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Pediatric Periodic Limb Movement Disorder: Sleep Symptom and Polysomnographic Correlates Compared to Obstructive Sleep Apnea

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SCIENTIFIC INVESTIGATIONS

Study Objectives: Although periodic limb movements in sleep (PLMS) have been described in multiple pediatric publications, periodic limb movement disorder (PLMD) has not. The aims of this study were to describe the prevalence, sleep-related correlates, and polysomnographic correlates of PLMD in a large pediatric case series, and compare these to pediatric obstructive sleep apnea (OSA).

Methods: All PLMD cases (defined by International Classification of Sleep Disorders, 2nd edition criteria + respiratory disturbance index [RDI] < 3) and OSA cases (defined by RDI ≥ 3 + PLMS < 5), from a single pediatric sleep practice, over a 2-year time span, were included. Chart, questionnaire, and polysomnographic data were compiled. Of 468 referred children, 66 PLMD cases were identified (14%).

Results: The PLMD cases, mean age 8.1 years (range 1-17), were clinically characterized by frequent sleep onset and maintenance problems, difficulty awakening, restless sleep, leg pain/discomfort at night, and parasomnias. Compared to 90 OSA children, those with PLMD had a history of significantly more sleep onset and maintenance problems, leg pain/discomfort at night, parasomnias, getting out of bed at night, and family history of restless legs syndrome. Polysomnographically, PLMD cases had more awakenings, stage 1 sleep, stage shifts, and spontaneous arousals.

Conclusions: These data indicate that pediatric PLMD has important clinical and polysomnographic correlates. In addition, PLMD has many characteristics that are different from pediatric OSA, suggesting that PLMD is a distinct pediatric sleep disorder, of which clinicians should be aware.

Keywords: Periodic limb movements in sleep, periodic limb movement disorder, sleep disorder, children, parasomnia, obstructive sleep apnea, polysomnography

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Although there are multiple publications on pediatric periodic limb movements in sleep (PLMS), little is known about periodic limb movement disorder (PLMD) in children. PLMS are brief leg or arm jerks during sleep, associated with negative physiological consequences, including cardiac acceleration, spikes in blood pressure, and cortical arousals.[1-6] PLMS occur in a variety of sleep disorders, including restless legs syndrome (RLS), PLMD, narcolepsy, obstructive sleep apnea (OSA), and REM sleep behavior disorder, or may be induced by certain medications.[7,8] Based on the current diagnostic criteria, PLMD is diagnosed when the following are present: (1) PLMS documented by polysomnography; (2) PLMS exceeding norms for age (≥ 5/h for children); (3) clinical sleep disturbance or daytime fatigue; and (4) the absence of another primary sleep disorder or reason for the PLMS, including RLS and OSA.[7,9] Prior to revision of the criteria at a workshop at the National Institutes of Health in 2002, PLMD was typically diagnosed by the presence of only criteria 1-2, which do not effectively differentiate PLMS as part of another condition or PLMS as an asymptomatic polysomnographic finding, from PLMD as a distinct disorder. However, there is very little adult or pediatric literature using this current definition, and controversy continues as to the clinical significance of PLMS.[10-14]

BRIEF SUMMARY

Current Knowledge/Study Rationale: There is very limited medical literature on pediatric periodic limb movement disorder (PLMD) based on the current definition. In this study we identify clinical and polysomnographic features of PLMD in a pediatric sleep center referral population, and compare these to children with obstructive sleep apnea (OSA).

Study Impact: In this large clinical case series, PLMD was found to be common,14% of 468 referred children. Important correlates of pediatric PLMD included disturbed sleep, leg discomfort/pain, parasomnias, and a family history of restless legs, more so than in the children with OSA.

