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Original Article

The validity of the PAM-RL device for evaluating periodic limb movements in sleep and an investigation on night-to-night variability of periodic limb movements during sleep in patients with restless legs syndrome or periodic limb movement disorder using this system

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ABSTRACT

Background: The status of night-to-night variability for periodic limb movements in sleep (PLMS) has not been clarified. With this in mind, we investigated the validity of PLMS measurement by actigraphy with the PAM-RL device in Japanese patients with suspected restless legs syndrome (RLS) or periodic limb movement disorder (PLMD) and the night-to-night variability of PLMS among the subjects.
Methods: Forty-one subjects (mean age, 52.1 ± 16.1 years) underwent polysomnography (PSG) and PAM-RL measurement simultaneously. Thereafter, subjects used the PAM-RL at home on four more consecutive nights.
Results: The correlation between PLMS index on PSG (PLMSI-PSG) and PLM index on PAM-RL (PLMI-PAM) was 0.781 ($P < .001$). When the PLMSI cutoff value on PSG was set at 15 episodes per hour, the cutoff value for predicting this PLMSI level was 16.0 episodes per hour. When the condition was set to the level in which the mean interclass correlation coefficient reached $\geqslant 0.9$, the number of required nights for repeated measurements was 26 nights for subjects with PLMI of <15 episodes per hour and three nights for those with PLMI $\geqslant 15$ episodes per hour on PAM-RL.
Conclusions: PAM-RL is thought to be valuable for assessing PLMS even in Japanese subjects. Recording of PAM-RL for three or more consecutive nights may be required to ensure the screening reliability of a patient with suspected pathologically frequent PLMS.

1. Introduction

Periodic limb movements in sleep (PLMS) may appear as stereotypic and intermittent involuntary movements mainly of the ankle or knee joints. PLMS is a rapidly evolving scientific topic, and the question if PLMS contributes to sleep disruption in RLS and if it should be treated or not is among the topics being discussed. Previous studies have found that PLMS frequently occur in patients with restless legs syndrome (RLS) [1], and the presence of PLMS is emphasized as an auxiliary diagnostic item for RLS [2]. Reportedly mean systolic blood pressure increases at the occurrence of PLMS in RLS patients [3], and this phenomenon is regarded as one of the factors of the increased risk for cardiovascular disorders including hypertension in the RLS population [4].

RLS usually is treated with dopaminergic agents, a type of drug also known to be effective for decreasing the frequency of PLMS [5]. Certain α2δ ligands such as gabapentin are less effective for decreasing the frequency of PLMS than dopaminergic agents, though they alleviate RLS symptoms and improve the subjective quality of sleep [6]. Therefore, it is important to assess the frequency of PLMS when selecting a medication for treatment.

In-laboratory polysomnography (PSG) is the gold standard for assessing the frequency of PLMS and calculation of the PLMS index (PLMSI) on PSG is particularly important for the diagnosis of periodic limb movement disorder (PLMD). The cutoff value of PLMSI for PLMD is set at 15 episodes per hour [7]. PSG examination is time-consuming and labor-intensive. In addition, large night-to-night variability of PLMS within individuals has been reported [8–10],

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and therefore it is doubtful if the frequency of PLMS can really be assessed from a single night of measurement.

The PAM-RL (Respironics, Inc., Murrysville, PA, USA) is a 3-axis motion sensor designed to record leg activities and to detect periodic limb movements (PLMs) with a specific software system (PAM-RL actigraph software version 7.6.2) [11]. Because it is capable of storing PLM data for up to five nights, it enables the evaluation of night-to-night variability in PLMs. However, there have been few reports on the reliability of this simple measurement device for the screening of pathologically frequent PLMS, and the studies on this issue have been limited to white individuals [8–11], with no evaluation of Japanese patients.

If the accuracy of PAM-RL measurements of PLM is sufficiently reliable, this device may have a wide range of clinical applications, such as the screening of RLS and PLMD and the assessment of the efficacy of drug treatment on PLMS at home. Moreover, if the characteristics of night-to-night variability in PLMS within individuals and the required number of recording nights to adequately identify the severity of PLMS can be established with this device, the level of certainty of the frequency assessment of PLMS would be improved. To clarify these issues, we evaluated the validity of the PAM-RL recording for the screening of pathologically frequent PLMS in Japanese patients with RLS or PLMD and investigated night-to-night variability in PLMS within affected individuals. The distribution of PLMs across the night, intermovement intervals (IMIs) of PLMs, and the periodicity index are helpful for distinguishing true PLMS from more irregular leg motor activity during sleep [10,12]. To confirm the reliability of PAM-RL for the evaluation of PLMS, we additionally compared these measurements between PLMs on PSG and those on PAM-RL.

2. Methods

Our study commenced after obtaining approval from the Ethics Committee of the Japan Somnology Center. Eligible cases comprised a series of 48 consecutive patients $\geqslant$20 years of age (mean age, 52.9 ± 16.2 years), who were examined at the Yoyogi Sleep Disorder Center with suspected RLS or PLMD and underwent PSG between May 2010 and January 2011. They provided written informed consent to participate in the study. Patients who were already receiving drug therapy for RLS at the time of PSG were excluded from our study, as were patients taking dopaminergic blockers or selective serotonin reuptake inhibitors, tricyclic antidepressants, antihistamines, and other medications that may cause RLS symptoms [13]. Patients who were obviously obese or were identified by family members as snoring or having apnea episodes during sleep also were excluded, as were patients with suspected narcolepsy or rapid eye movement sleep behavior disorder.

