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Effect of series of periodic limb movements in sleep on blood pressure, heart rate and high frequency heart rate variability

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ABSTRACT

Introduction. The phenomenon known as periodic limb movements in sleep (PLMS) has been linked to a change in autonomic nervous system (ANS) activity and its effect on circulatory regulation. Autonomic dysfunction or dysregulation in patients with PLMS has been described in some domains; however, any relationship between heart rate variability (HRV) and PLMS has not been clearly established. HRV analysis is a recognised, non-invasive research method that describes the influence of the ANS on heart rate (HR). The aim of our study was to further investigate the dysregulation of autonomic HR control in patients with PLMS.

Material and methods. We undertook a retrospective analysis of the polysomnographic (PSG), demographic and medical data of five patients with a total number of 1,348 PLMS. We analysed HR, HRV HF, systolic blood pressure (SBP), and diastolic blood pressure (DBP) for 10 heartbeats before the series of PLMS and 10 consecutive heartbeats as beat-to-beat measurements. The presented method of using successive, short, 10 RR interval segments refers to the time-frequency measurement, which is very clear and useful for presenting changes in the calculated parameters over time and thereby illustrating their dynamics. This method allowed us to assess dynamic changes in HRV HF during successive PLMS series. Statistical analysis was performed using IBM SPSS Statistics (v. 28.0.0.0). The Kruskal–Wallis test was performed to find statistically significant changes from baseline.

Results. No statistically significant changes in HR, SBP, or DBP were found in our group, although an increase in the value of the HRV HF was noted, suggesting an increase in intracardiac parasympathetic activity during the subsequent series of PLMS.

Conclusions. Our study indicates an increase in parasympathetic activity during the appearance of successive PLMS, which, with the simultaneous lack of changes in HR, may suggest an increase in sympathetic activity, and therefore the appearance of so-called 'autonomic co-activation' resulting in the possibility of life-threatening cardiac events.

Clinical implications. Our findings add to the literature information regarding HRV in PLMS, and highlight the need for further studies to elucidate the effects of these conditions on the ANS, and on cardiovascular health.

Keywords: periodic limb movements in sleep, periodic movement disorder of sleep, heart rate variability, autonomic nervous system, sleep-related movement disorder, autonomic co-activation

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Introduction

Periodic limb movements in sleep (PLMS) are defined as repetitive and stereotypical movements of the lower limbs occurring during sleep in a periodic pattern. They typically involve dorsiflexion of the ankle, extension of the big toe, and occasional flexion of the knee and hip [1]. A single movement may last from 0.5 to 10 s; however, the movements manifest in a series of four or more single movements separated by intervals of 5-90 s [1]. PLMS are present in 80% of patients with restless leg syndrome (RLS) [2], but also co-occur with a range of sleep disorders including obstructive sleep apnoea, insomnia, narcolepsy [3], and neurological pathologies associated with REM sleep behaviour disorder [4]. Interestingly, PLMS have also been associated with diverse psychiatric diseases in numerous studies. Longitudinal data demonstrates that patients with PLMS have an increased risk of depression and anxiety, and of dementia [5, 6].

It should be noted, however, that it remains unclear how a series of PLMS affects the autonomic nervous system (ANS), cardiovascular system, and mental health.

PLMS has been linked to a change in ANS activity and its effect on circulatory regulation. PLMS are regarded as being accompanied by an increase in HR preceding the occurrence of leg movements during PLMS. Cortical and sympathetic activations are supposed to lead these changes [7–11], supporting the association between PLMS and cardiovascular and hypertensive risks [12]. This sympathetic overactivity can lead to surges in nocturnal blood pressure (BP) and HR [13]. There have been some reports that PLMS onset is heralded by a significant increase of HR and BP [14, 15]. Indeed, the increase in systolic blood pressure (SBP) [14] and diastolic blood pressure (DBP) has been widely discussed in the literature [14–16]. PLMS are supposed to be followed by an increase in HR which starts immediately after the onset of leg movement and rises in the first few seconds after the limb movement [14, 15, 17].

Basic haemodynamic parameters, such as systolic and diastolic blood pressure, but also more sophisticated methods of assessing extracardiac regulation of heart rhythms such as HRV, can be used to assess the autonomic regulation of circulation. HRV analysis is a well-recognised, non-invasive research method that describes the influence of the ANS on HR. HRV analysis determines the contribution of total HR components that are dependent on endogenous oscillators of HR regulation. The basic components of the heart rhythm are affected by the sympathetic and parasympathetic activity of the ANS, which determines the short- and long-term variability of the sinus rhythm. HRV analysis also indicates the contribution of the respiratory component to the heart rhythm. Physiological respiratory irregularity is a change in HR that is closely related to the phase of breathing.

In general, high HRV is regarded as an index of cardiovascular health [18]. Moreover, low HRV parameters are related to diverse psychiatric illnesses including major depressive disorder [19], bipolar disorder [20], anxiety disorder [21], schizophrenia [22] and Parkinson's Disease (PD) [23, 24]. PLMS are frequently observed in individuals with PD, and are often accompanied by dysautonomia and cognitive impairment, which are among the non-motor symptoms associated with PD [24, 25]. Cardiovascular ANS dysautonomia in PD involve abnormalities such as decreased HRV and impaired baroreflex sensitivity which may contribute to the increased risk of cardiovascular events in individuals with PD [24]. It is possible that the dysregulation of autonomic cardiovascular control in PD could impact upon cerebral blood flow and oxygenation, and contribute to neuroinflammation and neurodegeneration, thus affecting cognitive function [24].

