Mimics of Childhood Restless Legs Syndrome

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KEYWORDS

• Pediatric restless legs syndrome/Willis-Ekbom disease • Restless legs syndrome mimics • Growing pains • Leg cramps • Positional discomfort • Periodic limb movement disorder • Restless sleep disorder

KEY POINTS

- Several mimics need to be considered in the differential diagnosis of pediatric restless legs syndrome/Willis-Ekbom disease (RLS/WED).
- Neither mimics do cause RLS nor do they exclude RLS diagnosis. In some cases, they also may co-occur or even precede later diagnosis of RLS.
- Mimics should receive specific treatment after careful diagnosis.

INTRODUCTION

Restless Legs Syndrome (RLS), also known as Willis-Ekbom Disease (WED), is a motor-sensory neurologic disorder first described by Thomas Willis in the 17th century and later characterized in adults by Karl-Axel Ekbom. Pediatric RLS, however, remained largely unrecognized until the 1990s, with formal diagnostic criteria established in 2003 and subsequently revised in 2013.[1]

Since RLS diagnosis in adults primarily relies on clinical history and symptom reports rather than nighttime polysomnography, diagnosing young children presents unique challenges, particularly due to their developing language and communication skills. As a result, additional supportive criteria—such as atypical daytime and nighttime behaviors, hyperactivity, mood disturbances, and cognitive or academic difficulties—can play a crucial role in identifying the disorder, especially in very young patients. A thorough family history is also essential, as early-onset RLS frequently runs in families, often affecting multiple relatives.[2]

The prevalence of RLS in the pediatric population remains relatively low, ranging from 1.3% in clinical settings to 5.9% in pediatric sleep clinics.[3] However, certain medical conditions, such as uremia, and neurologic disorders, particularly attention deficit hyperactivity disorder (ADHD), significantly increase its occurrence, with prevalence rates rising to 20% to 30% in affected groups.[4]

Additionally, while RLS is defined by its core diagnostic features—including a circadian pattern favoring nighttime onset during inactivity, an urge to move, and symptom relief through passive or voluntary movement—various motor and sensory manifestations may occur independently, further complicating diagnosis.

CLINICAL PRESENTATION

Motor and sensory mimics of (RLS) in pediatric patients differ from those commonly seen in adults. Their presentation is influenced by age-related variations in symptomatology and the evolving

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Abbreviations

ALMA	alternating leg muscle activation
IV	intravenous
PLMD	periodic limb movement disorder
PLMs	periodic limb movements
RLS	restless legs syndrome
RSD	restless sleep disorder
SHE	sleep hypermotor epilepsy
WED	Willis-Ekbom disease

spectrum of neurologic and musculoskeletal development.

As outlined by Chokroverty,[5] pediatric RLS mimics can be categorized into 4 distinct groups:

1. Conditions characterized by abnormal restlessness.
2. Disorders presenting with nocturnal leg discomfort or pain.
3. A combination of both restlessness and nocturnal discomfort (1 & 2).
4. Conditions presenting with hypermotor nocturnal activity.

The fourth category bears a striking resemblance to a potential RLS precursor observed in toddlers, described as hypermotor insomnia. This pediatric insomnia phenotype, as identified by Bruni and colleagues,[6] is often associated with a strong family history of conditions such as RLS, periodic limb movement disorder (PLMD), anemia, and growing pains.

For clarity and conciseness, I propose first distinguishing between common and uncommon pediatric RLS mimics involving sensory and pain-related conditions (**Table 1**) before addressing predominantly motor-related mimics (**Box 1**).

Among the most common sensory pain mimics of RLS are growing pains, which have been thoroughly described by Walters and colleagues,[7] particularly in their differentiation from RLS. Children with growing pains typically experience discomfort toward the end of the day, often exacerbated by physical activity. However, unlike RLS, these pains do not trigger an urge to move and are not alleviated by motor activity.

