



Original Article

Pediatric restless legs syndrome diagnostic criteria: an update by the International Restless Legs Syndrome Study Group[☆]



Daniel L. Picchietti^{a,*}, Oliviero Bruni^b, Al de Weerd^c, Jeffrey S. Durmer^d, Suresh Kotagal^e, Judith A. Owens^f, Narong Simakajornboon^g,
On behalf of the International Restless Legs Syndrome Study Group (IRLSSG)

^a University of Illinois School of Medicine and Carle Foundation Hospital, Urbana, IL, USA

^b Department of Developmental Neurology and Psychiatry, Sapienza University, Rome, Italy

^c EEG Department and Sleepcenter SEIN Zwolle, Netherlands

^d Georgia State University and Fusion Sleep Medicine Program, Atlanta, GA, USA

^e Division of Child and Adolescent Neurology, Department of Neurology, The Sleep Disorders Center, Mayo Clinic, Rochester, MN, USA

^f Children's National Medical Center, Washington, DC, USA

^g Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

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ABSTRACT

Background: Specific diagnostic criteria for pediatric restless legs syndrome (RLS) were published in 2003 following a workshop at the National Institutes of Health. Due to substantial new research and revision of the adult RLS diagnostic criteria, a task force was chosen by the International Restless Legs Syndrome Study Group (IRLSSG) to consider updates to the pediatric diagnostic criteria.

Methods: A committee of seven pediatric RLS experts developed a set of 15 consensus questions to review, conducted a comprehensive literature search, and extensively discussed potential revisions. The committee recommendations were approved by the IRLSSG executive committee and reviewed by the IRLSSG membership.

Results: The pediatric RLS diagnostic criteria were simplified and integrated with the newly revised adult RLS criteria. Specific recommendations were developed for pediatric application of the criteria, including consideration of typical words used by children to describe their symptoms. Pediatric aspects of differential diagnosis, comorbidity, and clinical significance were then defined. In addition, the research criteria for probable and possible pediatric RLS were updated and criteria for a related condition, periodic limb movement disorder (PLMD), were clarified.

Conclusions: Revised diagnostic criteria for pediatric RLS have been developed, which are intended to improve clinical practice and promote further research.

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1. Introduction

Restless legs syndrome (RLS), also known as Willis–Ekbom disease, is a common pediatric neurologic condition affecting 2–4% of school-aged children and adolescents [1–4]. Symptoms range from mild to severe with 25–50% of pediatric cases having moderate to severe symptoms [2]. Both adult and pediatric RLS can adversely impact sleep, mood, cognition, and quality of life [1,2,5–11]. Re-

cently the pathophysiology of RLS has been defined, with genetics, the brain dopamine system, and iron found to play important roles [1,12–15].

The current pediatric RLS diagnostic criteria were published in 2003 based on the consensus of experts at a National Institutes of Health workshop (2002) and sponsored in part by the International RLS Study Group (IRLSSG) [16]. These criteria (Supplementary Table 1) were intended to conservatively but broadly define pediatric RLS, incorporating previous criteria and research up to that time, with knowledge that further refinement would be needed. To promote further research, definite, probable, and possible RLS categories were defined. Weaknesses of these criteria include their complexity and the fact that they are substantially different than the adult RLS diagnostic criteria.

Because there have been numerous pediatric RLS publications since 2003 and because the adult RLS diagnostic criteria were

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* Corresponding author. Address: University of Illinois, School of Medicine and Carle Foundation Hospital, Department of Pediatrics, 602 W University Ave, Urbana, IL 61801, USA. Tel.: +1 217 383 3311; fax: +1 217 383 4468.

E-mail address: dpicchie@illinois.edu (D.L. Picchietti).

being updated [17], the IRLSSG Executive Committee appointed a pediatric RLS committee to reach consensus on possible revisions to the pediatric RLS diagnostic criteria and pediatric criteria for a related condition, periodic limb movement disorder (PLMD). In addition, the Sleep-Wake Work Group of the *Diagnostic and Statistical Manual Mental Disorders* (DSM) Task Force requested consideration that the pediatric RLS criteria be integrated with the adult RLS criteria, for inclusion of pediatric RLS in the fifth edition of the DSM (DSM-5)[18].

Our report summarizes the rationale and recommendations of the pediatric RLS committee. The IRLSSG has approved and endorsed these updates.

2. Methods

A panel of seven pediatric RLS experts was approved in spring 2010 by the IRLSSG Executive Committee to provide recommendations on revision of the pediatric RLS diagnostic criteria. The committee, composed of the authors of this paper, began correspondence in spring 2010 to identify key issues related to potential revisions. Fifteen consensus questions were agreed on; thirteen were discussed at a face-to-face meeting in June 2010 and two were discussed later. The questions were as follows, with responses elaborated in the next section: (1) Should the definite 1 RLS definition (Supplementary Table 1) require both urge and discomfort? (2) Should the statement, “in the child’s own words” be retained for definite RLS? (3) Should the lower age limit for definite RLS be left open or be specified? (4) Is criterion 5 (differential diagnosis) in the new IRLSSG adult criteria (Table 1) adequate for children? (5) Is the specifier for Clinical Significance in the new IRLSSG adult criteria adequate for children? (6) Does the specifier for Clinical Course in the new IRLSSG adult criteria apply to children? (7) Should the definite 2 RLS category be eliminated? (8) Do the supporting features in the IRLSSG adult criteria apply to children? (9) Should probable 1 RLS (not worse at night) be retained for children, perhaps without the supportive criteria needed? (10) Should probable 2 RLS (description of RLS symptoms by someone other than the child) be retained for children, perhaps as possible RLS? (11) Should the pediatric RLS diagnostic criteria be merged with the

adult RLS diagnostic criteria? (12) Should PLMD be retained as a pediatric diagnostic entity and what is its relationship to pediatric RLS? (13) How should clinical sleep disturbance be defined in the PLMD definition? Subsequently, two additional questions were discussed and agreed on: (14) What conditions commonly are comorbid with pediatric RLS and what is their relationship to RLS? (15) Are these criteria intended for both clinical and research applications?

