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Research Article

Periodic Limb Movements during Sleep in Children, Adolescents, and Adults with Narcolepsy: A Cross-Sectional Study in China

Xianchao Zhao,[1,2] **Jiafeng Ren**,[1,2] **Guoyan Chen**,[1,2] **Jinxiang Cheng**,[1,2] **Danqing Shang**,[1,2] **Min Wu**,[3,4] **Yiqing Yang**,[5] **Junying Zhou**,[6,7] **and Changjun Su**[1,2]

[1]*Department of Neurology, Tangdu Hospital, Fourth Military Medical University, Xi' an, China*
[2]*Sleep Medicine Center, Tangdu Hospital, Fourth Military Medical University, Xi'an, China*
[3]*West China School of Nursing, Sichuan University/Sleep Medicine Center, West China Hospital, Sichuan University, Chengdu, China*
[4]*Shihezi University School of Medicine, Shihezi University, Shihezi, China*
[5]*Basic Medical School of the Fourth Military Medical University, Xi'an, China*
[6]*Sleep Medicine Center, West China Hospital, Sichuan University, Chengdu, China*
[7]*Department of Neurology, West China Hospital, Sichuan University, Chengdu, China*

Correspondence should be addressed to Junying Zhou; zhoujy2016@scu.edu.cn and Changjun Su; changjunsu@163.com

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Objectives. This study is aimed at determining the prevalence and effects of periodic limb movements during sleep (PLMS) on nighttime sleep and daytime sleepiness in children/adolescents and adults with narcolepsy. *Methods*. A total of 94 patients with narcolepsy were recruited in this study. They were classified into two groups including children/adolescents (<18 years, $n = 41$) and adults (≥18 years, $n = 53$). All participants completed face-to-face interviews and underwent polysomnography assessment followed by multiple sleep latency test. Demographic, clinical, and sleep parameters were compared between narcoleptic patients with and without PLMS. Linear regression analysis was performed to determine the association between PLMS and sleep parameters. *Results*. Thirty-eight (40.4%) patients with narcolepsy were defined as having PLMS, and there was a higher prevalence of PLMS in the children/adolescents than in the adults with narcolepsy (56.1% vs. 28.3%, respectively, $P = 0.006$). Narcoleptic patients with PLMS had a significantly shorter total sleep time, lower sleep efficiency (SE), and more wakefulness after sleep onset (WASO) than those without PLMS in adults (all $P < 0.05$). After adjusting for the potential confounders, PLMS was significantly associated with lower SE (adjusted $\beta = -0.327$; 95% CI: -0.608, 0.044; $P = 0.025$) and more WASO (adjusted $\beta = 0.330$; 95% CI: 0.038, 0.520; $P = 0.028$) in adults with narcolepsy. *Conclusions*. There is a high prevalence of PLMS in narcolepsy, especially in children and adolescent patients. PLMS is associated with nighttime sleep disturbance in adults with narcolepsy but is not a risk factor for daytime sleepiness both in children/adolescents and adults with narcolepsy.

1. Introduction

Narcolepsy is a rare, chronic hypersomnolence with a prevalence of 0.02%-0.06%, which is recognized as a hypothalamic disorder associated with sleep-wake dysregulation [1, 2]. Currently, it has been classified into two classic subtypes including narcolepsy type 1 (with cataplexy) and narcolepsy type 2 (without cataplexy). The essential features of narcolepsy include excessive daytime sleepiness (EDS), cataplexy, hypnagogic hallucinations, sleep paralysis, and disrupted nocturnal sleep (e.g., insomnia, obstructive sleep apnea (OSA), and rapid eye movement sleep behavior disorder (RBD)). In addition, narcolepsy not only presents a sleep-wake disorder but also comorbid motor, psychiatric, emotional, cognitive, metabolic,

and autonomic dysfunctions. Periodic limb movements during sleep (PLMS) is one of the motor control dysfunctions during sleep, which might be present in 25–50% of patients with narcolepsy [3]. The dysfunction in the hypocretin/DA system is likely to be the most important mechanism related to the pathophysiology of narcolepsy, which presents not only with alterations in arousal systems but also with sleep-related motor activation such as PLMS [4–6].