HRV may be considered to be a link between psychiatric and neurological disorders, cardiovascular diseases, and mortality [26]. HRV has recently been reported to show associations with suicide attempts [26, 27]. HRV analysis has found wide recognition in medical research as a non-invasive method of assessing HR regulation and an indicator assessing the risk of serious cardiovascular events. It is reasonable to postulate that the sympathetic activation and HRV alterations associated with PLMS may play a role in the occurrence of desaturation episodes during sleep, potentially worsening stroke outcomes [28].

Conducting further research to explore the connection between PLMS, desaturation episodes, and stroke outcomes could offer valuable insights into the underlying pathophysiology and clinical implications of PLMS-related cardiovascular dysautonomia.

Smoking and excessive alcohol consumption reduce HRV, while conversely an active lifestyle, regular physical exercise, and the use of relaxation methods including meditation, raise HRV parameters.

Data from the literature indicates that HRV decreases in PLMS with a concomitant increase in sympathetic tone [29–31]. Some studies additionally have indicated decreased vagal activity [32]. Altered HRV in PLMS patients was also the result of the study by Barone et al., who observed a significant reduction of HRV HF (high-frequency HRV) and elevation of very-low-frequency HRV (HRV VLF) [11]. Previous reports have indicated elevation of HRV VLF, HRV LF and LF/HF in the period of a PLMS event [7, 13, 31, 33]. In one study [7], the increase of HRV VLF and HRV LF was described several tens of seconds before the beginning of the period with PLMS, with a subsequent increase of HRV HF fluctuation. However, Izzi et al. [34] found no significant difference in HRV in RLS patients with PLMS.

Clinical rationale for the study

Autonomic dysfunction or dysregulation in patients with PLMS reflecting in HRV has been described in some domains; however, detailed studies on this subject are limited and results

are conflicting. Therefore, the aim of this study was to verify the hypothesis that a series of PLMS is connected with a higher range of abnormalities in SBP and DBP, with particular interest in HRV HF scores before the series of PLMS and after the end of the series.

In the current work, we have applied an innovative approach to the assessment of autonomic regulation of the heart rhythm, including the measurement of the dynamics of changes in HR regulation indices during successive PLMS series.

Material and methods

We analysed polysomnographic (PSG) recordings from five patients (three males and two females) aged 32–62 with PLMS at the Vitalmed Helsinki Sleep Clinic, Helsinki, Finland. All of the patients had a diagnosis of RLS that had been verified by an experienced neurologist. The original studies were approved by the local ethics committees and all subjects provided informed written consent.

Each subject underwent a single night PSG study. Patients did not undergo any pharmacological therapies that might influence or induce PLMS, such as antipsychotics, sedatives, antidepressants, lithium, B-blockers, or Ca-blockers. Patients with renal disease, diabetes mellitus, depression, anxiety disorder, heart disease, psychotic disorder, or arrhythmia were excluded. Patients with an apnoea/hypopnoea index ≥ 5 were also excluded.

Treatments for other conditions, including drugs for hypertension, were stable for ≥ 2 weeks preceding the PSG. Inclusion and exclusion criteria are set out in Table 1.

All PSG recordings were performed with a SOMNOscreen plus PSG system (Somnomedics, Randersacker, Germany).

The following parameters were included in the PSG examination. Recordings included eight EEG leads, two bilateral electro-oculogram leads (EOG), bilateral chin electromyographic (EMG) leads, and two surface EMG of the left and right anterior tibialis muscles (for recording periodic limb movements). Electrocardiograms were recorded via three precordial leads. The sleep respiratory pattern was assessed with a nasal cannula, thoracic and abdominal strains, and a finger oximeter.

The PSG recording included beat-to-beat BP measurements performed automatically, using pulse transit time (PTT) [35]. The BP measurements were collected continuously (beat-to-beat).

To assess heart rhythm, QRS peaks were detected, and then the HR was calculated directly from the RR interval (RRi) automatically. ECG was recorded at a sampling rate of 4 kH.

We also assessed the stage of sleep and the duration of limb movement in each PLMS. The total number of analysed PLMS samples was 1,348. All the measurements were noninvasive, did not disturb sleep, and were unnoticeable by the patients. No awakenings were noted during the study in the sample group.

PLMS were scored following the standard criteria of the American Academy of Sleep Medicine (AASM) [36]. PLMS were included if they increased at least 8 μV above the resting line in EMG with a duration of 0.5–10 s before a drop in EMG to < 2 μV above the resting line. The episodes were defined as PLMS only when four or more such episodes appeared separated by intervals of 5-90 s. In this study, only PLMS were considered, and patients with PLMS with arousals in PSG were excluded from the study.

A series of PLMS was defined as a group of consecutive PLMS with an interval between leg movements shorter than 90 s. A leg movement appearing 90 s or more after the previous one was designated as the beginning of a new series or as a single leg movement.

The episodes of PLMS > 10 s were regarded as a PLMS series, and in the case of each patient there were no single PLMS, as they occurred only as series. The PLMS series was stopped when a limb movement appeared with an interval of < 10 s [37]. Limb movements overlapping with any breath event were not considered as PLMS. Movements appearing sooner than 0.5 s before the beginning of, or no more than 0.5 s after the end of, a breath event were not recognised as PLMS. A total of 1,348 PLMS without arousals were selected from the PSGs.

Methods

The first step was to identify the appropriate ECG fragments for further analysis. Based on these records, RRi were calculated and used to determine HRV in the short-term variability band — HRV HF. For each time series, we assessed also the mean HR, SBP and DBP.