To help integrate the medical literature into the recommendations, the committee conducted a formal literature search. Using the PubMed database, first in May 2010 and updated in March 2011, the search term *restless legs AND children* identified a total of 190 articles. Abstracts from these articles were reviewed to determine if the articles included information on children or adolescents and if they contained original data and any consensus statements on pediatric diagnosis. To be inclusive, no minimum number of subjects was applied, but review articles, per se, were not retained, unless diagnostic criteria consensus or discussion was included. Based on the literature search and pearling (checking of reference sections for any articles otherwise missed), 71 papers were selected for full review. Articles were divided among the seven committee members, with data pertinent to pediatric RLS diagnosis extracted and recorded on specific literature review forms. This information was then integrated into the subsequent recommendations.

After approval of the written report by all seven committee members, the recommendations were forwarded to the IRLSSG executive committee for review and approval and then to the IRLSSG membership for comment.

3. Revised diagnostic criteria for pediatric RLS

3.1. Integration with the essential RLS criteria for adults

The same diagnostic criteria for adults and children are desirable to promote accuracy, consistency, and fluency of application. In addition, it is unlikely that the basic underlying pathophysiology of RLS is different at different ages. However, there was concern at the National Institutes of Health workshop in 2002 that children

Table 1
International Restless Legs Syndrome Study Group consensus diagnostic criteria for restless legs syndrome.

Restless legs syndrome (RLS), a neurological sensorimotor disorder often profoundly disturbing sleep, is diagnosed by ascertaining a syndrome that consists of all of the following features:
(1) An urge to move the legs usually but not always accompanied by or felt to be caused by uncomfortable and unpleasant sensations in the legs ^{a,b}
(2) The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or sitting
(3) The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues ^c
(4) The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity only occur or are worse in the evening or night than during the day ^d
(5) The occurrence of the above features are not solely accounted for as symptoms primary to another medical or a behavioral condition (e.g., myalgia, venous stasis, leg edema, arthritis, leg cramps, positional discomfort, habitual foot tapping). ^e
Specifier for clinical significance of RLS The symptoms of RLS cause significant distress or impairment in social, occupational, educational, or other important areas of functioning by the impact on sleep, energy/vitality, daily activities, behavior, cognition, or mood
Specifiers for clinical course of RLS ^f (A) Chronic-persistent RLS: symptoms when not treated would occur on average at least twice weekly for the past year (B) Intermittent RLS: symptoms when not treated would occur on average <2/week for the past year, with at least five lifetime events

^a Sometimes the urge to move the legs is present without the uncomfortable sensations and sometimes the arms or other parts of the body are involved in addition to the legs.

^b For children, the description of these symptoms should be in the child’s own words.

^c When symptoms are very severe, relief by activity may not be noticeable but must have been previously present.

^d When symptoms are very severe, the worsening in the evening or night may not be noticeable but must have been previously present.

^e These conditions, often referred to as “RLS mimics,” have been commonly confused with RLS, particularly in surveys because they produce symptoms that meet or at least come close to meeting criteria 1–4 above. The list here gives some examples that have been noted as particularly significant in epidemiologic studies and clinical practice. However, RLS may also occur with any of these conditions, requiring a clear delineation of the RLS feelings from the other sensations.

^f The clinical course criteria do not apply for pediatric cases or for some special cases of provoked RLS such as pregnancy or drug-induced RLS, in which the frequency may be high but limited to the duration of the provocative condition.

might not understand the term *urge*. Furthermore, both *urge* and *discomfort* were required for diagnosis, to err toward under rather than over diagnosis, unless other supportive criteria were present (Supplementary Table 1). Subsequent research has shown that, in fact, children typically do not use the word *urge* to describe RLS sensations but use more age-appropriate terms such as *need to move*, *want to move*, and *got to kick* [19]. Thus the concept of *urge to move* is present but expressed in developmentally appropriate terms. Additionally, research has shown that most children report both the *urge* and *discomfort* components when given the opportunity and the correct prompts [19]. Furthermore, although the supportive criteria of a family history of RLS and periodic limb movements in sleep (PLMS) >5 per hour clearly are predictive of pediatric RLS, biologic family history or polysomnography may not be available for individual children, limiting the uniform applicability of these criteria [3,4,20].

The pediatric RLS committee found broad consensus that adult and pediatric diagnostic criteria should be combined, with pediatric-specific terms and prompts considered by the diagnostician when the criteria are applied in clinical and research settings. This consensus also eliminated the use of two different pathways for definitive RLS diagnosis in children, definite 1 and definite 2 RLS. Updated integrated RLS diagnostic criteria (2012) are listed in Table 1. Footnotes help clarify some of the items and Table 2 lists “Special considerations for the diagnosis of pediatric RLS,” which are further explained below.