Narcolepsy usually occurs in adolescence with the first peak (age 15 years), and the second peak occurs in adults at the age of 35 years. Dauvilliers et al. have shown that the increase in PLMS was more common in adult patients with narcolepsy than controls without narcolepsy. Furthermore, they reported that narcoleptics had a higher rate of periodic limb movement index (PLMI) greater than 5 per hour of sleep than controls (67% versus 37%, respectively), and similar results were also found with PLMI greater than 10 (53% versus 21%, respectively) [4]. In addition, previous data showed that up to 70% of patients with narcolepsy type 1 have PLMI ≥ 5 [7]. Interestingly, Nevsimalova et al. found that the prevalence of PLMS in narcolepsy had a positive correlation with age, especially above 40 years, which increased significantly [8]. In the general population, some studies have shown that participants with PLMI > 15/h have more propensity to self-reported insomnia symptoms and poor sleep architecture, but the association between PLMS and subjective/objective sleepiness is still controversial [9–11]. The current literature showed that PLMS was correlated with the severity of nocturnal sleep disruption in narcolepsy [4, 12]. Furthermore, narcoleptic patients with PLMS had shorter mean sleep latency in the multiple sleep latency test (MSLT) than those without PLMS in children and adolescent patients [12]. However, only a few studies have examined the disparities of sleep parameters and sleep-related adverse outcomes associated with PLMS in children or adult patients with narcolepsy [8, 11–13]. In the current study, we aimed to explore the characteristics and effects of PLMS on nighttime sleep and daytime sleepiness both in child/adolescent and adult patients with narcolepsy.

2. Methods

2.1. Study Participants. All participants were recruited from the Department of Neurology in Tangdu Hospital of the Fourth Military Medical University. This retrospective study was conducted on 94 consecutive newly diagnosed narcoleptic patients who underwent an overnight polysomnography (PSG) assessment and a subsequent multiple sleep latency test (MSLT) between January 2015 and December 2016. Patients fulfilled the narcolepsy criteria of the International Classification of Sleep Disorders, third edition (ICSD-3) [14]. They were classified into two groups, namely, children/adolescents and adults according to the age at diagnosis <18 years or ≥18 years, respectively. The study was approved by the Institutional Review Board of Tangdu Hospital of the Fourth Military Medical University, and all participants gave written informed consent.

2.2. Demography and Clinical Information. All participants completed face-to-face interviews to record demographic information and medical history. Demographic information including age of onset, age of diagnosis, sex, and body mass index (BMI) was collected. The clinical records related to narcolepsy included disease duration, symptoms of EDS, cataplexy, sleep paralysis, hypnagogic hallucinations, and disturbed nocturnal sleep (OSA, RBD, etc.). The Epworth Sleepiness Scale (ESS) was used to assess subjective daytime sleepiness. The participants self-rated the likelihood of daytime sleepiness in eight different situations on a four-point Likert scale from 0 to 3. The total score of ESS ranged from 0 to 24, and EDS was defined as ESS > 10 [15].

2.3. PSG and MSLT. All participants underwent an overnight PSG assessment followed by MSLT the next day (Philips Alice 6, Philips Respironics) at the Sleep Medicine Center of Tangdu Hospital. The recording of PSG included a standard electroencephalogram (EEG), electrooculogram (EOG), chin and bilateral anterior tibialis electromyogram (EMG), and electrocardiogram (ECG). Other measurements included oronasal thermal flow, nasal pressure, thoracic and abdominal respiratory efforts, oxygen saturation, snoring sound, and body position. The MSLT was used to measure objective daytime sleepiness and contained 5 scheduled naps according to the procedure recommended by the American Academy of Sleep Medicine (AASM) [16]. Sleep stages and associated events were manually scored by senior polysomnography technicians according to the AASM rule (version 2.3) [17]. OSA was defined as an apnea − hypopnea index (AHI) ≥ 1 event per hour in children and adolescents and AHI ≥ 5 events per hour in adults. PLMS was defined as PLMI > 5 events per hour in children and adolescents and PLMI > 15 events per hour in adults. The diagnosis of RBD was according to the criteria in ICSD-3 [14].