We are aware of only three publications that report pediatric PLMD based on this newer definition. Two were relatively small case series, which emphasized the relationship of pediatric PLMD to family history and subsequent onset of RLS, as well as potential significant associations with parasomnias and attention deficit hyperactivity disorder (ADHD).[15,16] In a recent report we looked at daytime behavioral correlates of pediatric PLMD, and found greater daytime mood and behavioral difficulties in children with PLMD when compared to children with OSA.[17] In addition, PLMD was found to predict these daytime difficulties better than PLMS index alone. Using a PLMD definition of PLMS > 5/h alone (not using the clinical sleep dis-

turbance criterion), studies have reported pediatric prevalences of 5.6% to 26% in clinical polysomnographic case series,[18-23] and a prevalence of 11.9% in the only population-based study.[20] Many of the clinical cases were found incidentally in children referred for potential OSA. In a recent pediatric study, correlates of PLMS > 5/h included male gender (61%) and snoring (45%), with PLMS index correlating negatively with total sleep time, sleep efficiency, and percent slow wave sleep on polysomnography.[18]

The specific aims of this study were to identify the demographic features, prevalence, sleep-related symptoms, and polysomnographic features of PLMD in a large pediatric sleep center referral population, as well as to compare the clinical and polysomnographic correlates of pediatric PLMD to pediatric obstructive sleep apnea (OSA).

METHODS

This was a retrospective case series of children and adolescents with PLMD referred to a private practice of sleep medicine in a Southeastern urban area over a period of 2 years. The pediatric patients were seen by a single sleep physician (JLG). After institutional review board approval, demographic, chart, questionnaire, and polysomnographic data were compiled. Sleep history was obtained by semi-structured interview during the course of comprehensive clinical assessment, which included consideration of differential diagnosis and other medical conditions. In addition, parents completed a detailed questionnaire developed by author JLG specifically for use in her clinical practice of pediatric sleep medicine and designed to query the behavioral sleep routines, sleep complaints, and daytime mood and behavioral problems in children as perceived by the parent and/or child. Items encompassing sleep-related behavior and routines were analyzed in this study. Daytime mood and behavior items have been reported in a separate study.[17] Possible responses to individual items were: 1 = never (0 out of 7 days per week); 2 = sometimes (1-4 out of 7 days); or 3 = frequently (5-7 out of 7 days).

Polysomnography

Polysomnography was performed in an accredited sleep laboratory specifically designed for pediatric studies, attended by a certified sleep technologist trained in pediatric polysomnography, and video recorded. The following parameters were measured: electroencephalogram, eye movements, chin electromyogram, bilateral anterior tibialis electromyogram, electrocardiogram, nasal airflow (Pro-Tech Thermal Airflow Sensors), chest and abdominal wall motion (Pro-Tech Piezo effort belts), snore recording (Pro-Tech Piezo Snore Sensor), pulse oximetry (Nellcor NPB 295), and body position. The PSGs were reviewed and interpreted by a board-certified Sleep Medicine Specialist also boarded in Pediatrics (JLG).

PLMD and OSA Definitions

PLMD was defined by ICSD-2 criteria: PLMS ≥ 5/h present on PSG; clinical sleep disturbance (difficulty falling or staying asleep, or waking unrefreshed after sufficient sleep); and PLMS were not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.[7] PLMS at the termination of respiratory events were not counted. PLMS were defined as a sequence of ≥ 4 limb movements of 0.5–5.0 s in duration, separated by > 5 s and < 90 s, and of an amplitude ≥ 25% of toe dorsiflexion during calibration.[7,24] Although the ICSD-2 criteria had not been published at the time of initial assessment for these patients (2001-2002), the criteria may nonetheless be applied retrospectively because they are similar to the ICSD-R criteria used at the time,[25] and the interviewer (JLG) was routinely asking for and recording all information relevant to the diagnosis, including "clinical sleep disturbance."

An obstructive apnea was defined as a decrease ≥ 75% in airflow from the baseline value for ≥ 2 breaths with continuing respiratory effort. A hypopnea was defined as a discernable decrease in airflow from the preceding baseline accompanied by either a decrease in oxygen saturation of ≥ 3% or followed by an arousal. Snore arousals were scored when snoring was associated with EEG arousals. Respiratory disturbance index (RDI) was defined as apneas + hypopneas + snore arousals per hour of sleep.

