INVITED EDITORIAL

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Periodic limb movements in sleep: evolving role of autonomic nervous system

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Periodic limb movements in sleep (PLMS) are polysomnogram-defined movements with a duration of 0.5–10 seconds, with a minimum amplitude increase in EMG voltage above resting EMG of 8 μV, and occur in a series of at least four limb movements (Fig. 1) [1]. The observed movements tend to occur in a triple flexion pattern of the lower extremities, with dorsiflexion at the ankle, and flexion of the knee and hip. However, movements can occur in upper extremities. PLMS are observed frequently on polysomnograms, and their prevalence in the general population is estimated at 5–8% [2]. Research over the last decade has shown that there may be an association between PLMS and cardiovascular disease. Unlike restless leg syndrome, which is a clinical diagnosis, PLMS are a polysomnogram diagnostic finding. The pathophysiology of PLMS is not fully understood. Theories in the literature include complex brainstem and spinal cord autonomic and motor activity, but the generator or generators have not been discovered [2–8].

There is a growing body of literature regarding the association of blood pressure and heart rate elevations occurring with PLMS. Further investigation into this association might provide greater clarity regarding the relationship between PLMS and the cardiovascular system. A systematic review examining HTN risk in patients with PLMS found a significant association between having PLMS and HTN, with an overall 1.26-fold increased risk of HTN compared to those who did not have PLMS [9]. The association between PLMS and cerebrovascular disease is uncertain in the literature, with some studies showing an association and others not [10, 11]. In order to better establish the relationship of this association, finding the cause of autonomic nervous system activity before, during, and/or after, a PLMS series was needed. Heart rate variability parameters were first reported in the 1970s to assess autonomic function [12].

Malkiewicz et al. examined heart rate (HR), high-frequency heart rate variability (HRV HF), systolic blood pressure (SBP), and diastolic blood pressure (DBP) for 10 heartbeats preceding a series of PLMS and 10 consecutive heartbeats as beat-to-beat-measures [13]. The aim of the study was to investigate the dysregulation of autonomic HR control in patients with PLMS. They found no statistically significant changes in HR, systolic blood pressure, or diastolic blood pressure. However, there was an increase in the value of HRV HF following eight PLMS in the series. Uniquely, they only analysed PLMS without arousals. This may account for the lack of association with blood pressure and HR.

Other data has suggested that perhaps the HRV and electroencephalogram changes associated with limb movements are not specific to PLMS, but in fact occur during all types of leg movement [14]. One study tried to answer this question by examining not only PLMS but also isolated leg movements during sleep, and found that HRV and EEG changes occur uniformly before and during all leg movements; however, the intensity of HRV was statistically greater in PLMS compared to isolated leg movements, suggesting sympathetic activity as the physiological process was most probably causally related to PLMS [14]. Other analyses have examined HRV and HRV HF compared to sleep with PLMS and sleep without PLMS, and have found elevation of the HRV HF tens of seconds prior to the PLMS series versus elevation at times of sleep without

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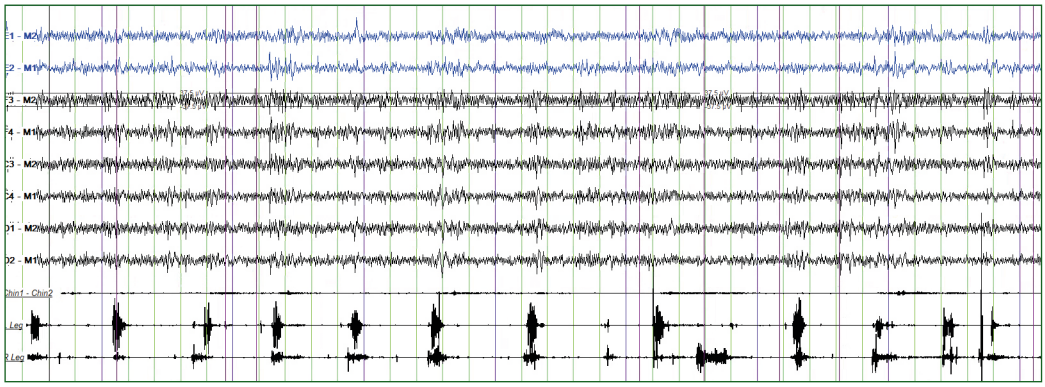

Figure 1. Example of series of periodic limb movements on a polysomnogram

PLMS [15]. Systolic blood pressure and heart rate evaluation have been examined relative to the timing of the PLMS; the authors found that HR increased within the first epoch after PLMS but systolic blood pressure increases occurred in the second and third epochs post-PLMS [16].

The findings by Malkiewicz et al. [13] have informed the discussion regarding the pathophysiology of PLMS and illuminated a new theory of the autonomic nervous system having co-activation of the sympathetic and parasympathetic pathways occurring parallel to each other during PLMS.

The role of the autonomic nervous system in the generation of PLMS is yet to be established. Further research is needed to better assess the changes occurring to aid in the prevention of cardiovascular and cerebrovascular disease.

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