2.4. Statistical Analysis. We used Shapiro-Wilk tests for all the data to assess the normal distribution. Quantitative variables were expressed as means ± standard deviation (SD), and qualitative variables were presented as frequency (percentages). Pairwise comparisons were performed using a *t* test or Mann-Whitney *U* test depending on data distributions. Qualitative variables were compared by means of the chi-square test or Fisher's exact test. Linear regression analysis was performed to determine the associations between PLMS and objective sleep parameters (sleep efficiency (SE) and wakefulness after sleep onset (WASO)) related to nocturnal sleep quality in children/adolescents and adults. Statistical analyses were performed using SPSS for Windows software (version 22.0; SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

3. Results

3.1. Demographic and Clinical Characteristics. In this study, the mean age at diagnosis was 23.9 ± 14.3 years, and 66 (70.2%) patients were male. All patients with narcolepsy were divided into the child/adolescent group ($n = 41$, 43.6%) and the adult group ($n = 53$, 56.4%). We found that

PLMS was presented in 40.4% (38/94) of patients with narcolepsy. The child/adolescent group had a higher rate of PLMS when compared to adult patients (56.1% vs. 28.3%, respectively, $P < 0.05$), but there were no significant differences in different cutoff values of PLMI (e.g., PLMI ≥ 5/h, PLMI ≥ 10/h, PLMI ≥ 15/h, PLMI ≥ 20/h, PLMI ≥ 25/h, and PLMI ≥ 30/h) between the two groups (Figure 1). The demographic and clinical characteristics of 94 narcoleptic patients are shown in Table 1. The adult patients had older age both at onset and diagnosis, a higher proportion of males, longer duration of the disease, and higher BMI (all $P < 0.01$). Furthermore, the adult group had more severe daytime sleepiness and a higher proportion of hypnagogic hallucinations (all $P < 0.01$) but had a lower proportion of RBD ($P < 0.05$). In addition, the adult group had a slightly higher proportion of sleep paralysis ($P = 0.077$). Notably, there was no significant difference in the proportion of cataplexy between the two groups. More importantly, there were no significant differences in the above demographic and clinical characteristics between patients with and without PLMS both in the child/adolescent and adult groups.

3.2. Sleep Parameters in PSG and MSLT. The comparisons of sleep parameters between narcolepsy with and without PLMS in child/adolescent and adult groups are presented in Table 2. In adults, narcoleptic patients with PLMS had significantly shorter total sleep time (TST) (391.0 ± 61.0 vs. 432.4 ± 40.3, respectively, $P = 0.011$), lower sleep efficiency (SE) (81.8 ± 12.8 vs. 89.4 ± 7.4, respectively, $P = 0.03$), and more WASO (77.5 ± 53.5 vs. 44.6 ± 34.4, respectively, $P = 0.021$) than those without PLMS. However, there were no significant differences in sleep latency, arousal index, percentage of sleep stages (N1-3 and REM sleep), AHI, and MSLT variables including mean sleep latency and sleep onset REM periods (SOREMPs) between the groups. In the child/adolescent group, no significant differences were found in nocturnal PSG and MSLT variables except for PLMI between patients with and without PLMS.

3.3. Association between PLMS and Nocturnal Sleep Quality. To further explore the effect of PLMS on nocturnal sleep quality in child/adolescent and adult patients with narcolepsy, the linear regression analysis is shown in Figure 2. SE and WASO were set as the dependent variables in the regression model. The linear regression models were adjusted for age, sex, BMI, disease duration, and narcolepsy type. The results showed that PLMS was significantly associated with lower SE (adjusted $\beta = -0.327$; 95% CI: -0.608, 0.044; $P = 0.025$) and more WASO (adjusted $\beta = 0.330$; 95% CI: 0.038, 0.520; $P = 0.028$) in adult patients with narcolepsy. However, there was no significant association between PLMS and SE/WASO after adjusting the same confounders in the child/adolescent group.

