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Original Article

Blood pressure changes associated with periodic leg movements during sleep in healthy subjects

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ABSTRACT

Background and objectives: Periodic leg movements during sleep (PLMS) are associated with important blood pressure (BP) increases in restless legs syndrome (RLS) patients. These movements also are highly prevalent in the healthy elderly population. The aims of our study were to evaluate if heart rate (HR) and BP changes associated with PLMS are present in healthy subjects with no report of health concerns and to compare the amplitude of cardiovascular changes in healthy subjects to that of RLS subjects.
Methods: Fourteen healthy subjects (six men, eight women; 46.6 ± 9.7 y) and 14 RLS subjects (six men, eight women; 47.6 ± 11.8 y) matched for age and gender participated in our study. Beat-to-beat noninvasive BP was continuously recorded during one night of polysomnography. HR, systolic BP (SBP) and diastolic BP (DBP) were measured for 10 beats before and 15 beats after onset of PLMS with and without microarousals (MA).
Results: PLMS were associated with sudden and significant increases of HR, SBP and DBP in both groups; however, cardiovascular increases were more pronounced in RLS subjects than in healthy subjects.
Conclusions: Because PLMS index increases with age in healthy subjects and aging is associated with higher cardiovascular risk, further studies should investigate the impact of PLMS-related BP changes on the development of cardiovascular diseases in healthy elderly populations.

1. Introduction

Periodic leg movements during sleep (PLMS) are short involuntary movements occurring repetitively during sleep at about 20- to 40-second intervals. They are described as a rhythmic extension of the big toe and dorsiflexion of the ankle with occasional flexion at the knee and hip. They have been extensively studied in patients with restless legs syndrome (RLS), in which they are considered a supportive criterion for diagnosis [1], but they also occur in other sleep disorders such as narcolepsy [2], rapid eye movement sleep behavior disorder (RBD) [3] and sleep apnea syndrome [4,5]. Several studies also have shown a high prevalence of PLMS in healthy subjects with no health concerns, especially after the age of 40 years [6,7]. A study determined that the prevalence of PLMS in a population-based sample of 592 subjects was 7.6%, considering a PLMS index > 15 as a criterion [8].

It is now well-established that PLMS are associated with a significant increase followed by a decrease in heart rate (HR) [9–12], with larger amplitude of these changes when PLMS are accompanied by microarousals (MA). Moreover bilateral PLMS are associated with more pronounced HR changes than unilateral ones [13]. Subsequently we found that in addition to HR changes, PLMS are associated with significant blood pressure (BP) increases in RLS subjects, whether or not movements are associated with MA [14]. These findings have been replicated in treated RLS subjects who therefore presented a lower PLMS index; however, the amplitude of cardiovascular activation associated with PLMS response seemed to be lower [15].

The first objective of our study was to verify if PLMS in healthy subjects without RLS also are associated with BP changes. The second objective was to compare HR and BP increases associated with PLMS in healthy subjects and in RLS subjects.

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2. Methods

2.1. Subjects

Thirty-two healthy subjects with no report of health concerns were recruited through newspaper advertisements. Subjects with a PLMS index < 5 per hour of sleep were not included in the study, as the principal objective was to evaluate cardiovascular changes associated with PLMS. Fourteen of these subjects ages 30 to 62 years (mean age, 46.6 ± 9.7 y; six men, eight women), had a PLMS index > 5 per hour of sleep and were included in our study. Fourteen RLS subjects matched for age and gender were included in the study (six men, eight women). The subjects were ages 29 to 69 years (mean age, 47.6 ± 11.8 y). Nine of these subjects were studied in previous work on PLMS and BP increase in RLS subjects [14]. RLS was diagnosed in a face-to-face interview with a specialist applying the four standard clinical criteria developed by the International Restless Legs Syndrome Study Group [1]. Only subjects who were never treated for RLS were enrolled in the study.

Exclusion criteria for both healthy subjects and RLS subjects were (1) the presence of other psychiatric or medical condition known to be associated with RLS such as uraemia, peripheral neuropathy, rheumatoid arthritis, or anemia; (2) serum ferritin level <10 μg/L; (3) the presence of hypertension; (4) the presence of other sleep disorders associated with PLMS or with cardiovascular changes during sleep such as sleep apnea syndrome (apnea-hypopnea index ⩾ 10/h), narcolepsy, RBD, or sleep bruxism; and (5) the use of psychotropic medications, BP medications, or other drugs known to influence sleep, autonomic nervous system function, or motor activity. An additional exclusion criterion for healthy subjects was the presence of RLS symptoms or a family history of RLS. The subjects were specifically questioned regarding the presence of urges to move associated with unpleasant leg sensations. All subjects signed a consent form, which was approved by the ethics committee of the Sacré-Coeur Hospital.