Sample Selection

From an initial pool of 468 consecutive children referred to a private pediatric sleep medicine practice over a period of 2 years (2001-2002), 347 received a clinical diagnosis of OSA, PLMD, or both. Of the other 121 children, 24 did not complete the diagnostic protocol, 34 did not receive a PSG, and 63 were diagnosed with a disorder outside the scope of the present study, such as narcolepsy (n = 6) or RLS (n = 9). Although narcolepsy and RLS are commonly associated with PLMS, the focus of this study was PLMD. Seventy of the 347 received a dual clinical diagnosis of PLMD and OSA, and because of potential "overlap" were excluded from analysis. Furthermore, to analyze unequivocal cases of PLMD and OSA, more stringent polysomnography-based inclusion criteria were implemented: for the PLMD cases, ICSD-2 defined PLMD *and* RDI < 3; for the OSA cases, RDI ≥ 3 *and* PLMS < 5/h. One hundred twenty-one of the remaining 277 children who had received a single clinical diagnosis of OSA or PLMD were excluded from these analyses because they did not meet these stringent study criteria for OSA or PLMD. Eighty-seven of the 121 were OSA cases with PLMS > 5/h but without a clinical diagnosis of PLMD, 30 were PLMD cases with an RDI ≥ 3 but no clinical symptoms for sleep disordered breathing, and 4 had missing data. This resulted in 66 distinct PLMD cases and, for comparison, 90 unequivocal OSA cases.

Although not a primary focus of the study, treatment data were available for 51 of 66 patients with a diagnosis of PLMD (77%). Treatment was open-label, with outcome assessed by clinician impression, through interview of the child and parent at follow-up clinic visits.

Statistical Analysis

Group differences in chart and questionnaire data (counts) were tested using χ^2 analyses. In an effort to reduce family-wise error, PSG data were grouped into categories (such as sleep time, wake time, awakenings) and analyzed using multivariate analyses, followed by univariate analyses. Pearson correlations

Table 1—Demographic data: PLMD compared to OSA group

Parameter	PLMD	OSA	PLMD vs OSA
Age (yrs; mean ± SD)	8.05 ± 3.93 (range 1-17)	7.47 ± 4.07 (range 1-15)	n.s.
Gender (% male)	58	61	n.s.
Ethnicity*			$\chi^2(3) = 8.88$, p = 0.03
Caucasian (n = 74)	36/74 (49%)	38/74 (51%)	
African American (n = 31)	8/31 (26%)	23/31 (74%)	
Asian (n = 2)	2	0	
Latino (n = 2)	0	2	

PLMD, periodic limb movement disorder; OSA, obstructive sleep apnea; n.s., not significant; *ethnicity data not available for 47 children.

examined associations between variables. An α of $p < 0.05$ was considered significant. Treatment results were evaluated by Kaplan-Meier survival analysis.

RESULTS

Prevalence and Demographics

Sixty-six of 468 consecutive children referred over a 2-year period were diagnosed with PLMD, a prevalence of 14% in this practice population. The average age was 8.05 years (range 1-17), with 58% males. Comparing children with PLMD to those with OSA, there were not significant group differences for age or gender (**Table 1**). However, comparing Caucasian to African American children, Caucasian children were more likely to have PLMD than were African American children (49% vs. 26%), while African American children were more likely than Caucasian children to have OSA (74% vs. 51%).

Chart and Questionnaire Data

As expected, many children with PLMD were reported by the parent and/or child to have sleep onset and maintenance problems (**Table 2**, chart data). In addition, restless sleep and kicking while asleep were commonly described. Many were also reported to be difficult to awakening in the morning (68%), complain of leg pain or discomfort at night (62%), have parasomnias (61%), and have a family history of RLS (49%). Remarkably, the sleep onset and maintenance problems, leg pain/discomfort at night, kicking in sleep, parasomnias, and family history of RLS were significantly more common in PLMD than OSA, while restless sleep, difficulty awakening, and excessive daytime sleepiness were not.

In the questionnaire data (**Table 2**), where responses are reported as percent frequent responses (5-7 out of 7 days), significantly more children with PLMD than OSA were described as getting out of bed, going to parents' bed, waking from nightmares, having frightening dreams, and having sleep terror-type awakenings, i.e., more sleep onset/maintenance problems and parasomnias. Interestingly, complaints of frequent crawling/aching sensations or leg pain were not significantly more common in children with PLMD. However, when responses of "sometimes" and "frequently" were recoded as "yes" answers for these items, children with PLMD were reported to have crawling/aching sensations and leg pain significantly more often ($\chi^2(1) = 5.00$, p = 0.02).