3.2. Application of integrated diagnostic criteria

The descriptions of the RLS sensations described in the adult’s own words are implied but not stated in the application of RLS criteria for adults. Proxy report of core sensory symptoms would not be considered appropriate in adult RLS or in other sensory conditions in children, such as pediatric migraine headaches. Thus description of the RLS sensations in the child’s own words was agreed on as essential by the committee. However, pediatric specific terms and prompts should be primarily considered during the diagnostic interview, rather than adult language. Simple straightforward pediatric prompts should be used, such as “Do your legs bother you?” and “Do your legs bother you at night?” Further details regarding the pediatric diagnostic interview are discussed in a recent review article [1].

Based on recent research and consensus, the child’s language and cognitive development should determine the applicability of the RLS diagnostic criteria, rather than age [19]. However, because the diagnostic criteria require (1) the verbal description of RLS sensations by the child (*urge*, *discomfort*), (2) the relationship to rest or inactivity (lying down, sitting), (3) relief with movement, (4) time of day or night of the occurrence (only or worse evening/

night), and (5) the differentiation from symptoms of other conditions, it is unlikely that most children less than 6 years of age will have the skills for accurate description of these aspects.

Due to periods of prolonged sitting during the day in class, the interaction of being worse with rest (criterion 2) and worse in the evening/night (criterion 4) may be difficult to sort out. Please see the *Research criteria for probable and possible RLS* section for further discussion.

The differentiation of RLS from other conditions or mimics is an important facet of the diagnostic process that has been emphasized in recent literature [21–23], including in two pediatric studies that found mimics in 11.8% and 27% of children who initially appeared to meet RLS diagnostic criteria [3,4]. Careful consideration of RLS mimics will substantially reduce the chance of misdiagnosis or overdiagnosis. In the updated criteria, this aspect has been formalized as a fifth essential element for RLS diagnosis (Table 1). To help with differential diagnosis in pediatric cases, the committee discussed possible pediatric RLS mimics; important mimics are enumerated in Table 3.

Four important points are relevant to the differential diagnosis of pediatric RLS: (1) Although some mimics meet criteria 1–4 for RLS, many do not. For example, sore leg muscles typically are worse with movement, not better. (2) Although pain is not an unusual descriptor for RLS with approximately 45% of children using the terms *pain* and *hurts* or *hurting*, all children in a recent study used other descriptors for RLS—at least two descriptors and a mean of three or more in the three age categories [19]. Thus while pain is a common element of RLS and RLS mimics, other descriptors are used for RLS. In particular, the *urge to move the legs* (e.g., “got to move,” “have to move”) is uncommonly a description for the mimics. (3) Growing pains are a common benign condition in childhood characterized by intermittent bilateral leg pain that occurs in the late afternoon or evening [24]. Pediatric RLS may be misdiagnosed as growing pains if adequate history is not obtained including the presence or absence of a need to move, which worsens with rest and is relieved with activity (RLS criteria 1–3) [2,25,26]. (4) There are some mimics that also may occur in an individual with RLS (e.g., sore leg muscles, dermatitis) requiring a clear delineation of the RLS feelings from the other sensations during the diagnostic interview [1].

3.3. Comorbidity

Co-occurrence of RLS with other medical conditions has clearly identified three exacerbating factors in adults, iron deficiency, pregnancy, and chronic renal failure [27–29]. Current evidence supports relative iron deficiency and renal failure as potential aggravating factors for pediatric RLS [30–34]. Comorbidity of RLS with attention-deficit/hyperactivity disorder, depressive symptoms, and anxiety more often has been found in adults and children with RLS than in comparison populations [1,35]. Approximately one-quarter of individuals with RLS have attentional problems and conversely, 13–35% with attention-deficit/hyperactivity disorder meet criteria for RLS [2,4,36–40]. However, the basis for these relationships is not known, though a common underlying dopamine/iron pathophysiology has been postulated [7,41]. In addition, parasomnias may be more common in children with RLS, possibly triggered by PLMS and sleep deprivation [3,4,20,42].

Associations between RLS and cardiovascular disease have been found in adult population-based studies [43,44]. The heart rate and blood pressure surges associated with PLMS may mediate this relationship and have been demonstrated with pediatric PLMS [45,46].

3.4. Clinical course

The pediatric RLS committee agreed that there was insufficient pediatric information to accept the adult *Specifiers for Clinical*

Table 2

Special considerations for the diagnosis of pediatric restless legs syndrome.

- The child must describe the RLS symptoms in his or her own words
- The diagnostician should be aware of the typical words children and adolescents use to describe RLS
- Language and cognitive development determine the applicability of the RLS diagnostic criteria, rather than age
- It is not known if the adult specifiers for clinical course apply to pediatric RLS
- As in adults, a significant impact on sleep, mood, cognition, and function is found. However, impairment is manifest more often in behavioral and educational domains
- Simplified and updated research criteria for *probable* and *possible* pediatric RLS are available (Table 5)
- Periodic limb movement disorder may precede the diagnosis of RLS in some cases

Abbreviation: RLS, restless legs syndrome.

Table 3
Differential diagnosis of pediatric restless legs syndrome.