All measurements were computed from a segment of 10 RR intervals immediately preceding the first PLMS series (baseline; –1), and at the start of the first PLMS series (point 0), as well as from subsequent 10 RR interval segments located after each successive PLMS series from 1 to 10 (Fig. 1).

Determination of the HRV HF parameter allowed the assessment of short-term HRV, represented by changes in high frequency (0.15–0.4 Hz) [38]. Short-term variability is

Table 1. Inclusion and exclusion criteria applied in study

Inclusion criteria	Exclusion criteria
Age 18–65	Age < 18
Diagnosis of RLS	Age > 65
PLMS without arousal	PLMS with arousal
Treatment of non-excluded medical conditions stable for ≥ 2 weeks preceding PSG	Respiratory events
	Apnoea/hypopnoea index ≥ 5
	Antipsychotics, sedatives, antidepressants, lithium, B-blockers, or Ca-blockers intake
	Renal diseases, diabetes mellitus, depression, anxiety disorders, heart diseases, psychotic disorders, and arrhythmias diagnosis

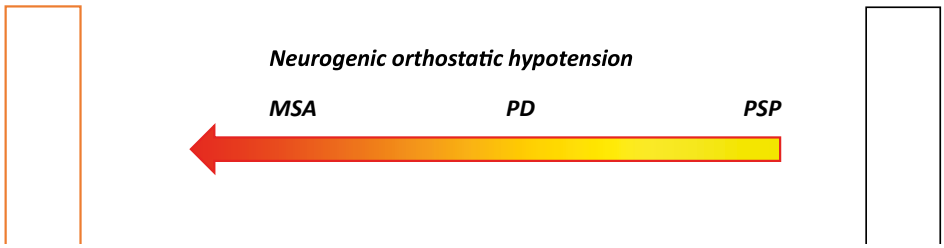

Figure 1. Demonstration of PLMS in a series; point 0 indicates start of 1st PLMS in series. Time window location (1–10) was assessed as 10 RR intervals after each PLMS (1–10). Baseline indicates point of 10 RR intervals before start of series. For each RR interval in window and baseline, value of HR, SBP, DBP and HRV HF was assessed

representative of parasympathetic influences on heart rhythm. The choice of HRV HF estimation was dictated by short time windows, which in turn were determined by the nature of the records.

The presented method of using successive, short, 10 RR interval segments refers to the time-frequency measurement, which is very clear and useful for presenting changes in the calculated parameters over time and thereby illustrating their dynamics. Calculation of HRV analysis parameters from many consecutive short time windows is widely used in time-frequency analysis. Using this method allowed us to assess any dynamic changes in HRV HF during successive PLMS series. To the best of our knowledge, we are the first to study dynamic changes in intracardiac ANS activity in conjunction with PLMS.

All tested parameters: HR, HRV HF, and BP (SBP and DBP) were averaged for all subsequent PLMS series. Moreover, the value of data was subtracted from the baseline rate, defined as the value of data before leg movement (in point "–1"), to obtain the rate of change for each data type.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (v. 28.0.0.0). A one-sample test was performed to check if these measurements differed significantly from each other. The analysis showed that only SBP changes had no statistically significant change ($p = 0.0589$; the other parameters had $p < 0.05$). None of the data had a normal distribution (normality test $p < 0.001$). The Kruskal–Wallis test was performed to find statistically significant changes from baseline. This analysis was carried out to compare responses to leg movement from each type of data compared to baseline values (before PLMS). The statistically significant changes showed data from HRV_HF between series "–1" and series "9" ($p = 0.026$).

Results

We found no statistically significant changes in HR, SBP, or DBP in our group (Tab. 2, 3). In the assessed group of patients, HRV HF changed after the series of eight PLMS (Fig. 2). The average of the evoked change in HRV HF, calculated as

Table 2. Average value of parameters obtained for each PLMS, where "–1" is period before beginning of limb movement ("0")

Movement	HR	SBP	DBP	HRV HF
–1	59.22	127.84	69.53	307.08
0	58.02	125.81	68.86	354.96
1	59.72	127.60	70.82	356.43
2	58.43	126.42	70.33	358.02
3	59.28	126.84	70.98	357.55
4	58.02	127.12	71.11	362.38
5	58.67	126.24	69.83	364.65
6	57.24	124.53	69.21	377.45
7	55.96	125.56	70.01	446.98
8	57.26	126.53	69.58	472.44
9	56.46	125.69	69.26	476.50
10	58.00	126.28	68.85	475.32

DBP — diastolic blood pressure, HR — heart rate; HRV HF — heart rate variability high frequency; SBP — systolic blood pressure

Table 3. Average changes in value (difference between value of each parameter and mean value before PLMS) of parameters obtained for each PLMS, where "–1" is period before beginning of limb movement ("0")

Movement	HR change	SBP change	DBP change	HRV HF change
–1	0.00	0.03	–0.05	0.03
0	–0.28	–0.43	–0.51	0.42
1	1.42	1.33	1.45	1.89
2	0.14	0.17	0.96	3.48
3	0.99	0.65	1.61	3.01
4	–0.72	–1.14	1.19	5.05
5	–0.08	0.23	–0.08	7.31
6	–2.29	0.78	0.71	11.86
7	–2.19	–0.46	0.83	22.50
8	–1.05	0.48	1.74	24.87
9	–1.85	–0.36	1.43	28.94
10	–0.11	0.25	0.91	32.13

DBP — diastolic blood pressure, HR — heart rate; HRV HF — heart rate variability high frequency; SBP — systolic blood pressure