4. Discussion

As far as we know, there is little literature investigating the characteristics and effects of PLMS both in child/adolescent and adult patients with narcolepsy. The present study found that the prevalence of PLMS was 56.1% in children/adolescents and 28.3% in adults with narcolepsy. After controlling for the potential influence factors, we also identified that PLMS was the risk factor associated with nighttime sleep disruption in adults, but not in children and adolescents with narcolepsy. In addition, we did not investigate the significant effect of PLMS on the subjective and objective daytime sleepiness both in adult and child/adolescent groups.

Our finding of PLMS prevalence in narcolepsy (40.4%) is rather similar to those previously reported (25-63.2%) [3, 6, 18], which is significantly higher than that reported in the general population (7.6%) [13]. The high prevalence of PLMS in narcolepsy has suggested that PLMS could be an intrinsic feature of narcolepsy [12]. Genetic diathesis, iron status, and dopaminergic impairment have been implicated in the pathophysiology of PLMS [4, 14, 19, 20]. The previous study showed that there is an age-associated increase in the prevalence of PLMS in the general population. And the increasing PLMS is probably associated with the decrease of D2 receptors which has been demonstrated in healthy humans and animals with advancing age [21, 22]. However, in our narcoleptic cases, although PLMI increased with age, the rate of PLMS was found to be higher in children and adolescents than in adults (56.1% vs. 28.3%, respectively) based on the cutoff value of PLMI (children/adolescents: PLMI > 5/h; adults: PLMI > 15/h). Previous studies had inconsistent findings in the prevalence of PLMS in children and adolescents with narcolepsy, in which two studies reported a high prevalence of 36-63% [12, 23], and the other two studies found a lower prevalence of PLMS of 7%-16.1% [8, 24]. In children and adolescents, PLMS have been observed more frequently in individuals with restless leg syndrome (RLS), OSA, narcolepsy, attention deficit and hyperactivity disorder (ADHD), and iron deficiency and those taking medications (e.g., selective serotonin reuptake inhibitors, lithium, and tricyclic antidepressants) than in healthy controls [25–28]. In particular, previous evidence highlighted an association between ADHD and narcolepsy in children, and there was a higher prevalence of ADHD symptoms in narcoleptics when compared to the controls (35.3% vs. 4.8%, respectively) [29]. Thus, the unknown distribution of other factors possibly associated with increased PLMS could be a confounder contributing to the high prevalence of PLMS in child/adolescent narcolepsy.

Disrupted nighttime sleep (DNS) is one of the core symptoms of narcolepsy, and it has been reported that the estimated prevalence ranges widely from 30% to 95% [30]. DNS includes underlying narcolepsy-related sleep symptoms and disorders (e.g., hallucinations, sleep paralysis, RBD, nightmares, RLS, PLMS, nocturnal eating, and sleep apnea), as well as intrinsic sleep instability [31]. Preclinical studies have also highlighted that orexin loss/deficiency plays an important role in sleep discontinuity and sleep motor dysregulation in narcolepsy [4, 30, 32, 33]. In the current study, the results showed that narcoleptic patients with PLMS in the adult group had decreased total sleep time (TST) and SE and increased WASO compared with those without PLMS. Surprisingly, we did not find any significant differences in the above sleep parameters that reflected the

