

# Practice Guideline: Treatment for Insomnia and Disrupted Sleep Behavior in Children and Adolescents with Autism Spectrum Disorder



This is a summary of the American Academy of Neurology (AAN) practice guideline, “Treatment for Insomnia and Disrupted Sleep Behavior in Children and Adolescents with Autism Spectrum Disorder,” which was published in *Neurology*<sup>®</sup> online on February 12, 2020, and appears in the March 3, 2020, print issue.

Please refer to the full guideline at [AAN.com/guidelines](http://AAN.com/guidelines) for more information, including full descriptions of the processes for classifying evidence, deriving conclusions, and making recommendations.

## Addressing Coexisting Medical Conditions and Concomitant Medications

### Recommendation 1

#### Rationale

Children and adolescents with autism spectrum disorder (ASD) are at increased risk of co-occurring conditions that contribute to sleep disturbance, such as intellectual disability, sleep apnea, epilepsy, gastrointestinal disturbances (including gastroesophageal reflux disorder), depression, anxiety, psychosis, bipolar disorder, and attention-deficit/hyperactivity disorder. Children and adolescents with ASD are also more likely to use medications that disrupt normal sleep patterns, such as stimulants, some anticonvulsants, and psychotropic medications.

Level	Recommendation
	Clinicians seeking to improve sleep in children and adolescents with ASD should perform an assessment for coexisting conditions that could be contributing to sleep disturbance.
	Clinicians seeking to improve sleep in children and adolescents with ASD should review concomitant medications that could be contributing to sleep disturbance.
<b>Level B</b>	Clinicians seeking to improve sleep in children and adolescents with ASD who have a coexisting condition that is contributing to their sleep disturbance should ensure they receive appropriate treatment for their coexisting condition.*
	Clinicians seeking to improve sleep in children and adolescents with ASD who have medications that could be contributing to sleep disturbance should address whether the potentially contributing medications can be stopped or adjusted.

\* Level B based on feasibility and cost relative to net benefit

## Behavioral Strategies

### Recommendation 2

#### Rationale

Environment and family factors, including child-rearing practices and bedtime routines that are not conducive to good sleep, contribute to sleep disturbance in children with ASD.<sup>1</sup> Although robust evidence for parental education and behavioral strategies to improve sleep in children and adolescents with ASD is lacking, suggested approaches include:

- Unmodified extinction: parents impose a set bedtime and wake-up time and ignore protest behavior that occurs after the bedtime and before the wake-up time
- Graduated extinction: parents ignore bedtime resistance for specified periods that are fixed or get progressively longer and then respond without reinforcing the resistant behavior (i.e., brief and boring verbal reassurance)
- Positive routines: parents develop and strictly adhere to regular pre-bed calming rituals
- Bedtime fading: parents put their child to bed close to the time the child begins to fall asleep<sup>2</sup>

In addition, this systematic review (SR) has shown that family-based cognitive behavioral therapy (CBT) with or without melatonin improves several aspects of sleep. In the study, families attended four weekly 50-minute sessions of CBT, where parents/caregivers received education and instruction on how to modify behavior regarding sleep and were required to complete homework practicing strategies, and then twice-monthly maintenance sessions over the 12 study weeks.<sup>3</sup> As a general tenet of pediatric practice, behavioral strategies are the preferred first treatment option before initiation of pharmacologic approaches. Successful application of behavioral approaches will require knowledgeable clinicians who can teach parents appropriate techniques and that parents implement the techniques consistently despite discomforts and challenges associated with behavioral modification.

Level	Recommendation
<b>Level B</b>	Clinicians seeking to improve sleep function in children and adolescents with ASD should counsel parents or guardians regarding strategies for improved sleep habits, with behavioral strategies as a first-line treatment approach either alone or in combination with pharmacologic or nutraceutical approaches, depending on individual circumstances.