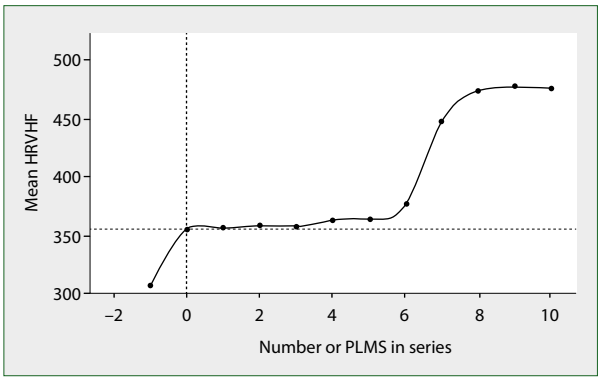

Figure 2. Average of evoked HRV HF for each PLMS. Horizontal dashed line represents mean HRV before limb movement, while vertical dashed line marks beginning of limb movement. HRV HF — heart rate variability high frequency; PLMS — periodic limb movements in sleep

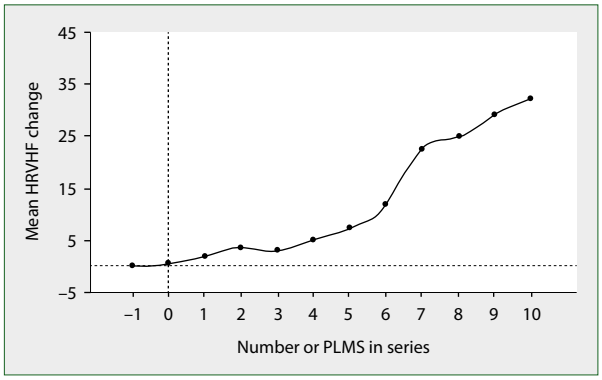

Figure 3. Average change in evoked HRV HF (calculated as difference between each HRV and mean HRV before limb movement) for each PLMS. Horizontal dashed line represents mean HRV before limb movement, while vertical dashed line marks beginning of limb movement. HRV HF — heart rate variability high frequency; PLMS — periodic limb movements in sleep; HR — .heart beats/ /min; HR change calculated as difference between actual HR and mean HR before leg movement; HR baseline calculated as mean HR before leg movement; SBP/DBP/HRV HF baseline calculated as difference between actual value and mean value before leg movement; movement calculated as number of series, where "–1" is before start of movement and "0" is start of movement

the difference between each HRV and mean HRV before leg movement for each PLMS, also increased after the series of eight PLMS (Fig. 3).

Discussion

The main finding of our study is that following eight PLMS in a series, HRV HF increased with no increase in HR and BP. To the best of our knowledge, we are the first to report such an effect.

We focused on sequential PLMS series and related changes in BP, HR and HRV HF. Previous research has analysed a single PLMS or limited numbers of PLMS patterns [7, 14, 29]. In our research, we focused on all the PLMS events during sleep in all five patients.

The results that we present do not indicate a significant and systematic increase in systolic and diastolic blood pressure as well as HR during subsequent series of PLMS. These results contradict some reports that have recorded both an increase in HR and in BP before PLMS. It has been reported that as much as 99% of PLMS is associated with changes in HR [39]. Increases in HR and BP are associated with increased sympathetic arousal, sometimes in combination with arousal in EEG, shortly before the onset of periodic limb movement [30, 40]. In our study however, PLMS with arousals were excluded, which could explain the lack of changes in HR and BP.

Sympathetic hyperactivity may also have an important effect on BP, increasing it up to 30 mmHg [41]. On the other hand, although our results did not indicate a change in HR and BP, we do not rule out an increase in intracardiac sympathetic activity. We believe that the increase in sympathetic activity was marked, as it counterbalanced the increase in intracardiac parasympathetic activity, which resulted in no change in HR and BP.

Since our results indicate a significant increase in short-term variability, expressed by the HRV HF, we hypothesise an increase in intracardiac parasympathetic activity, alongside the appearance of successive PLMS series. We postulate a simultaneous increase in intracardiac sympathetic and parasympathetic activity.

Although this assumption does not contradict the traditional view of the role of the ANS in the establishment of HR, associated with the opposing action of the sympathetic and parasympathetic systems on the heart rhythm, it does suggest the co-activation of the sympathetic and parasympathetic systems in such a way that they occur in parallel with each other.

Almost 30 years ago, Pagani et al. [42] proposed that HRV analysis be applied to evaluate the balance between two branches of the ANS. This was related to three core statements: 1) the power spectral density (PSD) of the HF component can be taken as an index of cardiac parasympathetic tone; 2) the PSD of the LF component may be a marker of cardiac sympathetic outflow; and 3) the balance between the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) can be assessed as the LF/HF ratio, usually interpreted as the relative SNS contribution to the control of HR. Surprisingly, despite evidence to the contrary [43–45], these measures are still extensively used to index the so-called 'sympathovagal balance'. The concept of autonomic balance and its LF/HF mathematical expression is based on the traditional doctrine of autonomic reciprocity.

The traditional view of the SNS and PNS is that they function in opposition to each other. The SNS is often considered the 'fight or flight' system, while the PNS is responsible for

'rest and digest' or 'feed and breed' activities [46]. The SNS is activated by exercise, cold and anxiety to divert bloodflow away from the gastro-intestinal tract and skin (via vasoconstriction) to the brain, heart, skeletal muscles and lungs. In addition, SNS activation increases HR and myocardial contractility, further enhancing bloodflow to the brain and skeletal muscles [47].

