

Sleep in the Pediatric Population



Jonathan P. Hintze, MD, Shalini Paruthi, MD*

KEYWORDS

• Restless legs syndrome • Narcolepsy • Parasomnia • Epilepsy • Headache • Pediatric • Sleep

KEY POINTS

- Pediatric sleep disorders are common and may have a significant impact on a child's daytime function and performance.
- Additionally having a co-morbid sleep disorder may worsen a neurologic disorder.
- Sleep disorders are well defined in the International Classification of Sleep Disorders, 3rd edition.
- The evaluation, diagnosis and treatments of common pediatric sleep disorders that frequently co-exist with neurologic disorders are reviewed here.

RESTLESS LEGS SYNDROME

Introduction

Restless legs syndrome (RLS) is a common neurologic sensorimotor disorder affecting 2% to 4% of the pediatric population.^{1–3} It is characterized by the urge to move the legs or by unpleasant sensations. These urges are worst at night and improve with movement or distraction. Sleep disturbance is the most common complaint in pediatric RLS, and is present in approximately 85% of patients (International Classification of Sleep Disorders, Third Edition [ICSD-3]⁴).

Impacts of RLS may include:

- Poor mood, irritability
- Increased risk of depression and anxiety
- Decreased daytime function at school
- Misdiagnosis of attention-deficit/hyperactivity disorder (ADHD)
- Headaches^{1,3–9}

Pathophysiology

Although not completely understood, dopamine has a prominent role in the pathophysiology of RLS. Inadequate dopamine production, use, and blockade are contributors. Iron is an essential cofactor for tyrosine hydroxylase, the enzyme of

the rate-limiting step of dopamine synthesis. Low iron availability may reduce dopamine production and transport. Therefore, low iron status is a common cause or contributor to RLS. Of note, iron shows a diurnal pattern with a nadir in the late evening and early night, which may contribute to increased symptom severity at night.^{10,11} Iron is also important in myelin synthesis, energy production, and other neurotransmitter systems that may play a role in RLS.^{12–14} Antidopaminergic medications are also contributors to RLS, although they are uncommon in children.

Genetics

Multiple genomewide studies have reported gene variants associated with RLS.^{15–20} Among children with RLS, at least 1 biological parent reported RLS symptoms in greater than 70% of families, with both parents affected in 16% of families.¹ Thus, individuals may have a genetic predisposition to RLS that combines with environmental factors, such as iron status, to determine clinical manifestations.

Diagnosis

The diagnosis of RLS is made by taking a specific history relevant to the diagnosis; a polysomnogram is not necessary to diagnose RLS. Special

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Department of Pediatrics, Saint Louis University School of Medicine, 1465 South Grand Boulevard, Glennon Hall 2712, St Louis, MO 63104, USA

* Corresponding author.

E-mail address: sparuthi@slu.edu

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consideration should be given to possible descriptions of symptoms based on the patient's age. Physical examination is usually nonfocal.

ICSD-3 criteria for the diagnosis of RLS for adults and children are the same and all criteria should be met:

- A. An urge to move the legs, usually accompanied by, or thought to be caused by, uncomfortable and unpleasant sensations in the legs. These symptoms must:
 1. Begin or worsen during periods of rest or inactivity, such as lying down or sitting
 2. Be partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
 3. Occur exclusively or predominantly in the evening or night rather than during the day
- B. The features listed earlier are not solely accounted for as symptoms of another medical or a behavioral condition (eg, leg cramps, positional discomfort, myalgia, venous stasis, leg edema, arthritis, habitual foot tapping).
- C. The symptoms of RLS cause concern, distress, sleep disturbance, or impairment in mental, physical, social, occupational, educational, behavioral, or other important areas of functioning.

Young patients should be encouraged to use their own words and have described RLS as:

- Pain
- Growing pains
- Shark bites
- Soda in my legs
- Need to stretch
- Cannot get comfortable

The differential diagnosis of common mimics includes (from Ref.²¹):

- Positional discomfort
- Sore leg muscles
- Ligament sprain/tendon strain
- Positional ischemia (numbness)
- Dermatitis
- Bruises
- Leg cramps

Management

Management includes:

- Avoidance of exacerbating factors
- Iron supplementation when ferritin level is less than 75 µg/L
- Medications (off-label) that are approved for RLS in adults, including gabapentin, ropinirole, pramipexole, and rotigotine

- Nonpharmacologic treatments: massage, warm bath, socks warmed for 5 to 10 minutes in a clothes dryer, compression stockings, or soccer socks in the evenings, and so forth

Avoidance of exacerbating factors

Exacerbating factors may include²²:

- Insufficient sleep for age
- Irregular sleep schedule
- Caffeine
- Nicotine
- Alcohol
- Medications (sedating antihistamines, serotonergic antidepressants, neuroleptics)

Serum ferritin and iron supplementation

Serum ferritin levels should be obtained on pediatric patients with RLS because more than 80% may have low levels.^{4,23,24} These patients often have improvement or resolution of symptoms with oral iron therapy.^{25–28} Serum ferritin results should be interpreted with caution because ferritin is an acute phase reactant and levels may remain increased for up to 4 weeks following a febrile illness.²⁹ Patients with serum ferritin levels less than 75 µg/L³⁰ should be treated with 2 to 4 mg/kg of elemental iron daily up to twice a day. Serum ferritin should be rechecked in 3 months, at which time symptoms are reassessed. Patients with ongoing iron therapy should continue to be monitored for iron overload, which is a rare but serious complication of iron therapy in individuals who carry hemochromatosis genes.³¹

Iron absorption is enhanced when taken with vitamin C (common in juices). Iron is more poorly absorbed when taken within 2 hours of calcium/dairy products and should be avoided.²²

Side effects of iron supplementation may include:

- Dark green or black stools while taking iron
- Temporary brown or gray teeth discoloration (resolves by brushing teeth with baking soda toothpaste)
- Constipation/diarrhea
- Abdominal pain

Other medications

Because there are no RLS treatments specifically labeled by the US Food and Drug Administration (FDA) for pediatric use, caution is advised to select treatment medications for off-label use. Medications that have been shown to improve RLS severity include gabapentin^{32,33} and dopaminergic medications, including ropinirole and pramipexole.^{4,23,28,34–38} Medications that are FDA approved for RLS in adults are often efficacious in children at

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