<i>Common mimics</i>
<ul style="list-style-type: none"> • Positional discomfort • Sore leg muscles • Ligament sprain/tendon strain • Positional ischemia (numbness) • Dermatitis • Bruises • Growing pains
<i>Less common mimics</i>
<ul style="list-style-type: none"> • Leg cramps • Arthritis • Other orthopedic disorders • Peripheral neuropathy • Radiculopathy • Myelopathy • Myopathy • Fibromyalgia • Complex regional pain syndrome • Drug-induced akathisia • Sickle cell disease

Course of RLS (Table 1) as applicable for children and adolescents. Clearly a chronic persistent course for pediatric RLS has been described, but it is not certain that at least twice weekly can be considered the best determinant of chronicity in pediatric cases, particularly because the motor components (e.g., PLMS) may predominate in some children [20,47,48].

3.5. Clinical significance

The pediatric RLS committee agreed that the specifier for Clinical Significance of RLS was appropriate for children and adolescents, based on the current literature and clinical experience. As in adults, a significant impact on sleep, mood, cognition, and function was found [2–4,49]. In particular, sleep disturbance was a common and distressing aspect of pediatric RLS [2–4,49]. However, functional consequences of RLS in children more often manifest in behavioral and educational domains than in adults [49]. In addition, the category of other important areas of functioning for children includes the home environment. The specifier for clinical significance is particularly important as it provides clear delineation of RLS severe enough to impact function, a key issue when treatment decisions are considered. However, there is a spectrum of disease from latent or subclinical to severe. In addition, RLS is more like migraine headache than anxiety, as the core symptoms of RLS are not universally experienced but are limited to a subset of the population, with genetic and environmental factors influencing severity of symptoms [1]. As such, latent or mild cases are important to identify for genetic and epidemiologic research and for determination of the risk for developing clinically significant disease, which can occur with iron deficiency [27,50,51] or during or subsequent to pregnancy [52,53].

Table 4
Clinical features supporting the diagnosis of pediatric restless legs syndrome.

The following features, though not essential for diagnosis, are closely associated with pediatric RLS and should be noted when present:
<ol style="list-style-type: none"> (1) PLMS >5 per hour (2) Family history of RLS among first-degree relatives (3) Family history of PLMS >5 per hour (4) Family history of PLMD among first-degree relatives

Abbreviations: RLS, restless legs syndrome; PLMS, periodic limb movements during sleep; PLMD, periodic limb movement disorder.

3.6. Supportive and associated features

Clinical features supporting the diagnosis of RLS for adults are as follows: (1) presence of PLMS or periodic limb movements during wakefulness at rates greater than expected for age, (2) reduction in symptoms at least initially with dopaminergic treatment, and (3) family history of RLS among first-degree relatives [16]. Although not essential for diagnosis, these are closely associated with RLS and should be noted when present. Features supporting the diagnosis of pediatric RLS are listed in Table 4.

The pediatric RLS committee agreed that PLMS and a family history of RLS among first-degree relatives are supportive of pediatric RLS. PLMS >5 per hour have been found in 63–74% of children with RLS (normal, <5 per hour for children [54–56]), based on single-night sampling [20,57,58]. It is important to recognize that PLMS significantly vary from night to night [59,60]. With sampling over five nights, 91% of adults with RLS have been found to have PLMS of >5 per hour compared to 70–80% using single-night sampling [61,62]. Early-onset RLS is highly familial, with recent adult studies showing high familial rates of 65.8% and 77% in early-onset cases [48,63], as well as in younger age of onset in familial cases [63,64]. A large pediatric population-based study found a positive parental history of RLS (at least one biological parent) in 71% of children ages 8–11 years and 80% of adolescents ages 12–17 years, with both parents affected in 16% of cases [2]. Other pediatric studies found rates of 15–87% based on widely varying methods of parental RLS ascertainment [3,4,20,39,58]. These parental RLS rates are in sharp contrast to adult population-based rates of 5–10% [10]. The presence of one or both of these two supportive features is considered to increase the diagnostic certainty of RLS for an individual child. This finding is particularly relevant for PLMS >5 per hour, as PLMS are an objective marker of RLS [65].

Regarding other supportive features, the committee found that there were insufficient data on periodic limb movements during wakefulness [56], and there was concern that supportive feature two might unintentionally imply a clinical trial of dopaminergic therapy when there is not a clear-cut diagnosis of RLS [66]. However, a family history of PLMS of >5 per hour or a family history of PLMD among first-degree relatives should be considered supportive of pediatric RLS based on genetic research [67]. There was discussion to determine if a low ferritin level, which is demonstrated by evidence to be an aggravating factor for RLS, should be considered supportive of RLS. Serum ferritin has been found to be lower in adults and children with RLS than in control subjects [1], with oral iron therapy suggested for serum ferritin of <50 mcg/L (reference range, 15–200 mcg/L) [1,68,69]. However, because many children in the general population have serum ferritin in this range [70], it is unlikely that ferritin could be a notable differentiating feature for pediatric RLS.

Sleep disturbance is a commonly associated feature of pediatric RLS in both population- and clinic-based studies. It often is the primary clinical complaint, is more common with more severe RLS, and is present in over 85% of pediatric patients with RLS [2,20,47,57,58].

3.7. Application in clinical vs research settings

These diagnostic criteria are intended for both clinical and research settings. However, additional work is recommended to optimize the criteria in specific situations. Development of a structured interview would help to insure consistent application in research studies. For epidemiologic and large scale clinical studies a simplified but sufficiently sensitive and specific set of diagnostic questions would be useful. For genetic studies, milder subclinical cases in which clinical significance criteria are not required should be considered part of the RLS spectrum. In addition, assessment for

Table 5

Research diagnostic criteria for probable and possible pediatric restless legs syndrome.