According to this doctrine, the sympathetic and parasympathetic branches of the ANS are subjected to reciprocal central nervous control, in the sense that increased activation of one system is accompanied by inhibition of the other [48]. This view, however, seems somewhat simplistic. Instead, the SNS and PNS interact in a dynamic fashion, and either reciprocity or co-activation of both branches may occur [44, 49].

Baroreflex represents a typical physiological example of reciprocal activation of the ANS. It allows for a powerful and quick, but not precisely controlled, response to a rise/decline in BP through activation of PNS or SNS outflow to the heart, respectively [47]. However, the SNS/PNS relation seems to be more like the yin-yang principle where the interrelation of opposites is essential, and the SNS and PNS are indispensable to each other [50, 51]. Examples of SNS/PNS co-activation include: peripheral chemoreflex (PChR) [50], trigemino-cardiac reflexes (TCRs) [52, 53], panic disorder [54], emotional sadness [55], and visceral pain [56], to name but a few.

Sympathetic and parasympathetic co-activation, however, can lead to life-threatening cardiovascular events [57]. This is due to the parasympathetic chromotropic effect, slowing down the speed of conduction of excitation between the atria and ventricles, which can cause partial or complete atrioventricular block or even lead to asystole for several seconds. On the other hand, an increase in sympathetic activity directed at ventricular cells may lead to the appearance of ectopic areas and associated ventricular extrasystoles. These are just a few examples of cardiac arrhythmias that may occur. There are also studies confirming the connection between a higher prevalence of cardiac arrhythmia such as atrial fibrillation in PLMS [58–60]. Any causal role for PLMS in the pathogenesis of cardiovascular diseases including arrhythmias requires further investigation.

In general, a regular cardiac rhythm is maintained by a strictly regulated balance of sympathetic and vagal tone. Simultaneous co-activation of both branches of the ANS is associated with a potential risk of cardiac arrhythmia [61] and might determine a possible additive notable risk factor of cardiovascular disease in PLMS patients. According to Koo et al., both sympathetic and parasympathetic activity are likely to be hyperactive in patients with PLMS and in older men with PLMS and structural heart disease, or in those who in the absence of anti-arrhythmic medication are more prone to cardiac arrhythmias [58].

Our data, combined with earlier reports suggesting sympathetic activity, may potentially highlight the co-activation of both the sympathetic and parasympathetic divisions of the ANS, determining possible autonomic dysregulation. Sasai et al. have also described a consecutive elevation of HRV HF fluctuation after these changes, suggesting that parasympathetic nervous activity becomes unstable, which is consistent with our findings [7].

There are some limitations to our work. Short time windows did not allow us to calculate the long-term variability of HRV. Spectral power in the low frequency (LF) range corresponds to HR changes of 2.4–9 beats per minute (0.04–0.15 Hz). Originally, the LF band was thought to be an indicator of intracardiac sympathetic activity. However, the assumption of a simple relationship between the sympathetic activity and HRV in the low frequency range was not confirmed in further studies. Intracardiac parasympathetic activity may contribute to some extent in the LF component. This is evidenced by research related to the blockade of muscarinic receptors — M1, which leads not only to the reduction of the HF band, but also the low-frequency component — LF [62].

The use of AASM rules might be considered another limitation of this study. Although PSG recordings were scored accordingly to AASM guidelines, the new guidelines of the IRLSSG/WASM were considered as far as respiratory event-related leg movements were concerned. In selecting PLMS episodes which underwent further analysis, special attention was given to exclude events that might have been triggered by a respiratory event.

Finally, our sample size was small. Nevertheless, there were no PLMS related to the arousals criteria [63] defined as transient increases in higher frequency EEG activity occurring with increases of SNS activity. In addition, in all patients, changes in the HRV were in the same direction, an observation that actually strengthens our reasoning. The process of 1,348 leg movements and its influence on used parameters was analysed, which we believe support our inferences.

Clinical implications

The findings of our current study add to the literature information regarding HRV in PLMS, and highlight the need for further studies to elucidate the effects of these conditions on the ANS, and cardiovascular health. In particular, the effects of the PLMS series on the ANS should be more closely monitored.

Article information

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Conflicts of interest: None.

References

1. Coleman RM, Pollak CP, Weitzman ED. Periodic movements in sleep (nocturnal myoclonus): relation to sleep disorders. Ann Neurol. 1980; 8(4): 416–421, doi: 10.1002/ana.410080413, indexed in Pubmed: 7436384.

