut-off values of the standard (15–16/hour) and alternative (13/hour) PLMS indices, and of the PI (0.5). The diagnostic accuracy of all indices for RLS vs controls was found to be acceptably high, with the new alternative PLMS index performing slightly higher than the other two indices.

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## 1. Introduction

An alternative periodic leg movement (PLM) index, which more closely reflects the 'genuine' periodic portion of leg movements, has recently been introduced and statistically evaluated [1]. The alternative PLM index adopts the same criteria as the 'standard' PLM index, but only considers leg movements separated by ≥10 seconds and ≤90 seconds and, differently from the standard rules [2,3], interrupts a possible PLM series if the interval between two consecutive LMs is <10 seconds [1]. This modification is based on the concern that the standard PLM detection criteria acted as a 'pattern extractor' by ignoring all 'non-fitting' leg movement activity, with the consequence that the PLM index could only increase as the number of LMs increases, which might be problematic in situations where

there is a high number of LMs, as the PLM index will no longer reflect the truly periodic LMs but rather the number of LMs [1].

In a previous study [1] of a large group of RLS patients and healthy controls, it was shown that the alternative PLM index was similar to the standard index when leg movement activity was genuinely periodic, as indicated by the Periodicity index [4], but was significantly lower when the periodicity was low. The present study investigated the cut-off value of the alternative index, and its diagnostic accuracy for restless legs syndrome (RLS) vs healthy controls, compared with that of the standard index.

## 2. Material and methods

A detailed description of subjects and methods can be found in a previous publication [1]. In short: 107 unmedicated patients with RLS (60 female, 47 male, mean age 56.9 years, SD 12.95) and 48 healthy controls (24 females, 24 males, 52.0 years, SD 19.30), who were matched for age ($t = 1.75$, N.S.) and sex (Chi-square = 0.49, N.S.), were included. All the participants had an AHI ≤ 5. All-night
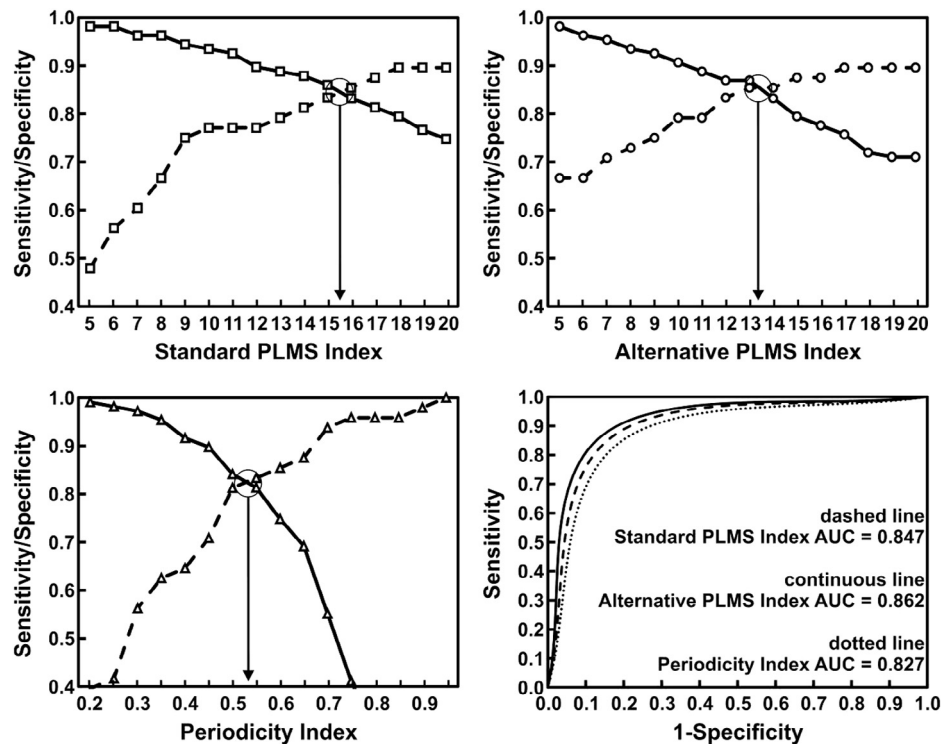
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**Fig. 1.** Scoring criteria for the standard and alternative periodic leg movement during sleep indices (PLMS) and periodicity index.

polysomnography was carried out according to standard procedures [5]. Leg movements during sleep were identified by automatic detection (Hypnolab) and fully supervised by a human scorer. The standard periodic leg movement during sleep (PLMS) index was calculated according to the criteria set by the International RLS Study Group and endorsed by the World Association of Sleep Medicine [2]. The alternative PLMS index only considered LMs separated by 10–90 seconds. Furthermore, if the interval between two consecutive LMs was <10 seconds, the periodic sequence was interrupted. In addition, the periodicity index (PI) during sleep [4,6] was computed. For all indices, sensitivity and specificity were calculated for a series of pre-set threshold values, which ranged from 5 to 20/hour for the standard and the alternative indices, and from 0.2 to 0.9 for the periodicity index.