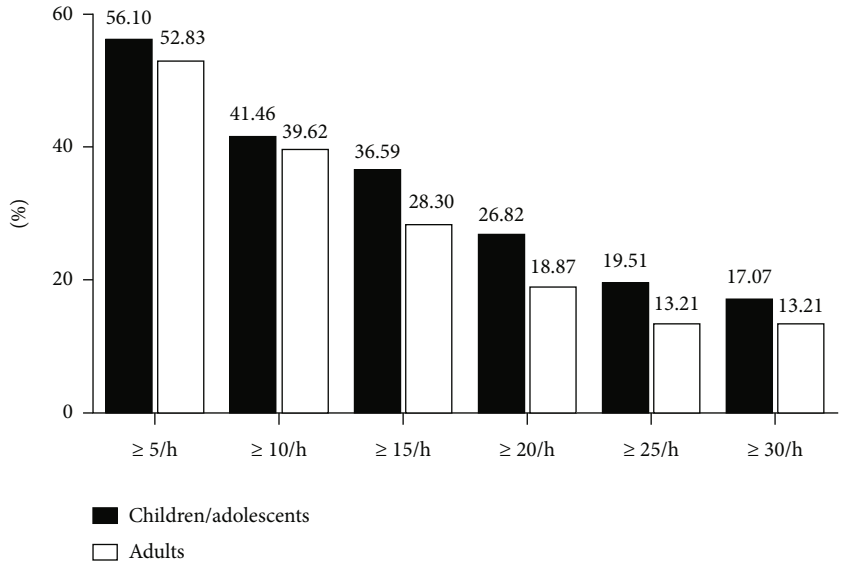


Figure 1: The rate of PLMI between child/adolescent and adult patients with narcolepsy.

Table 1: Demographic and clinical characteristics of patients with narcolepsy.

	Children/adolescents			Adults					
	All ($n = 41$)	N+PLMS ($n = 23$, 56.1%)	N-PLMS ($n = 18$, 43.9%)	All ($n = 53$)	N+PLMS ($n = 15$, 28.3%)	N-PLMS ($n = 38$, 71.7%)	P1	P2	P3
Age at diagnosis, years	11.9 ± 3.2	11.9 ± 3.1	11.8 ± 3.5	33.2 ± 12.4	34.5 ± 16.1	32.7 ± 10.8	<0.001	0.771	0.812
Age at onset, years	10.0 ± 3.4	10.0 ± 3.1	9.9 ± 3.8	26.1 ± 12.9	25.9 ± 12.6	26.2 ± 13.2	<0.001	0.958	0.929
Males, *n* (%)	23 (56.1)	12 (52.2)	11 (61.1)	43 (81.1)	12 (80.0)	31 (81.6)	0.008	0.567	0.895
BMI, kg/m^2	21.5 ± 4.2	21.5 ± 3.7	21.6 ± 4.8	26.3 ± 3.9	25.0 ± 3.1	26.9 ± 4.1	<0.001	0.916	0.054
Duration of the disease, years	2.0 ± 1.6	2.1 ± 1.8	1.9 ± 1.4	7.9 ± 9.7	8.7 ± 13.3	7.5 ± 7.8	0.001	0.967	0.695
Clinical symptoms									
ESS	11.5 ± 4.7	12.5 ± 4.5	10.1 ± 4.8	16.5 ± 5.0	15.7 ± 5.3	16.8 ± 5.0	<0.001	0.117	0.513
ESS > 10, *n* (%)	23 (56.1)	15 (65.2)	8 (44.4)	47 (88.7)	12 (80.0)	35 (92.1)	<0.001	0.183	0.334
Cataplexy, *n* (%)	32 (78.1)	18 (78.3)	14 (77.8)	42 (79.3)	14 (93.3)	28 (73.7)	0.888	0.970	0.640
Sleep paralysis, *n* (%)	6 (14.6)	5 (21.7)	1 (5.6)	16 (30.2)	4 (26.7)	12 (31.6)	0.077	0.205	0.985
Hypnagogic hallucinations, *n* (%)	9 (22.0)	5 (21.7)	4 (22.2)	27 (50.9)	7 (46.7)	20 (52.6)	0.004	0.970	0.696
PLMS, *n* (%)	23 (56.1)	23 (100.0)	NA	15 (28.3)	15 (100.0)	NA	0.006	NA	NA
RBD, *n* (%)	28 (68.3)	15 (65.2)	13 (72.2)	24 (45.3)	9 (60.0)	15 (39.5)	0.026	0.632	0.227
OSA, *n* (%)	8 (19.5)	4 (17.4)	4 (22.2)	17 (32.1)	5 (33.3)	12 (31.6)	0.172	0.698	0.920