Nocturnal PSGs were performed using the Alice5 (Respironics, Inc. Murrysville, PA, USA) or Comet (Astro-Med, Inc. West Warwick, RI, USA) system, with variables including electroencephalography (C3–A2, C4–A1, F3–A2, F4–A1, O1–A2, O2–A1), electrooculography, electromyography (EMG) of the mentalis muscle, nasal airflow, respiratory movement of the chest and abdomen, snoring sounds, percutaneous arterial oxygen saturation, body position information, electrocardiography, and leg surface EMGs.

On the day of PSG, the technician also attached a PAM-RL to both ankles of the patient to simultaneously record PAM-RL data. Subjects also were requested to use the PAM-RL at home for four more consecutive nights from the night after the PSG examination to collect data for evaluating night-to-night variability in PLMs.

Sleep stage on PSG was determined according to the American Academy of Sleep Medicine (AASM) 2007 criteria and was determined in 30-s epochs [14]. Arousal also was determined according to the AASM arousal criteria [14]. Apnea and hypopnea were determined according to the AASM Chicago criteria [15]. Leg movements (LMs) also were visually scored according to the AASM 2007 criteria [14], with the start of LM defined as an increase of $\geqslant$8 μV measured by the electrodes attached to the bilateral anterior tibial muscles from their potential at rest; and the end was defined as the point at which the difference with the EMG potential returned to $\leqslant$2 μV from the value at rest, with the duration being 0.5–10 s. A PLM sequence was determined when the appearance of four or more consecutive LMs at intervals of 5–90 s during sleep were observed [14]. We defined the PLMSI on PSG (PLMSI-PSG) as PLM events divided by total sleep time.

The PAM-RL is a calibrated (1 g = 9.82 kg/s^2) battery-powered accelerometer with central processing and memory to record movements [16]. This system has a 0.3- to 20-Hz band-pass filter and can continuously record acceleration with a sampling rate of 40 Hz. The data recorded in the memory of the PAM-RL device were imported into a computer via a special cable supplied with the PAM-RL. PAM-RL software was used to perform the automatic analysis. The algorithm first detected LM as LMs using an onset threshold set to 160 mg, with a decay threshold set to 100 mg [16]. Thereafter, the PAM-RL software system detects PLMs, with durations of 0.5–10 s and IMIs between 5 and 90 s, with a minimum number of four LMs chosen [16]. After the automatic PLM analysis, the data files for individual legs were exported as a comma-separated value file for combined analysis of left and right limb movements. Movement in different legs with onset-to-onset of LM intervals of 5 s or less were defined as one movement manually [14]. The analysis of the PAM-RL results was done for time in bed, as PLMI on PAM-RL cannot be calculated for total sleep time. In our study, we determined PLMI on PAM-RL by averaging the data of five consecutive nights.

To evaluate the internal consistency of the PAM-RL measurements, we calculated Pearson product moment correlation coefficient for the values of PLMI obtained from the PAM-RL and PLMSI from PSG. We then used a Bland–Altman plot to evaluate differences in the results of analyses of these two measurements [17]. Based on the diagnostic criteria for PLMD [7], we then created a receiver operating characteristic curve for the PLMI-PAM, with PLMSI $\geqslant$15 episodes per hour on PSG as the cutoff value for the pathologic level, and calculated the area under the curve. We also determined the sensitivity, specificity, and rate of both false-positive and false-negative cases for PLMI-PAM with PLMSI of $\geqslant$15 episodes per hour on PSG as a reference.

Moreover, we compared the hourly distribution of PLMs and distribution of the number of durations of IMIs between PLMs obtained from PSG (all the PLMs were PLMS) and those from PAM-RL (PLMs included both PLMS and PLMs of wakefulness [PLMW]). Additionally, IMIs for 10–90 s in length were divided by the total number of intervals to yield the periodicity index; this index can vary between 0 (absence of periodicity with none of the intervals showing a length between 10 and 90 s) to 1 (complete periodicity with all intervals showing a length between 10 and 90 s) [18,19]. The hourly distribution of PLMs and the number of IMIs in each time period between PLMs on PSG and those on PAM-RL were compared using the Wilcoxon signed rank test.

One-way analysis of variance was used to investigate differences in PLMI measured on different nights. The coefficient of variation (CV) (CV = $s \times 100/x$, in which s = standard deviation and x = mean PLMI value) was calculated as an index of night-to-night variability for consecutive nights of PAM-RL measurements. The number of repeated PAM-RL measurements required for adequately evaluating the level of PLMI was calculated as the number to achieve a mean interclass correlation coefficient (ICC) of $\geqslant$0.9 by using the Spearman–Brown formula ($\rho = \kappa\rho/1+(\kappa-1)\rho$, in which κ = number of repeats and ρ = confidence coefficient of the ICC) [20]. SPSS 11.5 software (SPSS Japan, Inc., Tokyo, Japan) was used