## 3. Results

The results are given in Fig. 1, with sensitivity decreasing and specificity increasing with increasing thresholds. The intersection between these two represents the best choice for a threshold to be used for diagnostic purposes. This optimal threshold was between 15 and 16/hour for the standard PLMS index, and close to 13/hour for the alternative index (Fig. 1). For the periodicity index, the optimal threshold was around 0.5. Table 1 reports the common parameters of diagnostic accuracy for the standard and the alternative PLMS index, and the periodicity index, with thresholds of 15/hour, 13/hour, and 0.5, respectively. All methods showed high values of sensitivity and specificity, with corresponding high positive and negative predictive values and accuracy. The alternative PLMS index tended to show marginally higher values. In addition, the receiver operating characteristic (ROC) curve areas were similar and the Kappa coefficient of agreement indicated a 'very good' agreement between the standard and alternative PLMS index, while there was a lower, but still 'good', agreement of the periodicity index with these measures (Table 1).

## 4. Discussion

A validation process of the alternative PLMS/PLMW index [1], described above, has recently been introduced and successfully initiated. It has been proven to be more adherent to the parameters that allow a reliable evaluation of LM periodicity. Although encouraging, additional validation, and analysis of this algorithm's performance are needed and the present study, by evaluating its accuracy for the diagnosis of RLS, has added a further important piece of information. The present results show this accuracy to be high, at least at the same level of that of the standard method.

It is important to mention that this analysis has also been undertaken for the standard method, and this data-driven approach has demonstrated that the arbitrary threshold of 15 PLMS/hour of sleep, as used in the American Academy of Sleep Medicine (AASM) International Classification of Sleep Disorders [7], is in good approximation to the empirically found threshold in the present study.

**Table 1**

Analysis of the accuracy of the standard and alternative periodic leg movement during sleep (PLMS) indices and of the periodicity index for the diagnosis of restless legs syndrome vs controls.

|  | Standard PLMS index (threshold 15/hour) | Alternative PLMS index (threshold 13/hour) | Periodicity index (threshold 0.5) |
|---|---|---|---|
| Sensitivity, % | 83.3 | 86.9 | 84.1 |
| Specificity, % | 86.0 | 85.4 | 81.3 |
| Positive predictive value, % | 92.0 | 93.0 | 90.9 |
| Negative predictive value, % | 72.7 | 74.5 | 69.6 |
| Accuracy, % | 85.2 | 86.5 | 83.2 |
| ROC area | 0.847 | 0.862 | 0.827 |

Alternative vs standard PLMS Index: Kappa = 0.944 (95% confidence interval 0.889–0.998); Alternative PLMS index vs periodicity index: Kappa = 0.783 (95% confidence interval 0.683–0.883); Standard PLMS index vs periodicity index: Kappa = 0.761 (95% confidence interval 0.655–0.868).

It is believed that there are no other data in the previous literature supporting the indication of this threshold. However, as far as the diagnosis of RLS is concerned, the thresholds of 15/hour for the standard PLMS index and of 13/hour for the new alternative index seem to represent a reliable and data-driven choice.

This study cannot take any position with regard to the level of PLMS that might have a 'clinical significance', which has often been indicated with a value of 5/hour or has been used in genetic studies of PLMS [8]. It is also noteworthy to state that the performance of all three indices was largely equivalent.

In conclusion, the cut-off value of the alternative PLMS index and its diagnostic accuracy for RLS vs controls were assessed; these were found to be acceptably high (at least comparable to that of the standard index and the periodicity index, if not higher). This strengthens the proposition to use the new PLMS index as a valid alternative to the standard algorithm. Future studies should test the alternative PLMS index in a different dataset than the one used to derive it, evaluate it in younger subjects (children), and explore its application in other clinical samples of patients with frequent PLMS, such as REM sleep behavior disorder and narcolepsy [9,10].

## Conflict of interest

The authors have indicated no financial conflicts of interest.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2015.11.018.

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