2. Montplaisir J, Boucher S, Poirier G, et al. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. Mov Disord. 1997; 12(1): 61–65, doi: 10.1002/mds.870120111, indexed in Pubmed: 8990055.
3. El-Ad B, Korczyn AD. Disorders of excessive daytime sleepiness — an update. J Neurol Sci. 1998; 153(2): 192–202, doi: 10.1016/s0022-510x(97)00291-8, indexed in Pubmed: 9511878.
4. Jo H, Kim D, Song J, et al. Sleep disturbances and phenoconversion in patients with REM sleep behavior disorder. J Clin Med. 2021; 10(20), doi: 10.3390/jcm10204709, indexed in Pubmed: 34682832.
5. Drakatos P, Olaithe M, Verma D, et al. Periodic limb movements during sleep: a narrative review. J Thorac Dis. 2021; 13(11): 6476–6494, doi: 10.21037/jtd-21-1353, indexed in Pubmed: 34992826.
6. Lin CC, Chou CH, Fan YM, et al. Increased Risk of Dementia Among Sleep-Related Movement Disorders: A Population-Based Longitudinal Study in Taiwan. Medicine (Baltimore). 2015; 94(51): e2331, doi: 10.1097/MD.0000000000002331, indexed in Pubmed: 26705224.
7. Sasai T, Matsuura M, Inoue Y. Change in heart rate variability precedes the occurrence of periodic leg movements during sleep: an observational study. BMC Neurol. 2013; 13: 139, doi: 10.1186/1471-2377-13-139, indexed in Pubmed: 24093585.
8. Allena M, Campus C, Morrone E, et al. Periodic limb movements both in non-REM and REM sleep: relationships between cerebral and autonomic activities. Clin Neurophysiol. 2009; 120(7): 1282–1290, doi: 10.1016/j.clinph.2009.04.021, indexed in Pubmed: 19505849.
9. Karadeniz D, Ondze B, Besset A, et al. EEG arousals and awakenings in relation with periodic leg movements during sleep. J Sleep Res. 2000; 9(3): 273–277, doi: 10.1046/j.1365-2869.2000.00202.x, indexed in Pubmed: 11012867.
10. Ferrillo F, Beelke M, Canovaro P, et al. Changes in cerebral and autonomic activity heralding periodic limb movements in sleep. Sleep Med. 2004; 5(4): 407–412, doi: 10.1016/j.sleep.2004.01.008, indexed in Pubmed: 15223001.
11. Barone DA, Ebben MR, DeGrazia M, et al. Heart rate variability in restless legs syndrome and periodic limb movements of Sleep. Sleep Sci. 2017; 10(2): 80–86, doi: 10.5935/1984-0063.20170015, indexed in Pubmed: 28966745.
12. Koo BB, Blackwell T, Ancoli-Israel S, et al. Osteoporotic Fractures in Men (MrOS) Study Group. Association of incident cardiovascular disease with periodic limb movements during sleep in older men: outcomes of sleep disorders in older men (MrOS) study. Circulation. 2011; 124(11): 1223–1231, doi: 10.1161/CIRCULATIONAHA.111.038968, indexed in Pubmed: 21859975.
13. Walters AS, Rye DB. Review of the relationship of restless legs syndrome and periodic limb movements in sleep to hypertension, heart disease, and stroke. Sleep. 2009; 32(5): 589–597, doi: 10.1093/sleep/32.5.589, indexed in Pubmed: 19480225.
14. Sieminski M, Pyrzowski J, Partinen M. Periodic limb movements in sleep are followed by increases in EEG activity, blood pressure, and heart rate during sleep. Sleep Breath. 2017; 21(2): 497–503, doi: 10.1007/s11325-017-1476-7, indexed in Pubmed: 28190164.
15. Pennestri MH, Montplaisir J, Colombo R, et al. Nocturnal blood pressure changes in patients with restless legs syndrome. Neurology. 2007; 68(15): 1213–1218, doi: 10.1212/01.wnl.0000259036.89411.52, indexed in Pubmed: 17420405.
16. Siddiqui F, Strus J, Ming X, et al. Rise of blood pressure with periodic limb movements in sleep and wakefulness. Clin Neurophysiol. 2007; 118(9): 1923–1930, doi: 10.1016/j.clinph.2007.05.006, indexed in Pubmed: 17588809.
17. Sforza E, Nicolas A, Lavigne G, et al. EEG and cardiac activation during periodic leg movements in sleep: support for a hierarchy of arousal responses. Neurology. 1999; 52(4): 786–791, doi: 10.1212/wnl.52.4.786, indexed in Pubmed: 10078729.
18. Thayer JF, Brosschot JF. Psychosomatics and psychopathology: looking up and down from the brain. Psychoneuroendocrinology. 2005; 30(10): 1050–1058, doi: 10.1016/j.psyneuen.2005.04.014, indexed in Pubmed: 16005156.
19. Koch C, Wilhelm M, Salzmann S, et al. A meta-analysis of heart rate variability in major depression. Psychol Med. 2019; 49(12): 1948–1957, doi: 10.1017/S0033291719001351, indexed in Pubmed: 31239003.
20. Faurholt-Jepsen M, Kessing LV, Munkholm K. Heart rate variability in bipolar disorder: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2017; 73: 68–80, doi: 10.1016/j.neubiorev.2016.12.007, indexed in Pubmed: 27986468.
21. Chalmers JA, Quintana DS, Abbott MJA, et al. Anxiety disorders are associated with reduced heart rate variability: a meta-analysis. Front Psychiatry. 2014; 5: 80, doi: 10.3389/fpsyt.2014.00080, indexed in Pubmed: 25071612.
22. Clamor A, Lincoln TM, Thayer JF, et al. Resting vagal activity in schizophrenia: meta-analysis of heart rate variability as a potential endophenotype. Br J Psychiatry. 2016; 208(1): 9–16, doi: 10.1192/bjp.bp.114.160762, indexed in Pubmed: 26729841.
23. Heimrich KG, Lehmann T, Schlattmann P, et al. Heart rate variability analyses in Parkinson's disease: a systematic review and meta-analysis. Brain Sci. 2021; 11(8), doi: 10.3390/brainsci11080959, indexed in Pubmed: 34439578.
24. Kwaśniak-Butowska M, Dulski J, Pierzchlińska A, et al. Cardiovascular dysautonomia and cognition in Parkinson's Disease - a possible relationship. Neurol Neurochir Pol. 2021; 55(6): 525–535, doi: 10.5603/PJNNS.a2021.0040, indexed in Pubmed: 34037978.
25. Siuda J. Importance of non-motor symptoms in PD and atypical parkinsonism. Neurol Neurochir Pol. 2021; 55(6): 503–507, doi: 10.5603/PJNNS.a2021.0085, indexed in Pubmed: 34939662.
26. Lee D, Baek JiH, Cho YJi, et al. Association of resting heart rate and heart rate variability with proximal suicidal risk in patients with diverse psychiatric diagnoses. Front Psychiatry. 2021; 12: 652340, doi: 10.3389/fpsyt.2021.652340, indexed in Pubmed: 33995148.
27. Kang GuE, Patriquin MA, Nguyen H, et al. Objective measurement of sleep, heart rate, heart rate variability, and physical activity in suicidality: A systematic review. J Affect Disord. 2020; 273: 318–327, doi: 10.1016/j.jad.2020.03.096, indexed in Pubmed: 32421619.
28. Wojtasz I, Tomski A, Kaźmierski R. Association between nocturnal oxygen desaturation and ischaemic stroke outcomes. Neurol Neurochir Pol. 2022; 56(3): 267–275, doi: 10.5603/PJNNS.a2022.0033, indexed in Pubmed: 35607842.
29. Lavoie S, de Bilbao F, Haba-Rubio J, et al. Influence of sleep stage and wakefulness on spectral EEG activity and heart rate variations around periodic leg movements. Clin Neurophysiol. 2004; 115(10): 2236–2246, doi: 10.1016/j.clinph.2004.04.024, indexed in Pubmed: 15351364.
30. Guggisberg AG, Hess CW, Mathis J. The significance of the sympathetic nervous system in the pathophysiology of periodic leg movements in sleep. Sleep. 2007; 30(6): 755–766, doi: 10.1093/sleep/30.6.755, indexed in Pubmed: 17580597.
31. Sforza E, Juony C, Ibanez V. Time-dependent variation in cerebral and autonomic activity during periodic leg movements in sleep:

implications for arousal mechanisms. Clin Neurophysiol. 2002; 113(6): 883–891, doi: 10.1016/s1388-2457(02)00066-4, indexed in Pubmed: 12048047.
32. Walter LM, Foster AM, Patterson RR, et al. Cardiovascular variability during periodic leg movements in sleep in children. Sleep. 2009; 32(8): 1093–1099, doi: 10.1093/sleep/32.8.1093, indexed in Pubmed: 19725261.
33. Sforza E, Pichot V, Barthelemy JC, et al. Cardiovascular variability during periodic leg movements: a spectral analysis approach. Clin Neurophysiol. 2005; 116(5): 1096–1104, doi: 10.1016/j.clinph.2004.12.018, indexed in Pubmed: 15826850.
34. Izzi F, Placidi F, Romigi A, et al. Is autonomic nervous system involved in restless legs syndrome during wakefulness? Sleep Med. 2014; 15(11): 1392–1397, doi: 10.1016/j.sleep.2014.06.022, indexed in Pubmed: 25266501.
35. Gesche H, Grosskurth D, Küchler G, et al. Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method. Eur J Appl Physiol. 2012; 112(1): 309–315, doi: 10.1007/s00421-011-1983-3, indexed in Pubmed: 21556814.
36. IBER, C. The AASM Manual for the Scoring of Sleep and Associated Events: Rules. Terminol Tech Specif [Internet]. 2007. https://ci.nii.ac.jp/naid/10024500923 (26.01.2022).
37. Ferri R, Fulda S, Allen RP, et al. International and European Restless Legs Syndrome Study Groups (IRLSSG and EURLSSG). World Association of Sleep Medicine (WASM) 2016 standards for recording and scoring leg movements in polysomnograms developed by a joint task force from the International and the European Restless Legs Syndrome Study Groups (IRLSSG and EURLSSG). Sleep Med. 2016; 26: 86–95, doi: 10.1016/j.sleep.2016.10.010, indexed in Pubmed: 27890390.
38. Dodds KL, Miller CB, Kyle SD, et al. Heart rate variability in insomnia patients: A critical review of the literature. Sleep Med Rev. 2017; 33: 88–100, doi: 10.1016/j.smrv.2016.06.004, indexed in Pubmed: 28187954.
39. Gosselin N, Lanfranchi P, Michaud M, et al. Age and gender effects on heart rate activation associated with periodic leg movements in patients with restless legs syndrome. Clin Neurophysiol. 2003; 114(11): 2188–2195, doi: 10.1016/s1388-2457(03)00206-2, indexed in Pubmed: 14580618.
40. Winkelman JW. The evoked heart rate response to periodic leg movements of sleep. Sleep. 1999; 22(5): 575–580, doi: 10.1093/sleep/22.5.575, indexed in Pubmed: 10450592.
41. Cuellar NG. The effects of periodic limb movements in sleep (PLMS) on cardiovascular disease. Heart Lung. 2013; 42(5): 353–360, doi: 10.1016/j.hrtlng.2013.07.006, indexed in Pubmed: 23998383.
42. Pagani M, Lombardi F, Guzzetti S, et al. Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circ Res. 1986; 59(2): 178–193, doi: 10.1161/01.res.59.2.178, indexed in Pubmed: 2874900.
43. Goldstein DS, Bentho O, Park MY, et al. Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes. Exp Physiol. 2011; 96(12): 1255–1261, doi: 10.1113/expphysiol.2010.056259, indexed in Pubmed: 21890520.
44. Reyes del Paso GA, Langewitz W, Mulder LJM, et al. The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: a review with emphasis on a reanalysis of previous studies. Psychophysiology. 2013; 50(5): 477–487, doi: 10.1111/psyp.12027, indexed in Pubmed: 23445494.
45. Ritz T. Studying noninvasive indices of vagal control: the need for respiratory control and the problem of target specificity. Biol Psychol. 2009; 80(2): 158–168, doi: 10.1016/j.biopsycho.2008.08.003, indexed in Pubmed: 18775468.
46. Massaro S, Pecchia L. Heart rate variability (HRV) analysis: a methodology for organizational neuroscience. Organ Res Methods. 2016; 22(1): 354–393, doi: 10.1177/1094428116681072.
47. Kawano H, Okada R, Yano K. Histological study on the distribution of autonomic nerves in the human heart. Heart Vessels. 2003; 18(1): 32–39, doi: 10.1007/s003800300005, indexed in Pubmed: 12644879.
