Review Article: Special Edition

Tourette disorder and sleep

Justin L. Blaty, Lourdes M. DelRosso

Seattle Children’s Hospital, University of Washington, Seattle, WA, United States

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A B S T R A C T

Healthy sleep is of utmost importance for growth, development, and overall health. Strong evidence shows that sleep is affected negatively in patients and particularly children with Tourette Disorder (TD). There is also a frequent association of TD with Attention Deficit Hyperactivity Disorder (ADHD) which alone has negative effects on sleep and cumulatively worsens the associated sleep findings. The most consistent polysomnographic findings in patients with TD is decreased total sleep time, lower sleep efficiency and an elevated arousal index. Polysomnography studies have confirmed the presence of movements and persistence of tics during both Rapid Eye Movement (REM) and NREM sleep [1]. In general Patients with TD are found to have an increased incidence of sleep onset and sleep maintenance insomnia. Some studies have shown increased incidence of parasomnias (including sleepwalking, sleep talking and night terrors), but this may be confounded by the increased underlying sleep disruptions seen in TD. The hypersomnolence found in patients with TD is also suggested to be secondary to the underlying TD sleep disruption. There is not a significant association with sleep disordered breathing or circadian rhythm disorders and TD. Treatment of underlying TD is important for the improvement of sleep related TD manifestations and is outlined in this review.

Gilles ‘de la Tourette or more commonly known as Tourette Syndrome or Tourette Disorder (TD) was first published in the literature in 1885 [1]. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classifies TD as a motor disorder characterized by both motor and vocal tics that persist for more than a year [2]. The onset of the disorder is usually prior to 18 years old and is more prevalent in boys [3]. The overall worldwide prevalence is 0.9% [3]. The frequency of tics usually increases in the second decade of life and starts decreasing during adolescence, but still tics persist into adulthood in a third of patients [3]. There is strong evidence that sleep is affected negatively in patients and particularly children with TD, with some studies suggesting a direct correlation between tic severity and sleep disruption [4]. Furthermore, motor tics have been reported to persist during sleep. Up to 65% of children with TD have shown sleep
disturbances of various types including but not limited to difficulty with sleep initiation, increased sleep disruption with associated decreased sleep efficiency [5]. The exact mechanism of this effect in sleep is not fully understood. Furthermore there is a high prevalence of comorbidities in children with TD, in particular 55% of children with TD also are diagnosed with attention deficit hyperactivity disorder [5] and 27% are diagnosed with Obsessive Compulsive Disorder (OCD) (range 2–66%) along with other conditions including anxiety and depression [7]. Freeman et al. and others have demonstrated that children with TD and comorbidities have worse sleep problems than children with TD alone [7]. Also notable, is the finding that effective management of sleep problems has been reported to improve tic control in both severity and impact on life [8,9] emphasizing the importance of adequately identifying and treating sleep complaints in children with TD. In this manuscript we will summarize the most important findings associated with the presence of sleep disorders in children with TD.

Sleep and Tourette Disorder (TD)

Healthy sleep is of utmost importance for growth, development, and overall health. Healthy sleep includes obtaining the right amount of sleep for age, with good quality of sleep, appropriate consolidation, continuity, and absence of a sleep disorder. Adequate sleep is important for brain development, learning, memory consolidation, emotion regulation, executive function, among other important functions [10]. Lack of sleep, sleep disruption or sleep disorders have been associated with cognitive deficits, executive dysfunction, emotional dysregulation, increased sympathetic activation, hormone dysregulation, decreased seizure threshold among other consequences [11].

The American Academy of Sleep Medicine (AASM) has published an expert consensus on sleep requirements for adults and children [Table 1] [12,13]. The AASM also has published the international classification of sleep disorders that divides sleep disorders into 6 main group categories: insomnia, parasomnias, hypersomnias, sleep related movement disorders, sleep related breathing disorders (SRBD) and circadian rhythm disorders [14]. Polysomnography is the gold standard for evaluation of sleep disorders. Polysomnography assesses sleep latency, sleep continuity, arousal index, among other parameters that help identify disturbances in sleep quality or quantity [15]. These parameters are calculated from a total sleep time which is the time (in minutes) from lights off to lights on in the sleep lab during which the patient is asleep. Sleep latency is the time from lights off to the start of the first epoch of any stage of sleep, and the sleep efficiency index is the total time spent sleeping divided by the total recorded time in bed (from lights out to lights on). The time spent awake during the night after initially falling asleep detracts from the sleep efficiency index. People who are tired or have a significant sleep debt may spend more time in bed in an attempt to increase their total sleep time, but oftentimes if there is a comorbid sleep disorder or medication effect, they may not be able to fall asleep quickly despite sleepiness, or may wake up through the night, resulting in prolonged sleep latency, lower sleep efficiency and lack of resolution of daytime sleepiness symptoms. Polysomnography can identify sleep disorders such as obstructive sleep apnea (OSA) and periodic leg movement disorders and the addition of video can help in the recognition of movements and tics which may be disrupting sleep. Other methods to assess sleep include objective actigraphy which estimates total sleep time and sleep disruption, and subjective sleep diaries and questionnaires.