Polysomnographic Data

Based on inclusion criteria, the PLMD and OSA groups had markedly different mean PLMS and respiratory disturbance indices (**Table 3**), with a mean PLMS index of 23.5 in the PLMD group and mean RDI of 19.2 in the OSA group. In an effort to determine whether the relative severity of each disorder was roughly equivalent, a severity variable was calculated, equal to the standardized PLMS index for children with PLMD and the standardized apnea-hypopnea index (AHI) for children with OSA. The groups were equivalent for this estimate of severity ($t_{154} = 0.79$, p = 0.43).

Comparing PLMD to OSA, total recording time, total sleep time, and REM latency did not differ. However, children with PLMD had significantly more awakenings, stage 1 sleep, stage shifts, stage 1 shifts, and spontaneous arousals (**Table 1**). Conversely, children with OSA had significantly more total arousals. Both PLMD and OSA groups had equivalent, but remarkably low sleep efficiencies of 83.8% and 84.9%, and long sleep latencies of 41.7 and 38.3 minutes, respectively. Comparable pediatric polysomnographic normative values are 89.3% to 90.8% for sleep efficiency and 23 minutes for sleep latency.[26,27]

The PLMS index was not significantly correlated with age, total sleep time, sleep efficiency, sleep onset latency, awakenings, waking after sleep onset, percent slow wave sleep, or minimum SaO_2 NREM. It was significantly correlated with stage shifts ($r(155) = 0.27$, $p < 0.01$), stage 1 shifts ($r(155) = 0.27$, $p < 0.01$), percent stage 1 sleep ($r(155) = 0.17$, p = 0.03), and minimum SaO_2 REM ($r(153) = 0.19$, $p < 0.02$), but negatively correlated with snore arousals ($r(155) = -0.38$, $p < 0.01$).

Treatment

Treatment data were available for 77% (51/66) of the PLMD cases. Of the 15 children not included in the treatment analysis, 14 never began treatment, and one saw another provider for follow-up (data unavailable). Children who began treatment but subsequently were lost to follow-up or their treatment was not successful during the period of the analysis were included in the analysis. In this cohort, 76% (39/51) were successfully treated as defined by resolution of their sleep complaint, determined by clinician assessment at follow-up visits. Sixty percent of these successes occurred by the second visit, and 88% by the fourth visit. The mean number of visits to successful treatment was 2.54 visits (see **Figure S1**). Although treatment choices were individualized,

Table 2—Sleep-related chart and questionnaire data

Chart data	PLMD (n = 66) % yes	OSA (n = 90) % yes	PLMD vs OSA
Difficulty falling asleep	67	22	$\chi^2(1) = 31.09$, $p < 0.01$
Difficulty staying asleep	50	29	$\chi^2(1) = 7.22$, $p < 0.01$
Difficulty awakening	68	67	n.s.
Restless sleep	89	87	n.s.
Kicking in sleep	53	21	$\chi^2(1) = 17.14$, $p < 0.01$
Leg pain/discomfort at night	62	18	$\chi^2(1) = 32.89$, $p < 0.01$
Apnea observed	15	59	$\chi^2(1) = 30.26$, $p < 0.01$
Excessive daytime sleepiness	30	24	n.s.
Parasomnias	61	36	$\chi^2(1) = 9.62$, $p < 0.01$
Family history of RLS	49	18	$\chi^2(1) = 8.40$, $p < 0.01$
Questionnaire data	**PLMD (n = 66) % frequent**	**OSA (n = 90) % frequent**	**PLMD vs OSA**
Regular bedtime	73	59	$\chi^2(1) = 3.19$, $p = 0.07$
Goes to bed awake	74	72	n.s.
Has bedtime ritual	61	48	n.s.
Has caffeine before bed	3	3	n.s.
Uses sleep medication	8	2	n.s.
Refuses to go to bed	21	10	$\chi^2(1) = 3.81$, $p = 0.05$
Gets out of bed	35	20	$\chi^2(1) = 4.33$, $p = 0.04$
Refuses to sleep alone	23	18	n.s.
Sleeps with family member	26	19	n.s.
Wakes, goes to parents' bed	36	20	$\chi^2(1) = 5.18$, $p = 0.02$
Wakes up tired	39	33	n.s.
Wakes irritable, in bad mood	38	31	n.s.
Difficult to awaken	38	34	n.s.
Morning headache	3	8	n.s.
Appears drowsy during day	9	12	n.s.
Falls asleep inappropriately	24	17	n.s.
Moves during sleep	67	54	n.s.
Sleeps in unusual positions	21	24	n.s.
Jerks arms and legs	21	17	n.s.
Crawling, aching	14	8	n.s.
Leg pain	18	9	$\chi^2(1) = 2.94$, $p = 0.09$
Wets bed	2	10	$\chi^2(1) = 3.81$, $p = 0.05$
Grinds teeth	15	10	n.s.
Talks in sleep	23	12	$\chi^2(1) = 3.02$, $p = 0.08$
Walks in sleep	9	3	n.s.
Wakes from nightmares	12	1	$\chi^2(1) = 8.49$, $p < 0.01$
Frightening dreams	11	2	$\chi^2(1) = 4.92$, $p = 0.03$
Screams/difficult to fully awaken	12	3	$\chi^2(1) = 4.88$, $p = 0.03$