48. Crick SJ, Wharton J, Sheppard MN, et al. Innervation of the human cardiac conduction system. A quantitative immunohistochemical and histochemical study. Circulation. 1994; 89(4): 1697–1708, doi: 10.1161/01.cir.89.4.1697, indexed in Pubmed: 7908612.
49. Behnke M, Kreibig S, Kaczmarek L, et al. Autonomic nervous system activity during positive emotions: a meta-analytic review. Emotion Review. 2022; 14(2): 132–160, doi: 10.1177/17540739211073084.
50. Kollai M, Koizumi K. Reciprocal and non-reciprocal action of the vagal and sympathetic nerves innervating the heart. J Auton Nerv Syst. 1979; 1(1): 33–52, doi: 10.1016/0165-1838(79)90004-3, indexed in Pubmed: 553085.
51. Paton JFR, Boscan P, Pickering AE, et al. The yin and yang of cardiac autonomic control: vago-sympathetic interactions revisited. Brain Res Brain Res Rev. 2005; 49(3): 555–565, doi: 10.1016/j.brainresrev.2005.02.005, indexed in Pubmed: 16269319.
52. Chen CY, Luo CF, Hsu YC, et al. Comparison of the effects of atropine and labetalol on trigeminocardiac reflex-induced hemodynamic alterations during percutaneous microballoon compression of the trigeminal ganglion. Acta Anaesthesiol Taiwan. 2012; 50(4): 153–158, doi: 10.1016/j.aat.2012.11.001, indexed in Pubmed: 23385037.
53. Malinowski KS, Wierzba TH, Neary JP, et al. Heart rate variability at rest predicts heart response to simulated diving. Biology (Basel). 2023; 12(1), doi: 10.3390/biology12010125, indexed in Pubmed: 36671817.
54. Ito T, Inoue Y, Sugihara T, et al. Autonomic function in the early stage of panic disorder: power spectral analysis of heart rate variability. Psychiatry Clin Neurosci. 1999; 53(6): 667–672, doi: 10.1046/j.1440-1819.1999.00623.x, indexed in Pubmed: 10687748.
55. Rash JA, Prkachin KM. Cardiac vagal reactivity during relived sadness is predicted by affect intensity and emotional intelligence. Biol Psychol. 2013; 92(2): 106–113, doi: 10.1016/j.biopsycho.2012.11.009, indexed in Pubmed: 23182876.
56. Paine P, Kishor J, Worthen SF, et al. Exploring relationships for visceral and somatic pain with autonomic control and personality. Pain. 2009; 144(3): 236–244, doi: 10.1016/j.pain.2009.02.022, indexed in Pubmed: 19398272.
57. Hansel J, Solleder I, Gfroerer W, et al. Hypoxia and cardiac arrhythmias in breath-hold divers during voluntary immersed breath-holds. Eur J Appl Physiol. 2009; 105(5): 673–678, doi: 10.1007/s00421-008-0945-x, indexed in Pubmed: 19034490.
58. Koo BB, Mehra R, Blackwell T, et al. Osteoporotic Fractures in Men (MrOS) Study Group. Periodic limb movements during sleep and cardiac arrhythmia in older men (MrOS sleep). J Clin Sleep Med. 2014; 10(1): 7–11, doi: 10.5664/jcsm.3346, indexed in Pubmed: 24426814.
59. Mirza M, Shen WK, Sofi A, et al. Frequent periodic leg movement during sleep is an unrecognized risk factor for progression of atrial fibrillation. PLoS One. 2013; 8(10): e78359, doi: 10.1371/journal.pone.0078359, indexed in Pubmed: 24147132.

60. May AM, Blackwell T, Stone KL, et al. Osteoporotic Fractures in Men (MrOS) Study Group. Longitudinal relationships of periodic limb movements during sleep and incident atrial fibrillation. Sleep Med. 2016; 25: 78–86, doi: 10.1016/j.sleep.2016.08.009, indexed in Pubmed: 27823721.
61. Shattock M, Tipton M. 'Autonomic conflict': a different way to die during cold water immersion? J Physiol. 2012; 590(14): 3219–3230, doi: 10.1113/jphysiol.2012.229864, indexed in Pubmed: 22547634.
62. Pomeranz B, Macaulay RJ, Caudill MA, et al. Assessment of autonomic function in humans by heart rate spectral analysis. Am J Physiol. 1985; 248(1 Pt 2): H151–H153, doi: 10.1152/ajpheart.1985.248.1.H151, indexed in Pubmed: 3970172.
63. Ferri R, Rundo F, Zucconi M, et al. An evidence-based analysis of the association between periodic leg movements during sleep and arousals in restless legs syndrome. Sleep. 2015; 38(6): 919–924, doi: 10.5665/sleep.4740, indexed in Pubmed: 25581922.