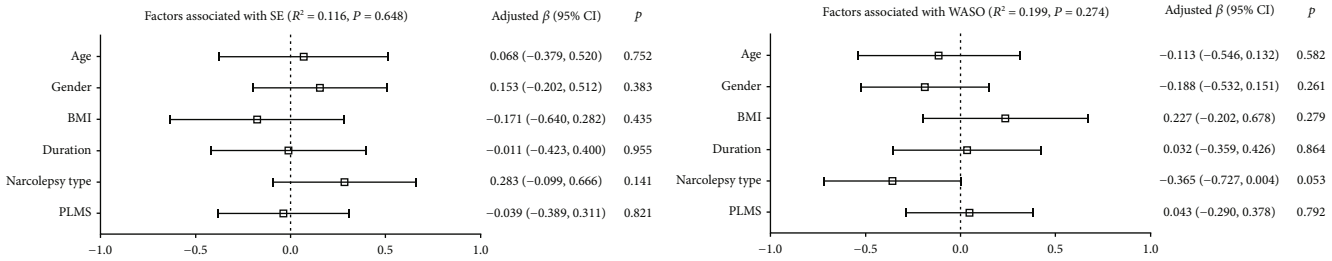
BMI: body mass index; ESS: Epworth Sleepiness Scale; NA: not applicable; N+PLMS: narcolepsy with PLMS; N-PLMS: narcolepsy without PLMS; OSA: obstructive sleep apnea; PLMS: periodic limb movements during sleep; RBD: rapid eye movement sleep behavior disorder. P1: all children/adolescents vs. all adults; P2: children/adolescents with PLMS vs. without PLMS; P3: adults with PLMS vs. without PLMS.

sleep quality between patients with and without PLMS in the child/adolescent group. Furthermore, after adjusting for potential confounding variables, PLMS was the risk factor associated with poor nocturnal sleep quality in adult patients with narcolepsy. This finding in the adult group is in keeping with the previously reported result that adult narcoleptic patients with PLMS had worse nighttime sleep than those without PLMS [2, 34]. However, our results in the child/adolescent group conflict with previous studies which showed increased awakenings and stage shifts during nighttime in narcoleptic patients with PLMS [4, 35]. These inconsistent results between adult and child/adolescent narcoleptic

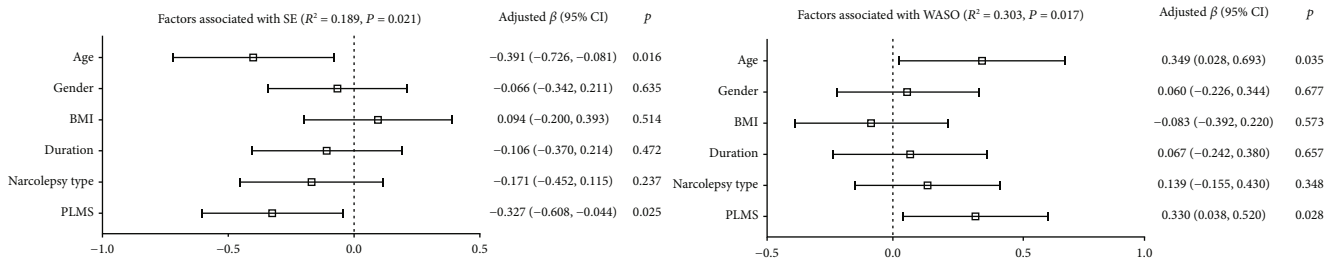
Table 2: Sleep parameters of narcolepsy with and without PLMS in child/adolescent and adult groups.