<i>Probable RLS</i>
The child meets all five essential criteria for RLS, except criterion 4 (occurrence only or worsening in the evening or night)
<i>Possible RLS</i>
The child is observed to have behavior manifestations of lower extremity discomfort when sitting or lying, accompanied by motor movement of the affected limbs. The discomfort is characterized by RLS criteria 2–5 (is worse during rest and inactivity, relieved by movement, worse in the evening or night, and is not solely accounted for as primary to another medical or a behavioral condition)

Abbreviation: RLS, restless legs syndrome.

Table 6

Criteria for the diagnosis of pediatric periodic limb movements during sleep.

(1) Polysomnography shows repetitive stereotyped limb movements that are:
(a) 0.5–10 s in duration,
(b) minimum amplitude of 8 μ V above resting EMG,
(c) in a sequence of four or more movements,
(d) separated by an interval of more than 5 s (from limb movement onset to limb movement onset) and less than 90 s (intermovement intervals often are short and variable in children)
(2) The PLMS index exceeds 5/h in pediatric cases
(3) The PLMS cause clinically significant sleep disturbance or impairment in mental, physical, social, occupational, educational, behavioral, or other important areas of functioning
(4) The PLMS are not better explained by another current sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder (e.g., exclude from PLMS counts the movements at the termination of cyclically occurring apneas)

Abbreviations: s, seconds; EMG, electromyogram; PLMS, periodic limb movements during sleep.

Table modified from Allen et al. [16].

PLMS is likely to enhance genetic research work [67,71]. Importantly accurate translation of the pediatric diagnostic criteria to other languages besides English is recommended for both clinical and research applications.

3.8. Research criteria for probable and possible RLS

Daytime leg sensations are reported by two-thirds of children and adolescents, possibly related to prolonged periods of sitting in class [19]. Because of this, it is important to contrast an equal duration of sitting or lying down in the day to the evening and night when applying diagnostic criterion 4 (worse evening/night). However, even when considering equal duration of sitting or lying down, a significant subset of children do not report worsening at evening and night, yet they meet all other diagnostic criteria and have supportive features for RLS including a positive family history [2,20,47]. For this reason the pediatric RLS committee recommended probable RLS to be retained as a definition for further research. However, the essential feature of a positive family history of RLS was eliminated, as a biologic family history is not available for some children (Table 5 and Supplementary Table 1).

A research diagnosis based on behavioral observations rather than direct report by the child or adolescent was changed from probable 2 RLS to possible RLS (Table 5). The behavioral observations must meet RLS criteria 2–5. We found only one publication on this behavioral observation approach to pediatric RLS diagnosis, which concluded that it was useful and needed [58]. The committee agreed that further exploration of this issue is warranted, but also that more work is needed to assign probable or definite RLS status to this approach. Accurate diagnosis by behavioral observation could be particularly helpful for children younger than 6 years of age. In addition, children with neurodevelopmental disabilities that involve language or cognitive impairments could potentially

benefit from this approach. A positive family history of RLS was eliminated as an essential feature, as was recommended for the new version of probable RLS.

The specifier for clinical significance applies to both probable and possible RLS. In pediatric RLS research studies, it is important to specify definite, probable, and possible RLS whenever possible.

3.9. Pediatric PLMD

Considering the latest genetic research, which indicates that PLMS characterize a common endophenotype for RLS [71], the documentation of PLMD evolving to RLS in children over time [47] and new literature on pediatric PLMS and PLMD [20,72–74], the committee agreed that PLMD should be retained as a diagnostic entity related to RLS, particularly for children. Criterion 1 defines the polysomnographic features of PLMS (Table 6). For children the intermovement intervals may be short and variable in contrast to the typical 15–40 s intervals in adults [56,75,76]. Criterion 3 has been expanded, linking disturbed sleep or daytime symptoms to the PLMS rather than some other cause. Sleep disturbance in criterion 3 is defined as difficulty with sleep initiation, sleep maintenance, or unrefreshing sleep. It is important to note that RLS supersedes a diagnosis of PLMD. Thus a child can have RLS with PLMS, but he or she cannot have RLS and PLMD [77]. In addition, children with PLMS >5 per hour and hypersomnia should be evaluated for narcolepsy, as PLMS are commonly found in narcolepsy and moderate to severe daytime sleepiness is uncommon in children with PLMD [20,47].

4. Conclusions

These revised, simplified, and integrated diagnostic criteria for pediatric RLS have been developed to replace the previous criteria and are intended to improve clinical practice and to promote pediatric RLS research.

4.1. Directions for future research

Important areas for future research include diagnosis in young children aged <6 years, diagnosis in children with neurodevelopmental disabilities, circadian issues related to RLS expression in children, the longitudinal course of RLS in children, comorbidity of RLS with psychiatric conditions, and further work on the relationship of PLMS to pediatric RLS. In addition, further research is recommended on the typical periodicity of PLMS in children [76], normative PLMS data for children ages <2 years, and techniques other than polysomnography to accurately measure PLMS [78]. Although a pediatric rating scale has been developed, validation is needed for clinical and research applications [49].

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <http://dx.doi.org/10.1016/j.sleep.2013.08.778>.

References

- Picchetti MA, Picchetti DL. Advances in pediatric restless legs syndrome: iron, genetics, diagnosis and treatment. *Sleep Med* 2010;11:643–51.