Table 1
Pediatric Restless legs syndrome/Willis Ekbom Disease sensory/painful mimics

Common Mimics	Less Common Mimics
Growing pains	Sickle cell disease
Sleep-related leg cramps	Arthritis
Ligament/tendon strain	Fibromyalgia
Myalgias	Myelopathy/Radiculopathy
Positional discomfort	Peripheral/polyneuropathy
Dermatitis	

Box 1
Motor periodic limb movements/restless legs syndrome mimics

PLMs/RLS Mimics

- Sleep Starts/hypnic jerks
- Hypnogogic foot tremor and ALMA
- Partial hypnic myoclonus
- Fragmentary myoclonus
- Propriospinal myoclonus of sleep onset
- Benign sleep myoclonus of infancy
- Sleep hypermotor epilepsy (SHE)
- Periodic limb movement disorder (PLMD)
- Restless sleep disorder (RSD)
- Rhythmic movement disorder
- Iatrogenic akathisia/dyskinesia

Diagnostic confusion frequently arises due to a familial history of RLS and potential genetic overlap between the 2 conditions. Notably, some children diagnosed with growing pains have later gone on to develop RLS in adulthood, further complicating the clinical distinction.[8]

Sleep-related leg cramps in children[9,10] manifest as painful, involuntary muscle contractions, primarily affecting the calf, and foot muscles. Unlike (RLS), these cramps do not exhibit a circadian pattern and are not alleviated by walking. Instead, relief is typically achieved through massage or stretching. Additionally, they do not respond to standard RLS treatments, such as dopaminergic therapy or iron supplementation. However, when necessary, magnesium supplementation may provide symptomatic relief.

Ligament and tendon strains commonly occur during sports activities, resulting in minor injuries. Similar to myalgias, neither these strains do improve with movement and typically aggravated by nighttime, nor are they confined to the distal regions of the lower limbs.

Positional discomfort refers to unpleasant sensations in the legs that arise from holding the same position for an extended period. This type of discomfort does not follow a circadian rhythm, and simply changing positions is usually sufficient to relieve it.

Dermatitis, particularly in atopic children, can also cause nocturnal pain, which is alleviated by local (topical) treatment of the affected areas.

Less frequently, painful mimics in children may include *sickle cell disease*, where pain crisis occurs due to hemolysis in the distal regions.

Arthritis and other painful rheumatologic conditions are typically aggravated by walking the floor at night, rather than alleviated by it. In these cases, the joints—rather than neuronal fibers—are primarily affected, and the pain does not follow a circadian rhythm.

Fibromyalgia, a rare, serum-negative rheumatic condition in adolescents, predominantly affects females and is characterized by a low pain threshold, allodynia, diffuse and poorly localized pain, and disrupted natural sleep. Unlike RLS, these patients typically do not wake during the night to temporarily relieve their pain.

Myelopathy and *radiculopathy*, though rare in children, are associated with prior traumatic, vascular, or inflammatory conditions. These disorders present with severe pain that follows a specific distribution, depending on the spinal regions involved.

Peripheral neuropathy, particularly *polyneuropathy*, causes burning, painful sensations in the upper and lower extremities, typically with a stocking-glove distribution. This condition is a common complication of diabetes and uremia, even in children. While the urge to move and a circadian preference may occasionally be observed, they are infrequent.

RLS mimics involving abnormal nocturnal restlessness encompass a wide range of conditions, from "isolated symptoms and normal variants" (as described by the International Classification of Sleep Disorders – Third Edition, Text Revision [ICSD-3-TR][11]) to a variety of benign and less benign myoclonic variants.

Among the former, *hypnic jerks*—also known as *sleep starts*—are physiologic phenomena experienced by about 70% of the adult population,[12] though they are less common during developmental periods. These jerks involve simultaneous contractions of multiple body segments at sleep onset and, like RLS, have both sensory and motor components, often creating the sensation of falling. When particularly intense or frequent, hypnic jerks can lead to sleep onset insomnia, much like RLS.[12]

Various types of myoclonus that occur at sleep onset include:

- *Benign sleep myoclonus of infancy*: Distal myoclonic jerks affecting the limbs and face, which must be distinguished from infantile epileptic seizures.
- *Partial hypnic myoclonus*: Sporadic, isolated contractions resembling fasciculations in the distal muscles that unlike periodic limb movements (PLMs) occur mostly during non-rapid eye movement (NREM) sleep, stage 1 (N1) and rapid eye movement (REM) sleep.
- *Fragmentary myoclonus*: Brief, bilateral, symmetric muscle twitches affecting the distal muscles, primarily occurring at sleep onset, and generally asymptomatic.
- *Hypnagogic foot tremor and alternating leg muscle activation (ALMA)*[13]: These typically benign symptoms are most often noticed by caregivers or incidentally recorded via video-polysomnography at sleep onset. Unlike RLS, these stereotypic movements do not cause discomfort to the affected individual.

Less benign and rarer myoclonic variants include:

- *Hyperplexia*: Excessive and generalized hypnic jerks, often causing startling and leading to stiffness and falls during both sleep and wakefulness.
- *Propriospinal myoclonus*: A chronic condition, rarely observed in children, characterized by sleep onset insomnia due to spontaneous jerks originating from the neck, trunk, and abdominal muscles, with slow upward and downward propagation. This condition is unique in that it occurs during relaxed wakefulness and resolves with mental activation or sleep, unlike RLS.
- *Epileptic myoclonus*: This condition coexists with electroencephalogram (EEG) discharges and other epileptic seizure features, often manifesting at sleep onset.
- *Sleep hypermotor epilepsy (SHE)*: An epileptic syndrome marked by partial motor seizures, predominantly originating from the frontal or temporal lobes. While restless, abnormal behaviors and postures may mimic the motor activity seen in RLS, they are, in fact, involuntary, complex stereotyped movements, distinct from the locomotor activity typical of RLS. The resulting sleep disturbances can be chronic and severe, leading to cognitive impairments and a reduction in verbal intelligence quotient (IQ), which is often more pronounced than in RLS-related conditions, including ADHD.[14]

ADHD frequently coexists with RLS,[15] as well as with other motor disorders like PLMD, bruxism, and disorders of arousal. A recent systematic review and meta-analysis suggests that 11% to 42.9% of children with ADHD also have RLS.[16] However, an interesting study showed that RLS mimics are more common than RLS in ADHD, with a ratio of 23%-11% mimics to RLS.[17] These

mimics encompass a broad range of conditions, from positional discomfort and habitual foot tapping to myalgia. ADHD comorbidity with RLS is more strongly predicted by a family history of RLS and by a more consistent functional impairment in daily and academic life, compared to RLS mimics.

PLMs, initially described as nocturnal myoclonus, are now defined as a sequence of 4 or more movements involving 1 or both anterior tibialis muscles, each lasting 0.5 sec, with intervals of 10 to 90 sec between them.[18] PLMs are observed in up to 74% of children diagnosed with RLS.[19]

PLMD is characterized by an elevated index of PLMs during sleep, accompanied by significant sleep disturbances and daytime impairment, in the absence of other medical, psychiatric, or sleep disorders that could explain the symptoms. Thus, while PLMD is distinct from RLS, it may serve as a rare pediatric mimic of RLS. A recent systematic review[20] found that when strict diagnostic criteria are applied, the prevalence of PLMD in children is very low. However, the frequent family history of RLS in children with PLMD suggests potential shared risk factors and genetic susceptibility.

Restless Sleep Disorder (RSD) is a recently defined sleep-related movement disorder, introduced to explain sleep-related restlessness.[21] It is characterized by gross body movements occurring in sequences throughout the sleep period, particularly in children who experience daytime behavioral and academic challenges, unrelated to sleep deprivation or sleep onset insomnia. Unlike children with RLS, those with RSD are generally unaware of and undisturbed by their movements during sleep. However, the behavioral consequences and lower ferritin levels suggest shared underlying mechanisms between RLS and RSD, suggesting possible similar therapeutic algorithms.