Studies have demonstrated that children with TD get less sleep than children without TD and sleep disruption gets worse with age. In fact, older adolescents have less nights of good sleep than younger children with TD; in a recent study neither medications or comorbidities appear to predict adequate amount of sleep in children with TD suggesting that sleep disruption is inherent to TD and not only secondary to comorbidities or medications [16]. Lee et al. found that comorbid anxiety was associated with the highest risk of sleep disorders, followed by ADHD, and allergic rhinitis [17]. A study using sleep diaries showed that sleep initiation affects approximately 48% of children with TD and 56% of children with TD with Attention Deficit Hyperactivity Disorder (ADHD) while sleep maintenance is affected in 27% of children in the former group and 47% in the latter [5]. Fig. 1 illustrates the contribution of comorbidities and medications to the sleep disturbance seen in patients with TD.

Sleep architecture which is the distribution of sleep into different sleep stages and frequency of sleep disruption (arousals and awakenings), has been studied if patients with TD using polysomnography and important differences have been identified, although findings have been variable. The most consistent findings are decreased total sleep time, lower sleep efficiency and elevated arousal index [18]. There is inconsistency in the literature with regard to the effect of TD on percentage of REM and N3 delta wave sleep. Most polysomnographic studies assessing sleep parameters in children with TD also include children with comorbidities, particularly ADHD. It is difficult to identify TD specific effects on sleep architecture besides the increase numbers of arousals and effect in sleep continuity. Studies have also shown increased periodic limb movements (PLM) during sleep which appear to be additive and worse in the context of comorbid ADHD [1,19,20].

Pathophysiology of sleep disorders in TD

The pathophysiology of sleep disruption in children with TD is not completely understood but several potential mechanisms have been postulated. Early studies have pointed toward a dopaminergic dysfunction with likely increase in dopaminergic activity as evidenced by improvement of symptoms with medications that produce dopamine depletion (tetrabenazine) [21].

Most recently an epigenetic basis of environmental influences over genetic predisposition has been postulated. There are currently no consistent neuroimaging markers of TD but studies with magnetic resonance spectroscopy and
...neurotransmitters are also implicated including GABA and glutamate [22]. Overall, there is strong evidence to support involvement of the cortical-basal ganglia-thalamocortical circuits which are crucial for regulation and control of movement. This may indicate involved neurotransmitters including serotonin, histamine, acetylcholine, norepinephrine, endogenous cannabinoids, opioids, and adenosine may form a dynamic interplay in the pathophysiology of tics [8]. Many of these neurotransmitters (most significantly acetylcholine, norepinephrine, serotonin, histamine, and GABA) have important implications in the regulation of sleep and wakefulness supporting a pathologic explanation for increased sleep disruption in TD.

**Findings related to sleep**

As discussed, the international classification of sleep disorders third edition (ICSD-3) [14] classifies sleep disorders in 6 major groups. In this section we discuss the findings associated with each group in children with TD.

**Table 1 Recommended Amount of Sleep for Pediatric & Adult Populations to promote optimal health AASM Consensus Recommendations [12,13].**

| Age Group               | Recommendation                                      |
|------------------------|-----------------------------------------------------|
| Infants 0–4 months     | Not well established with wide variation & insufficient evidence for associations with health outcomes |
| Infants 4–12 months    | 12 to 16 h per 24 h (including naps)                |
| Children 1–2 years     | 11 to 14 h per 24 h (including naps)                |
| Children 3–5 years     | 10 to 13 h per 24 h (including naps)                |
| Children 6–12 years    | 9 to 12 h per 24 h                                  |
| Teenagers 13–18 years  | 8 to 10 h per 24 h                                  |
| Adults 18–60 years     | 7 or more hours per night on a regular basis        |

Insomnia

Insomnia is defined as a frequent and persistent difficulty initiating or maintaining sleep that results in general sleep dissatisfaction despite having adequate time and circumstances each night to obtain necessary sleep. This sleep complaint is accompanied by distress about poor sleep and/or impairment in important areas of functioning and can occur in isolation or comorbidly [23]. The classically used Spielman model of chronic insomnia “the 3P model” describes an implication of predisposing, precipitating, and perpetuating factors which all contribute to the development and maintenance of chronic insomnia [24].