- [2] Picchietti D, Allen RP, Walters AS, Davidson JE, Myers A, Ferini-Strambi L. Restless legs syndrome: prevalence and impact in children and adolescents—the Peds REST study. *Pediatrics* 2007;120:253–66.
- [3] Turkdogan D, Bekiroglu N, Zaimoglu S. A prevalence study of restless legs syndrome in Turkish children and adolescents. *Sleep Med* 2011;12:315–21.
- [4] Yilmaz K, Kilincaslan A, Aydin N, Kor D. Prevalence and correlates of restless legs syndrome in adolescents. *Dev Med Child Neurol* 2011;53:40–7.
- [5] Hornyak M, Feige B, Voderholzer U, Philipsen A, Riemann D. Polysomnography findings in patients with restless legs syndrome and in healthy controls: a comparative observational study. *Sleep* 2007;30:861–5.
- [6] Hornyak M, Kopasz M, Berger M, Riemann D, Voderholzer U. Impact of sleep-related complaints on depressive symptoms in patients with restless legs syndrome. *J Clin Psychiatry* 2005;66:1139–45.
- [7] Walters AS, Silvestri R, Zucconi M, Chandrashekariah R, Konofal E. Review of the possible relationship and hypothetical links between attention deficit hyperactivity disorder (ADHD) and the simple sleep related movement disorders, parasomnias, hypersomnias, and circadian rhythm disorders. *J Clin Sleep Med* 2008;4:591–600.
- [8] Abetz L, Allen R, Follet A, Washburn T, Early C, Kirsch J, et al. Evaluating the quality of life of patients with restless legs syndrome. *Clin Ther* 2004;26:925–35.
- [9] Abetz L, Allen R, Washburn T, Early C. The impact of restless legs syndrome (RLS) on sleep and cognitive function. *Eur J Neurol* 2004;9(Suppl. 2):S50.
- [10] Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med* 2005;165:1286–92.
- [11] Earley CJ, Silber MH. Restless legs syndrome: understanding its consequences and the need for better treatment. *Sleep Med* 2010;11:807–15.
- [12] Clemens S, Rye D, Hochman S. Restless legs syndrome: revisiting the dopamine hypothesis from the spinal cord perspective. *Neurology* 2006;67:125–30.
- [13] Allen R. Dopamine and iron in the pathophysiology of restless legs syndrome (RLS). *Sleep Med* 2004;5:385–91.
- [14] Trenkwalder C, Hogl B, Winkelmann J. Recent advances in the diagnosis, genetics and treatment of restless legs syndrome. *J Neurol* 2009;256:539–53.
- [15] Trotti LM, Bhadriraju S, Rye DB. An update on the pathophysiology and genetics of restless legs syndrome. *Curr Neurol Neurosci Rep* 2008;8:281–7.
- [16] Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. a report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101–19.
- [17] International Restless Legs Study Group. IRLSSG Diagnostic Criteria for RLS (2012). www.irlssg.org. Updated 2013. Accessed July 25, 2013.
- [18] American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th ed. Arlington (VA): American Psychiatric Association; 2013.
- [19] Picchietti DL, Ar buckle RA, Abetz L, Durmer JS, Ivanenko A, Owens JA, et al. Pediatric restless legs syndrome: analysis of symptom descriptions and drawings. *J Child Neurol* 2011;26:1365–76.
- [20] Picchietti DL, Rajendran RR, Wilson MP, Picchietti MA. Pediatric restless legs syndrome and periodic limb movement disorder: parent–child pairs. *Sleep Med* 2009;10:925–31.
- [21] Benes H, Walters AS, Allen RP, Hening WA, Kohnen R. Definition of restless legs syndrome, how to diagnose it, and how to differentiate it from RLS mimics. *Mov Disord* 2007;22(Suppl. 18):S401–8.
- [22] Hening WA, Allen RP, Washburn M, Lesage SR, Earley CJ. The four diagnostic criteria for Restless legs syndrome are unable to exclude confounding conditions (“mimics”). *Sleep Med* 2009;10:976–81.
- [23] Popat RA, Van Den Eeden SK, Tanner CM, Kushida CA, Rama AN, Black JE, et al. Reliability and validity of two self-administered questionnaires for screening restless legs syndrome in population-based studies. *Sleep Med* 2010;11:154–60.
- [24] Evans AM. Growing pains: contemporary knowledge and recommended practice. *J Foot Ankle Res* 2008;1:4.
- [25] Rajaram SS, Walters AS, England SJ, Mehta D, Nizam F. Some children with growing pains may actually have restless legs syndrome. *Sleep* 2004;27:767–73.
- [26] Walters AS. Is there a subpopulation of children with growing pains who really have restless legs syndrome? A review of the literature. *Sleep Med* 2002;3:93–8.
- [27] Rangarajan S, D’Souza GA. Restless legs syndrome in Indian patients having iron deficiency anemia in a tertiary care hospital. *Sleep Med* 2007;9:88–93.
- [28] Manconi M, Govoni V, De Vito A, Economou NT, Cesnik E, Casetta I, et al. Restless legs syndrome and pregnancy. *Neurology* 2004;63:1065–9.
- [29] Araujo SM, de Bruin VM, Nepomuceno LA, Maximo ML, Daher Ede F, Correia Ferrer DP, et al. Restless legs syndrome in end-stage renal disease: clinical characteristics and associated comorbidities. *Sleep Med* 2010;11:785–90.
- [30] Picchietti D. Is iron deficiency an underlying cause of pediatric restless legs syndrome and of attention-deficit/hyperactivity disorder? *Sleep Med* 2007;8:693–4.
- [31] Davis ID, Baron J, O’Riordan MA, Rosen CL. Sleep disturbances in pediatric dialysis patients. *Pediatr Nephrol* 2005;20:69–75.
- [32] Sinha R, Davis ID, Matsuda-Abedini M. Sleep disturbances in children and adolescents with non-dialysis-dependent chronic kidney disease. *Arch Pediatr Adolesc Med* 2009;163:850–5.
- [33] Applebee GA, Guillot AP, Schuman CC, Teddy S, Attarian HP. Restless legs syndrome in pediatric patients with chronic kidney disease. *Pediatr Nephrol* 2009;24:545–8.