Sleep-related rhythmic movement disorder is a pediatric condition marked by repetitive, stereotypical rhythmic motor behaviors that engage large muscle groups, particularly at sleep onset. These movements are typically slow and affected individuals do not rise from their beds. Unlike RLS, there are no voluntary limb movements—rather, the movements involve the head and trunk, such as head and body rocking or rolling. Sleep and daytime functioning, as in RLS, are significantly impacted; however, there is no clear circadian pattern.

Furthermore, several tremors, stereotypies, and instances of restlessness in children may be induced by psychoactive drugs, including neuroleptics, antidepressants, and seizure medications.

Medications with the potential to cause RLS mimics include:

- Antidopaminergic medications can induce *dyskinesia* or *akathisia*, a rare pediatric condition marked by pervasive, persistent motor restlessness. Unlike RLS, this restlessness is not alleviated by movement, is not triggered by periods of rest, and generally does not disrupt sleep. Often, autistic children[22] report sleep onset restlessness akin to RLS behaviors, induced or worsened by antidopaminergic drugs, optimally responding to intravenous (IV) ferric carboxymaltose.[23]
- As for antidepressants, both serotonin selective reuptake inhibitors and dual serotonin and norepinephrine reuptake inhibitors increase leg movements in children,[24] whereas trazodone[25] and bupropion[26] have less or no detrimental effects.

DISCUSSION

Among the various RLS mimics discussed, a select few hold greater clinical significance and respond more effectively to treatment once accurately diagnosed. Notably, these include leg cramps, RSD, SHE, and both primary and iatrogenic restlessness in neurodevelopmental disorders.

The primary treatment approach involves discontinuing offending medications, such as neuroleptic antidepressants, and restoring iron levels through oral or IV supplementation. Iron repletion remains the sole universally acknowledged and well-tolerated strategy for alleviating sleep-related restlessness, particularly when ferritin levels fall below 50 μg/L[27] in cases of RLS[28,29] and RSD.[30] Moreover, restless sleep in neurodevelopmental disorders may be responsive by melatonin. In fact, a recent evaluation by an International Pediatric Sleep Association (IPSA) task force concluded that a cautious approach to melatonin therapy—beginning with the lowest effective dose and increasing gradually only when necessary, up to a maximum of 10 mg—can be beneficial in managing insomnia among children and adolescents with autism and neurogenetic disorders.[31]

Lastly, the diagnosis and treatment of nocturnal epilepsy—by targeting glutamate and N-methyl-D-aspartate transmission—share a common pharmacologic pathway with (RLS). This parallel suggests that altered membrane excitability and sleep deprivation serve as common triggers for a range of motor and sensory disturbances, impacting behavior and cognitive function during a crucial period of development. Pediatric RLS mimics may, therefore, reveal a fundamental vulnerability in the circadian regulation of movement during neurodevelopment.

SUMMARY

RLS has several mimics that may present either independently or alongside the condition. While some are benign, others necessitate a thorough, stepwise diagnostic approach followed by targeted treatment. The diversity of these mimics underscores the complexity of RLS as a multifaceted clinical conundrum, with mechanisms and characteristics that are distinct and not easily replicated as a whole within similar neurologic variants.

CLINICS CARE POINTS

- Use a thorough history (including family history) and physical examination, supported by laboratory testing, to differentiate RLS from its mimics.
- The classic RLS features—nocturnal onset during rest, an urge to move, and symptom relief with movement—are critical for diagnosis.
- Be aware that children may present with atypical features such as hyperactivity, mood disturbances, or academic difficulties, especially in younger patients with limited communication skills.
- Consider iron repletion (particularly when ferritin levels are <50 μg/L) and review medications (eg, SSRIs, neuroleptics) that may exacerbate symptoms.
- Distinguish sensory/pain mimics (growing pains, leg cramps, positional discomfort) from motor phenomena (hypnic jerks, periodic limb movements, sleep hypermotor epilepsy) for appropriate management.
- Overlooking the high frequency of RLS mimics in children with ADHD can result in overtreatment with RLS-specific therapies.
- Neglecting to consider atypical daytime or nighttime behaviors in young children can delay or obscure an accurate diagnosis.

DISCLOSURES

The authors have nothing to disclose.

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