	Children/adolescents		P	Adults		P
	N+PLMS ($n = 23$)	N-PLMS ($n = 18$)		N+PLMS ($n = 15$)	N-PLMS ($n = 38$)	
Nocturnal sleep						
TST, min	437.0 ± 38.2	428.0 ± 50.2	0.703	391.0 ± 60.9	432.4 ± 40.3	0.011
Sleep efficiency, %	88.5 ± 7.3	88.3 ± 10.6	0.655	81.8 ± 12.8	89.4 ± 7.4	0.030
Sleep latency, min	10.5 ± 9.7	7.9 ± 4.9	0.895	12.1 ± 12.3	9.1 ± 6.9	0.514
REM latency, min	57.6 ± 51.9	104.8 ± 77.5	0.060	77.7 ± 83.3	63.3 ± 58.2	0.708
WASO, min	48.5 ± 35.3	49.3 ± 52.5	0.337	77.5 ± 53.5	44.6 ± 34.4	0.021
Arousal index, /h	3.0 ± 2.0	3.9 ± 2.7	0.358	7.6 ± 6.5	4.8 ± 3.0	0.101
Stage N1, %	24.9 ± 9.4	22.1 ± 12.2	0.446	32.4 ± 13.4	29.2 ± 11.6	0.418
Stage N2, %	36.5 ± 9.6	37.3 ± 12.7	0.563	41.8 ± 10.0	43.4 ± 13.5	0.353
Stage N3, %	18.7 ± 5.5	22.3 ± 7.8	0.217	8.8 ± 7.7	9.7 ± 5.2	0.244
Stage REM, %	19.9 ± 4.6	18.3 ± 7.7	0.331	17.0 ± 6.4	17.7 ± 7.0	0.859
AHI, /h	1.0 ± 1.2	1.0 ± 1.5	0.361	3.7 ± 3.8	3.8 ± 4.6	0.968
PLMI, /h	25.9 ± 20.3	1.6 ± 1.5	<0.001	36.3 ± 39.9	4.4 ± 4.1	<0.001
MSLT						
Mean sleep latency, min	3.3 ± 2.2	3.2 ± 2.2	0.813	3.2 ± 2.0	2.6 ± 1.5	0.363
SOREMPs, *n*	4.1 ± 1.4	3.7 ± 1.2	0.117	3.9 ± 0.9	4.1 ± 1.0	0.416

AHI: apnea-hypopnea index; MSLT: multiple sleep latency test; N+PLMS: narcolepsy with PLMS; N-PLMS: narcolepsy without PLMS; N1: stage 1 of nonrapid eye movement sleep; N2: stage 2 of nonrapid eye movement sleep; N3: stage 3 of nonrapid eye movement sleep; PLMI: periodic limb movement index; REM: rapid eye movement; SOREMPs: sleep onset rapid eye movement periods; TST: total sleep time; WASO: wake after sleep onset.



(a) Child/adolescent narcoleptic patients



(b) Adult narcoleptic patients

Figure 2: The associations between PLMS and SE/WASO in patients with narcolepsy. All models were adjusted for age, sex, BMI, disease duration, and narcolepsy type. BMI: body mass index; CI: confidence interval; PLMS: periodic limb movements during sleep; SE: sleep efficiency; WASO: wake after sleep onset.

patients in our study may suggest that nighttime sleep quality was influenced by the increased PLMI but not PLMS, which was defined by different cutoff values [35].

Notably, no significant differences in demographic and clinical characteristics were found between narcolepsy with and without PLMS both in child/adolescent and adult groups, which seems that the intrinsic symptoms of narcolepsy including EDS have not been affected by PLMS. We did not find significant differences in the ESS score and MSLT characteristics between patients with and without

PLMS both in adult and child/adolescent groups. These results indicated that PLMS could not be a potential risk factor associated with subjective and objective daytime sleepiness in narcolepsy. But, some studies showed that patients with PLMS have more severe objective EDS based on the shorter mean sleep latency in MSLT both in adults and children/adolescents with narcolepsy [34, 36, 37]. Jimenez-Correa and colleagues reported that both subjective daytime sleepiness and objective daytime sleepiness were associated with disrupted night sleep (e.g., WASO, awakenings, short TST, and low percentage of stage N3) in narcolepsy [38]. Nonetheless, a multicenter narcolepsy study concluded that disrupted night sleep may exacerbate daytime sleepiness, but not be the primary cause of EDS [39]. As indicated in the earlier studies and our finding, the contribution of PLMS to the perceived sleep quality and daytime sleepiness in narcoleptic patients still needs further study, whereas it is important to note that the age itself should be considered when exploring the effects of PLMS in patients with narcolepsy [40].