- [34] Riar SK, Leu RM, Turner-Green TC, Rye DB, Kendrick-Allwood SR, McCracken C, et al. Restless legs syndrome in children with chronic kidney disease. *Pediatr Nephrol* 2013;28:773–95.
- [35] Pullen SJ, Wall CA, Angstman ER, Munitz GE, Kotagal S. Psychiatric comorbidity in children and adolescents with restless legs syndrome: a retrospective study. *J Clin Sleep Med* 2011;7:587–96.
- [36] Wagner ML, Walters AS, Fisher BC. Symptoms of attention-deficit/hyperactivity disorder in adults with restless legs syndrome. *Sleep* 2004;27:1499–504.
- [37] Zak R, Fisher B, Couvadedelli BV, Moss NM, Walters AS. Preliminary study of the prevalence of restless legs syndrome in adults with attention deficit hyperactivity disorder. *Percept Mot Skills* 2009;108:759–63.
- [38] Oner P, Dirik EB, Taner Y, Caykoğlu A, Anlar O. Association between low serum ferritin and restless legs syndrome in patients with attention deficit hyperactivity disorder. *Tohoku J Exp Med* 2007;213:269–76.
- [39] Silvestri R, Gagliano A, Arico I, Calareso T, Cedro C, Bruni O, et al. Sleep disorders in children with attention-deficit/hyperactivity disorder (ADHD) recorded overnight by video-polysomnography. *Sleep Med* 2009;10:1132–8.
- [40] Wiggs L, Montgomery P, Stores G. Actigraphic and parent reports of sleep patterns and sleep disorders in children with subtypes of attention-deficit hyperactivity disorder. *Sleep* 2005;28:1437–45.
- [41] Hornyak M. Depressive disorders in restless legs syndrome: epidemiology, pathophysiology and management. *CNS Drugs* 2010;24:89–98.
- [42] Guilleminault C, Palombini L, Pelayo R, Chervin RD. Sleepwalking and sleep terrors in prepubertal children: what triggers them? *Pediatrics* 2003;111:e17–25.
- [43] Walters AS, Rye DB. Evidence continues to mount on the relationship of restless legs syndrome/periodic limb movements in sleep to hypertension, cardiovascular disease, and stroke. *Sleep* 2010;33:287.
- [44] Innes KE, Selve TK, Agarwal P. Restless legs syndrome and conditions associated with metabolic dysregulation, sympathoadrenal dysfunction, and cardiovascular disease risk: a systematic review. *Sleep Med Rev* 2012;16:309–39.
- [45] Walter LM, Foster AM, Patterson RR, Anderson V, Davey MJ, Nixon GM, et al. Cardiovascular variability during periodic leg movements in sleep in children. *Sleep* 2009;32:1093–9.
- [46] Wing YK, Zhang J, Ho CK, Au CT, Li AM. Periodic limb movement during sleep is associated with nocturnal hypertension in children. *Sleep* 2010;33:759–65.
- [47] Picchietti D, Stevens HE. Early manifestations of restless legs syndrome in childhood and adolescence. *Sleep Med* 2008;9:770–81.
- [48] Xiong L, Montplaisir J, Desautels A, Barhaddi A, Turecki G, Levchenko A, et al. Family study of restless legs syndrome in Quebec, Canada: clinical characterization of 671 familial cases. *Arch Neurol* 2010;67:617–22.
- [49] Arbuckle R, Abetz L, Durmer JS, Ivanenko A, Owens JA, Croenlein J, et al. Development of the Pediatric Restless Legs Syndrome Severity Scale (P-RLS-SS): a patient-reported outcome measure of pediatric RLS symptoms and impact. *Sleep Med* 2010;11:897–906.
- [50] Silber MH, Richardson JW. Multiple blood donations associated with iron deficiency in patients with restless legs syndrome. *Mayo Clin Proc* 2003;78:52–4.
- [51] Ulfberg J, Nystrom B. Restless legs syndrome in blood donors. *Sleep Med* 2004;5:115–8.
- [52] Cesnik E, Casetta I, Turri M, Govoni V, Granieri E, Strambi LF, et al. Transient RLS during pregnancy is a risk factor for the chronic idiopathic form. *Neurology* 2010;75:2117–20.
- [53] Neau J-P, Marion P, Mathis S, Julian A, Godeneche G, Larrieu D, et al. Restless legs syndrome and pregnancy: follow-up of pregnant women before and after delivery. *Eur Neurol* 2010;64:361–6.
- [54] Traeger N, Schultz B, Pollock AN, Mason T, Marcus CL, Arens R. Polysomnographic values in children 2–9 years old: additional data and review of the literature. *Pediatr Pulmonol* 2005;40:22–30.
- [55] Montgomery-Downs HE, O’Brien LM, Gulliver TE, Gozal D. Polysomnographic characteristics in normal preschool and early school-aged children. *Pediatrics* 2006;117:741–53.
- [56] Pennestri MH, Whittom S, Adam B, Petit D, Carrier J, Montplaisir J. PLMS and PLMW in healthy subjects as a function of age: prevalence and interval distribution. *Sleep* 2006;29:1183–7.
- [57] Kotagal S, Silber MH. Childhood-onset restless legs syndrome. *Ann Neurol* 2004;56:803–7.
- [58] Muhle H, Neumann A, Lohmann-Hedrich K, Lohnau T, Lu Y, Winkler S, et al. Childhood-onset restless legs syndrome: clinical and genetic features of 22 families. *Mov Disord* 2008;23:1113–21.
- [59] Picchietti MA, Picchietti DL, England SJ, Walters AS, Couvadedelli BV, Lewin DS, et al. Children show individual night-to-night variability of periodic limb movements in sleep. *Sleep* 2009;32:530–5.
- [60] Hornyak M, Kopasz M, Feige B, Riemann D, Voderholzer U. Variability of periodic leg movements in various sleep disorders: implications for clinical and pathophysiologic studies. *Sleep* 2005;28:331–5.
- [61] Trotti LM, Blwiese DL, Greer SA, Sigurdsson AP, Gudmundsdottir GB, Wessel T, et al. Correlates of PLMs variability over multiple nights and impact upon RLS diagnosis. *Sleep Med* 2009;10:668–71.
- [62] Montplaisir J, Boucher S, Poirier G, Lavigne G, Lapierre O, Lesperance P. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. *Mov Disord* 1997;12:61–5.
- [63] Whittom S, Dauvilliers Y, Pennestri MH, Vercauteren F, Molinari N, Petit D, et al. Age-at-onset in restless legs syndrome: a clinical and polysomnographic study. *Sleep Med* 2007;9:54–9.