PLMD, periodic limb movement disorder; OSA, obstructive sleep apnea; RLS, restless legs syndrome; χ^2, chi-square; n.s., not significant.

dopamine agonists (pramipexole or ropinirole) were tried first in 88% of cases, with clonazepam as first choice in 6%. Final treatment status is summarized in **Table S1**. Fourteen percent of children who were treated reported adverse effects. The most common to the dopamine agonists were a paradoxical alerting reaction (7%) and headache (3%). Less than 1% reported nausea. The most common adverse effect to clonazepam was a paradoxical alerting reaction (13%). Iron status was not routinely assessed, and iron supplementation was not used because at the time there was not evidence for efficacy of iron in PLMD.

DISCUSSION

This is the largest case series to date of pediatric PLMD, as defined by current diagnostic criteria,[7,9] that reports sleep-related symptoms and polysomnographic correlates. In addition, it is the first large case series to compare pediatric PLMD to pediatric OSA.

As expected, prominent sleep onset and maintenance problems were reported in PLMD children, as was difficulty awakening in the morning. About one-third got out of bed many nights

Table 3—Polysomnographic data (means and standard deviations)

Parameter	PLMD (n = 66)	OSA (n = 90)	PLMD vs OSA
AHI	0.6 ± 0.6	13.0 ± 17.1	*
RDI	1.13 ± 0.9	19.2 ± 18.1	*
PLMS index	23.5 ± 17.6	1.3 ± 1.5	*
Total recording time (min)	537.9 ± 77.6	531.1 ± 157.8	n.s.
Total sleep time (min)	450.8 ± 77.2	440.5 ± 87.6	n.s.
Sleep efficiency (%)	83.8 ± 8.5	84.9 ± 13.0	n.s.
Sleep onset latency (min)	41.7 ± 31.7	38.3 ± 65.8	n.s.
REM latency (min)	166.2 ± 80.2	171.7 ± 80.0	n.s.
Awake time (mult.)			$F_{1,152} = 3.93$, $p = 0.02$, $\eta_p^2 = 0.05$
# Awakenings	15.3 ± 10.0	11.7 ± 8.3	$F_{1,153} = 5.97$, $p = 0.02$, $\eta_p^2 = 0.04$
WASO (min)	45.4 ± 50.2	51.2 ± 93.7	n.s.
Time in each stage (mult.)			$F_{5,150} = 85.82$, $p < 0.01$, $\eta_p^2 = 0.10$
Stage 1 (% TST)	6.7 ± 3.9	4.9 ± 3.19	$F_{5,150} = 9.26$, $p < 0.01$, $\eta_p^2 = 0.06$
Stage 2 (% TST)	57.9 ± 11.3	57.5 ± 12.4	n.s.
Stage 3 (% TST)	8.5 ± 6.2	9.9 ± 7.3	n.s.
Stage 4 (% TST)	11.2 ± 10.2	12.6 ± 12.4	n.s.
Stage REM (% TST)	15.7 ± 5.8	15.0 ± 6.6	n.s.
Shifts (mult.)			$F_{5,149} = 2.52$, $p = 0.03$, $\eta_p^2 = 0.08$
Stage shifts	88.5 ± 33.1	66.8 ± 29.2	$F_{1,153} = 18.76$, $p < 0.01$, $\eta_p^2 = 0.11$
Stage 1 shifts	27.3 ± 11.5	19.3 ± 11.2	$F_{1,153} = 18.94$, $p < 0.01$, $\eta_p^2 = 0.11$
Arousals (mult.)			$F_{5,150} = 85.82$, $p < 0.01$, $\eta_p^2 = 0.74$
Spontaneous arousal index	3.1 ± 4.1	2.0 ± 2.4	$F_{1,154} = 4.80$, $p = 0.03$, $\eta_p^2 = 0.03$
AH arousal index	0.4 ± 0.6	11.0 ± 16.6	$F_{1,154} = 26.83$, $p < 0.01$, $\eta_p^2 = 0.15$
Snore arousal index	0.6 ± 0.7	6.2 ± 5.0	$F_{1,154} = 83.32$, $p < 0.01$, $\eta_p^2 = 0.15$
PLMS arousal index	9.6 ± 4.6	0.8 ± 1.2	$F_{1,154} = 297.29$, $p < 0.01$, $\eta_p^2 = 0.66$
Total arousals index	13.7 ± 7.20	20 ± 16.6	$F_{1,154} = 8.29$, $p < 0.01$, $\eta_p^2 = 0.05$