This study also found more severe subjective EDS and higher proportions of sleep paralysis and hypnagogic hallucinations in the adult group than the child/adolescent group. In terms of sleepiness in narcolepsy, an earlier study has also shown an age-related increase trend in the subjective EDS assessed by ESS, but not in objective EDS by MSLT, which is consistent with our finding [8]. In contrast, several studies reported that there were no significant differences that appeared in ESS, mean sleep latency, and SOREMPs in MSLT among different age groups [41, 42]. The adults had higher ESS scores and similar objective sleep propensity on the MSLT compared with the children/adolescents, which possibly relates to the sleep misperception [36] and the reduced homeostatic pressure and impaired circadian arousal process in older narcoleptics [37]. In our study, the proportion of RBD in child/adolescent narcoleptics (68.3%) is significantly higher than that in the adult group (45.4%), which is inconsistent with Nevsimalova et al.'s reported study [8]. RBD is regarded as a commonly seen nocturnal symptom in narcolepsy with a prevalence of approximately 60-70% based on questionnaires/clinical interviews, while 2-50% based on video-PSG diagnosis [43]. Our finding showed that the prevalence of RBD was 55.3% in all patients with narcolepsy, which seemed to be higher than that in the previous studies using video-PSG confirmation. The main reason might be due to the disparity of diagnosis criteria between ICSD-2 and ICSD-3 [14]. It means that more broad clinical and PSG features were included in the RBD criteria of ICSD-3, which could result in more patients meeting the diagnosis of RBD. However, the prevalence of RBD assessed by questionnaires is generally higher than that diagnosed by PSG [44–47]. There are two important reasons that could explain the disparity. Firstly, the subjective screening questionnaires mostly assess sleep-related vocalization and/or complex motor behaviors, which are probably associated with other diseases such as NREM parasomnias, nocturnal seizures, and OSA. Thus, these mimic RBD symptoms due to a higher prevalence of RBD by using a questionnaire assessment. Secondly, some authors have previously found that a single night of video-PSG may not be sufficient for the diagnosis of RBD due to reduced or absent REM sleep [48, 49]. Nowadays, some authors pointed out that PLMS and RBD may share a common pathophysiology related to a central dopaminergic dysfunction or brain iron deficiency [50–52]. This hypothesis could explain the higher proportion of RBD with the increased PLMS in child/adolescent narcolepsy.

The strengths of the current study included that we compared the effect of PLMS on nighttime sleep and daytime sleepiness both in children/adolescents and adults and fully considered the variability of PLMS due to age itself. In addition, we defined PLMS in different age groups by using the standard cutoff values according to the ICSD-3, which is more consistent than the previous studies with the variable definition of PLMS. However, there are several limitations that should be noted in the current study. First, the sample size was relatively small and from a single center. Further studies with a larger sample are needed to verify our findings. Second, the evaluation of night sleep quality was only based on the PSG but lacks scoring by the subjective questionnaires. Third, the data regarding the presence of RLS and ADHD are not available. Thus, it is unclear if the PLMS are isolated or comorbid with RLS or ADHD symptoms which may lead to difficulty explaining the potential pathogenetic mechanism. Finally, several related factors such as PLMS arousal index, "periodicity" of leg movements during sleep, and iron level were not evaluated in the study. These factors help understand the effects and etiology of PLMS in narcolepsy.

5. Conclusions

In summary, the present study showed a high prevalence of PLMS in patients with narcolepsy, especially in the child/adolescent group. PLMS is associated with worse sleep quality in adults with narcolepsy but is not a risk factor for EDS both in children/adolescents and adults with narcolepsy. These results may suggest that PLMS play a different role in different age groups of narcolepsy.

Data Availability

If any want the data for research, he/she can contact the corresponding author Junying Zhou (zhoujy2016@scu.edu.cn).

Ethical Approval

Enrollment was conducted based on guidelines specified by the Institutional Review Board of Tangdu Hospital of the Fourth Military Medical University.

Consent

All participants gave written informed consent.

Conflicts of Interest

The authors disclose no potential conflicts of interest.

Authors' Contributions

XCZ and JYZ contributed to the conception and design of the study. The patients were diagnosed by XCZ, GYC, JXC, and CJS. XCZ, JFR, DQS, and YQY contributed to the scoring of sleep and associated events. The data was collected by XCZ, JFR, and MY, who prepared the tables and figures and performed the statistics. XCZ and JYZ drafted the manuscript, which was reviewed and approved by all authors.

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