2.2. Data collection

In the evening preceding polysomnographic (PSG) sleep recordings, brachial arterial BP was measured at rest in the sitting position with a cuff on the nondominant arm to provide a baseline clinical systolic BP (SBP) and diastolic BP (DBP). All healthy subjects SBP, 113.1 ± 10.7 mmHg; DBP, 69.1 ± 9.0 mmHg) and RLS subjects (SBP, 116.5 ± 13.9 mmHg; DBP, 68.5 ± 8.7 mmHg) had BP levels within reference range at rest, and there were no between-group differences on these baseline measures (SBP, $p = 0.5$; DBP, $p = 0.9$). One night recording was performed in a sleep laboratory using four electroencephalogram (EEG) leads (C3, C4, O1, and O2), two bilateral electrooculograms (EOG), and one chin electromyogram (EMG). Respiration was assessed by nasal cannula and thoracoabdominal strain gauges and finger pulse oximetry. Surface EMG electrodes placed 3-cm apart on the right and left anterior tibialis muscles were used to record PLMS. The electrocardiogram (ECG) included leads one, two, and three. Continuous BP recordings were obtained using a TNO Portapres Model-2 (TNO TPD Biomedical Instrumentation, the Netherlands), which provides noninvasive beat-to-beat BP recording through a continuous finger arterial pressure waveform. Although this method has shown consistent underestimation compared to direct measurements on the brachial artery, it provides an accurate measure of sudden BP changes in response to various stimuli [16]. It is therefore an appropriate noninvasive alternative method to measure beat-to-beat BP changes associated with episodic events during sleep.

2.3. Data analyses

Sleep was scored by the standard method [17] and PLMS were scored using the criteria set by the International Restless Legs Syndrome Study Group [18]. Only movements lasting 0.5 to 10 seconds, separated by intervals of 5 to 90 seconds and occurring in a series of at least four consecutive movements, were counted. The amplitude criterion for detecting leg movements was an increase in EMG to ⩾8 μV above the resting baseline for movement onset and a decrease in EMG to <2 μV above the resting level for movement offset. MA were scored according to standard American Sleep Disorders Association criteria [19] and respiratory events were scored according to American Sleep Disorders Association and the Academy of Sleep Medicine recommendations [20].

2.4. PLMS selection and cardiovascular analyses

A total of 157 PLMS without MA and 132 PLMS with MA were selected in healthy subjects, and 139 PLMS without MA and 136 PLMS with MA were selected in RLS subjects. All movements were selected in stage two sleep to avoid sleep stage interaction. In addition to the standard criteria for PLMS, only movements separated by at least 20 seconds were selected for analysis to avoid overlapping HR and BP responses to successive leg movements. Only movements free of any physiologic (e.g., rhythmic masticatory muscle activity, arrhythmias, flow limitation, apneas, and hypopneas based on nasal cannula and thoracoabdominal strain gauges) or technical factor that would potentially affect HR or BP signals were selected.

HR, SBP and DBP were automatically measured on segments lasting 25 heartbeats, comprising 10 beats before the movement (−10 to −1) and 15 beats after the movement (+1 to +15). Beat-to-beat values of HR, SBP and DBP were calculated for each movement and were averaged for each subject. Baseline was defined as the mean value from beats −10 to −4. To assess if PLMS in healthy subjects were associated with cardiovascular changes, HR, SBP and DBP changes were first calculated by subtracting baseline from each value following PLMS. Then to compare cardiovascular activation between the two groups of subjects, HR, SBP, and DBP changes were converted as a percentage of baseline value. In addition, the mean SBP and DBP amplitude (highest value obtained after movement onset compared to baseline) and the mean HR amplitude (highest value obtained during the increase-lowest value obtained during the decrease) was calculated in each subject for PLMS with or without MA.

2.5. Statistical analyses

Independent *t*-tests were performed to compare sleep architecture in RLS subjects and healthy subjects. Beat-to-beat HR, SBP and DBP changes associated with PLMS with and without MA were assessed by repeated measures one-way analysis of variance (ANOVA) followed by planned comparisons. Greenhouse–Geisser correction for sphericity was applied. Each value of HR, SBP and DBP (beat −3 to +15) was compared to baseline (mean value from beats, −10 to −4).

Percentage of HR, SBP and DBP changes associated with PLMS with and without MA in patients with RLS and healthy subjects were assessed by two-way ANOVA with one factor (group) and one repeated measure (heartbeat) followed by planned comparisons. Greenhouse–Geisser correction for sphericity was applied. Between-group differences were assessed on each value of HR, SBP, and DBP (beats −3 to +15).

Pearson product moment correlation coefficients were calculated between HR, SBP and DBP increments associated with both