- [64] Hanson M, Honour M, Singleton A, Crawley A, Hardy J, Gwinn-Hardy K. Analysis of familial and sporadic restless legs syndrome in age of onset, gender, and severity features. *J Neurol* 2004;251:1398–401.
- [65] Fulda S, Wetter TC. Where dopamine meets opioids: a meta-analysis of the placebo effect in restless legs syndrome treatment studies. *Brain* 2008;131:902–17.
- [66] Stiasny-Kolster K, Kohnen R, Möller J, Trenkwalder C, Oertel WH. Validation of the “L-DOPA test” for diagnosis of restless legs syndrome. *Mov Disord* 2006;21:1333–9.
- [67] Stefansson H, Rye DB, Hicks A, Petursson H, Ingason A, Thorgeirsson TE, et al. A genetic risk factor for periodic limb movements in sleep. *N Engl J Med* 2007;357:639–47.
- [68] Silber MH, Becker PM, Earley C, Garcia-Borreguero D, Ondo WG. Willis-Ekbom disease foundation revised consensus statement on the management of restless legs syndrome. *Mayo Clin Proc* 2013;88:977–86.
- [69] Garcia-Borreguero D, Stillman P, Benes H, Buschmann H, Chaudhuri KR, Gonzalez Rodriguez VM, et al. Algorithms for the diagnosis and treatment of restless legs syndrome in primary care. *BMC Neurol* 2011;11:28.
- [70] Centers for Disease Control and Prevention. National report on biochemical indicators of diet and nutrition in the U.S. population 1999–2002, Iron-Status Indicators. 2008. http://www.cdc.gov/nutritionreport/99-02/part_3.html. Accessed August 19, 2013.
- [71] Winkelman JW. Periodic limb movements in sleep—endophenotype for restless legs syndrome? *N Engl J Med* 2007;357:703–5.
- [72] Gaultney JF, Merchant K, Gingras JL. Parents of children with periodic limb movement disorder versus sleep-disordered breathing report greater daytime mood and behavior difficulties in their child: the importance of using ICSD-2nd Edition criteria to define a PLMD study group. *Behav Sleep Med* 2009;7:119–35.
- [73] Bokkala S, Napalinga K, Pinninti N, Carvalho KS, Valencia I, Legido A, et al. Correlates of periodic limb movements of sleep in the pediatric population. *Pediatr Neurol* 2008;39:33–9.
- [74] Gingras JL, Gaultney JF, Picchiatti DL. Pediatric periodic limb movement disorder: sleep symptom and polysomnographic correlates compared to obstructive sleep apnea. *J Clin Sleep Med* 2011;7:603–9.
- [75] Ferri R, Bruni O, Novelli L, Picchiatti MA, Picchiatti DL. Time structure of leg movement activity during sleep in attention-deficit/hyperactivity disorder and effects of levodopa. *Sleep Med* 2013;14:359–66.
- [76] Ferri R, Manconi M, Lanuzza B, Cosentino FI, Bruni O, Ferini-Strambi L, et al. Age-related changes in periodic leg movements during sleep in patients with restless legs syndrome. *Sleep Med* 2008;9:790–8.
- [77] American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester (IL): American Academy of Sleep Medicine; 2005.
- [78] Gschliesser V, Frauscher B, Brandauer E, Kohnen R, Ulmer H, Poewe W, et al. PLM detection by actigraphy compared to polysomnography: a validation and comparison of two actigraphs. *Sleep Med* 2009;10:306–11.