PLMD, periodic limb movement disorder; OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; RDI, respiratory disturbance index; PLMS, periodic leg movements in sleep; TST, total sleep time; mult, multivariate analysis; *differences defined by group inclusion criteria; n.s., not significant.

per week and went to their parents' bed, significantly more than in the OSA group. While restless sleep was commonly described for children with PLMD, this was equally as often reported for children with OSA and, thus, not a differentiating feature. Similarly, for both groups fewer than one-third were described as exhibiting signs of excessive sleepiness, frequent drowsiness, or frequent falling asleep inappropriately. Supporting previous work, which indicates history alone is not accurate for the determination of PLMS, almost 50% of children with PLMD were not noted by families to have kicking or frequent jerking during sleep.[15,21,28,29] Also supportive of previous studies related to pediatric PLMS, an unusually high rate of parasomnias were reported, particularly sleep terrors and nightmares.[15,16,28,30] Arousals associated with PLMS are the presumed mechanism for the triggering of parasomnias.[30] Interestingly, parasomnias in this study were significantly more in PLMD than OSA children, in spite of the OSA children having somewhat higher total arousal rates, suggesting other possible factors.

Although we excluded cases of pediatric RLS for this study, to better define the correlates of PLMD in childhood, there were significantly more children with PLMD than OSA who complained of leg pain/discomfort at night (62% vs. 18%) during the clinical interview. However, in the questionnaire data, children with PLMD were not more likely to report to their parents crawling/aching sensations or leg pain, when analyzed as a percent of *frequent* responses (5-7 nights/week). Nonetheless, when "sometimes" and "frequent" responses were combined, complains of crawling/aching sensations and leg pain were significantly more likely in children with PLMD, suggesting relatively infrequent sensations or reporting of sensations to parents. In combination with a remarkably high family history of RLS (49% vs. 18%), these data suggest that pediatric PLMD may be a precursor to RLS in some cases, as other studies have indicated.[15,16] Because of the relatively young mean age in this sample (8.1 years, range 1-17), we would expect some of these children to meet RLS criteria over time, simply due to the development of better language and cognitive skills, which are needed to adequately report RLS symptoms.[15,31]

The polysomnographic results provide objective data that document sleep disruption in pediatric PLMD, which was compared to that in pediatric OSA. Both groups had long sleep latencies, relatively low sleep efficiencies, increased WASO, and frequent arousals. Although we did not have concurrent normal controls, historical normative data clearly support the impairment of sleep in these cases.[26,27,32] Some of the polysomnographic findings were more common in children with PLMD as compared to the cases with OSA—awakenings, stage 1 sleep, stage shifts, stage 1 shifts, and spontaneous arousals—while

children with OSA had significantly more total arousals. These differences, the careful attention to only scoring PLMS independent of overt or subtle respiratory events, and the differences in clinical symptoms, indicate that PLMD (as currently defined) is not simply a variant of OSA, as has been suggested.[22]

While the prevalence of 14% in this pediatric sleep clinic population is not directly comparable to other studies, which defined PLMD as PLMS > 5/h only (not using the clinical sleep disruption criterion), it is within the broad range of those other studies, 5.6% to 26%.[18-23] Importantly, PLMD was purposely assessed for in this clinical population, rather than found as an incidental finding. Consistent with previous literature we found PLMS/PLMD to be significantly more common in Caucasian children and OSA more common in African American children,[33] but interpretation should be cautious since in about 30% ethnicity was not reported.