## Melatonin

### Recommendation 3

#### Rationale

When managing coexisting conditions and adopting behavioral strategies are unsuccessful at improving sleep of children and adolescents with ASD, pharmacologic strategies are an additional treatment approach. There is low to moderate confidence that melatonin improves various aspects of sleep in children and adolescents with ASD. In the studies included in the SR, pharmaceutical-grade melatonin preparations were used and the exact administration amounts ascertained. One study used prolonged-release melatonin up to 10 mg per day,<sup>4</sup> one used three mg of prolonged-release melatonin, and one started two mg of immediate-release melatonin with titration to effect up to 10 mg (modal dose seven mg).<sup>5</sup> In practice, variable concentrations of melatonin are found in over-the-counter (OTC) preparations,<sup>6</sup> such that melatonin obtained by prescription is more representative of what was used in studies than OTC forms. Melatonin is generally administered 30 to 60 minutes before bedtime.<sup>7</sup> Because immediate-release melatonin has a short half-life (40 minutes), it is assumed that the immediate-release formulations are more helpful for sleep onset insomnia and controlled-release forms more helpful for sleep maintenance.

No study in the SR reported serious adverse events (AEs). AEs reported with melatonin include morning drowsiness, increased enuresis, headache, dizziness, diarrhea, rash, and hypothermia.<sup>8–11</sup> Melatonin is currently used safely as neuroprotection in preterm infants,<sup>12</sup> suggesting that it may also be safe in other pediatric populations, but long-term safety data are lacking for all pediatric populations. Possible long-term AEs are of particular concern given melatonin's ability to suppress the hypothalamic–gonadal axis and potentially initiate precocious puberty.<sup>13</sup> Risk associated with melatonin use in ASD must be weighed against the harms of persistently disordered sleep for individuals with ASD and their families. It is axiomatic of good care that use of any behavioral or medical treatment be periodically reevaluated to ensure there is continued benefit and no new AEs have occurred.

Level	Recommendation
<b>Level B</b>	Clinicians should offer melatonin to children and adolescents with ASD if behavioral strategies have not been helpful and contributing coexisting conditions and use of concomitant medications have been addressed.
<b>Level B</b>	Clinicians offering melatonin for sleep disturbance in children and adolescents with ASD should write a prescription for melatonin or recommend using a high-purity pharmaceutical grade of melatonin when available.

Level	Recommendation
<b>Level B</b>	Clinicians offering melatonin for sleep dysregulation in children and adolescents with ASD should start by initiating a low dose (one to three mg per day), 30 to 60 minutes before bedtime, and titrate to effect, not exceeding 10 mg per day.
<b>Level B</b>	Clinicians offering melatonin for sleep disturbance in children and adolescents with ASD should counsel children and adolescents with ASD and sleep disturbance (as appropriate) and their parents regarding potential AEs of melatonin use and the lack of long-term safety data.

## Complementary and Alternative Medicine (CAM) Approaches

### Recommendation 4

#### Rationale

Families of children and adolescents with ASD are often interested in CAM approaches. The SR identified that Sound-to-Sleep (STS) Mattress Technology possibly results in higher sleep efficiency (SE) over two weeks but possibly fails to improve sleep onset latency (SOL), wake after sleep onset (WASO), or time to sleep (TST). Weighted blankets possibly fail to improve SOL, SE, WASO, night awakenings, TST, and daytime behavior over two weeks. No high-quality studies of other CAM approaches were identified. AEs were not described in the STS mattress study. The only AE in the weighted blanket study was a two-day skin rash on one child that might have been blanket related. Weighted blankets vary in approach to production; in the available study, weighted blankets were chosen to avoid extreme thickness and weighed two and one-fourth kilograms (kg) (small) or four and one-half kg (large) by using three-millimeter steel shot pellets embedded evenly throughout the blanket.

Level	Recommendation
<b>Level B</b>	Clinicians should counsel children and adolescents with ASD and sleep disturbance (as appropriate) and their parents that there is currently no evidence to support the routine use of weighted blankets or specialized mattress technology for improving disrupted sleep.*
<b>Level B</b>	Although evidence of efficacy is lacking, clinicians should counsel children and adolescents with ASD and sleep disturbance (as appropriate) and their parents asking about weighted blankets that the reviewed trial reported no serious AEs with blanket use and that blankets could be a reasonable nonpharmacologic approach to try for some individuals.

\* Level B based on importance of outcomes, variation in preferences

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This guideline was endorsed by the American Academy of Sleep Medicine, Autism Speaks, the Child Neurology Society, and the Society for Developmental and Behavioral Pediatrics. The American Epilepsy Society affirmed the value of this guideline to epileptologists.

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American Academy of Neurology, 201 Chicago Avenue, Minneapolis, MN 55415

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