It is relevant to note that there are no FDA-approved treatments for PLMD, or for most other sleep disorders, in children. The need for rigorous treatment trials in children is evident based on this study and other studies.[34,35] While we have included the results of medications tried clinically for this cohort of children with PLMD, the open-label use and non-polysomnographic outcome assessment limit conclusions about treatment based on these data. Two recent review papers more comprehensively discuss potential treatment considerations, including iron assessment and therapy.[13,14] In addition, a newer small, double-blind, placebo-controlled study has shown benefit of dopaminergic treatment for PLMS in children.[36]

The major strengths of this study are the large sample size, the fact that PLMD was purposefully assessed for based on ICSD-2 criteria, and the stringent criteria used to define distinct PLMD and OSA groups. A strength and limitation of this study was the exclusion of "overlap" cases, children with both PLMD and OSA. This was done to accurately characterize PLMD and compare it to OSA. However, in clinical practice overlap does occur, often with uncertainty about the potential significance of PLMD. Other limitations include that we did not have data available on inter-movement interval for PLMS, which new research suggests may be important in distinguishing various causes for PLMS.[37] Also, we did not have data on autonomic or "subcortical" arousals related to PLMS, which have been shown to occur in children[38] and may mediate the cardiovascular morbidity reported with RLS.[39] Lastly, we did not have consistently obtained information on ADHD, depression, anxiety, or iron deficiency, conditions that have been associated with RLS, PLMS, and PLMD.[13,14,40]

In conclusion, these data support PLMD as a distinct pediatric disorder, with significant sleep-related symptom correlates, polysomnographic correlates, and, when combined with our previous work, significant daytime mood and behavior correlates. Rather than dismissing PLMS as an incidental polysomnographic finding in children, we suggest that clinicians consider these data to help sort out the potential significance of a diagnosis of PLMD in pediatric sleep assessment. Future research on pediatric PLMD should include full iron assessment and other research techniques, such as home infrared videography, actigraphy, and leg accelerometry to assess sleep and leg movement patterns over extended periods of time.

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Figure S1—Number of clinical visits to attain successful treatment by Kaplan-Meier survival analysis

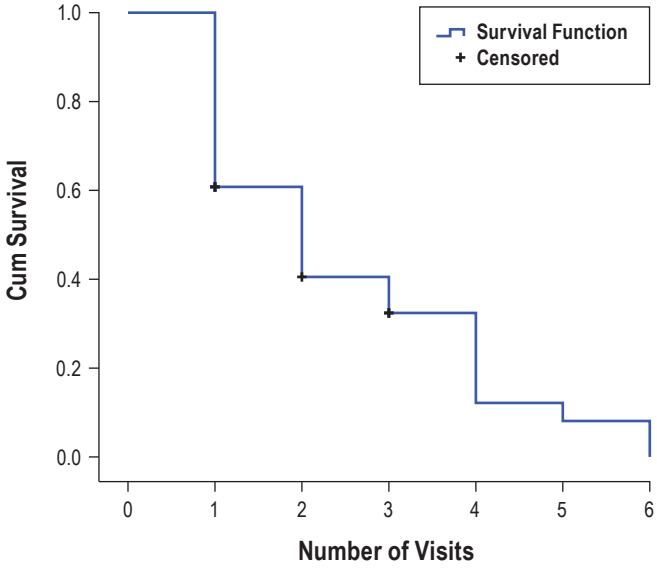

Table S1—Treatment outcomes for PLMD patients (N = 51)

Outcome	Cases
Dopamine agonist	28
Clonazepam	6
Dopamine agonist + Clonazepam	5
Lost to follow up or not successful	12

PLMD, periodic limb movement disorder.