As described above, there is a pathophysiologic neurochemical disruption of sleep wake regulation which predisposes TD patients to develop insomnia. Precipitating factors “push” someone to the state of clinically significant insomnia and can be the result of a single or multiple recurrent events. In patients with TD, negative effects of tic symptoms on school, work, or other performance can for example lead to reduced sleep opportunity from compensating with late nights. Patients with comorbid ADHD have also been shown to have an increased incidence of insomnia over TD alone [5]. Finally, perpetuating factors further contribute to the maintenance of chronic insomnia. Patients often report distress, anxiety and fear during drowsiness [25], reluctance to going to bed, and presence of myoclonic jerks or startle episodes on falling asleep [26]. This high prevalence of sleep onset and sleep maintenance insomnia have been described in both studies using subjective questionnaires and objective polysomnographic and actigraphy data [27].

Parasomnias

Parasomnias are defined as undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousal from sleep. This abnormal activity may occur during transitions to and from sleep, during NREM sleep (sleepwalking, sleep talking, night terrors or confusional arousals) or REM sleep (nightmares or REM behavior disorder) [23].

The NREM sleep disorders are viewed as a state of sleep-wake consciousness that is not fully declared and may be consciously disassociated with motor function retained. Other sleep disorders such as OSA have demonstrated an increase in comorbid night terrors or sleepwalking due to the increase sleep disruption [28]. One can speculate that movements during TD & the biochemical factors described could affect sleep continuity predisposing to increase in parasomnias. This was seen with a report of 14.3% of 56 young patients with TD or chronic tic disorder talking or walking during sleep [29].

Sleepwalking (somnambulism) is defined as ambulation and other complex behaviors out of bed while meeting NREM disorder criteria. One study of 247 children with TD and 47 random controls showed a threefold increased frequency of sleepwalking compared to controls [30]. A threefold increase was also seen in younger patients with TD age 6–17 compared to TD age >18 [31]. A defined prevalence of parasomnias in patients with TD is not clearly established.

![Image](82x85 to 252x246)

**Fig. 1 Contribution of ADHD, other comorbidities and medication effect to sleep disruption in patients with Tourette Disorder.**
There is also a confounding known age association with general population of some parasomnias (such as confusional arousals, sleep walking or sleep talking) which are generally more common in childhood and tend to decrease with age.

Sleep terrors (night terrors) are characterized by sudden scream from sleep usually during slow wave sleep (N3), with signs of autonomic arousal. Like in sleepwalking, there is dissociation and patients are not aware of the surroundings and do not recall of the event. Although the evidence is similarly not robust, Comings et al. also showed that 15.8%–49% of patients with TD had night terrors, and was higher than that found in controls [30].

REM sleep behavior disorder (RBD) is rare in children and always associated with a pathological process. RBD is characterized by dream enacting behaviors arising from REM sleep when atonia should occur. The pathophysiology of RBD is based on disruption this atonia mechanism during REM and is found commonly in neurodegenerative conditions particularly synucleopathies [32]. The prevalence is therefore higher in older individuals and very rare in children unless associated with other neurologic disorder (i.e. narcolepsy) [33]. There was only one case report found of a 7-year-old with the co-existence of Tourette’s syndrome with RBD confirmed after polysomnographic studies [34]. The authors proposed possible overlap in the pathophysiological mechanisms underlying the two disorders.

**Central disorders of hypersomnolence**

Hypersomnia refers to excessive daytime sleepiness (inability to stay awake or alert during wakeful portions of the day) and as a primary diagnosis is defined as not being caused by disturbed nocturnal sleep or misaligned circadian rhythms. Other sleep disorders may be present, but these must be adequately treated before a hypersomnia diagnosis can be established [23].

Disorders of hypersomnolence include narcolepsy type 1 or 2 (with physiologic basis on absence of neurons containing the sleep and wake regulating hormone orexin/hypocretin), idiopathic hypersomnia (diagnosis of exclusion with objective decreased sleep latency as seen on MSLT), Kleine-Levin syndrome and secondary hypersomnia.

There are no studies reporting cases of Kleine-Levin syndrome in children with TD. There are very few reported cases of TD and narcolepsy including 2 comorbid cases of TD & narcolepsy by Ghosh et al. [5] and one case of a patient with TD with a gene mutation of the orexin system implicated in narcolepsy [35]. The association with TD and narcolepsy is unknown at this time.

Results of questionaries used to evaluate other disorders of hypersomnolence in patients with TD vary in the literature. Modafferi et al. [26] described a significantly higher frequency of “daytime somnolence” and “falling asleep at school” in patients with tic disorders compared to healthy controls, but as described above also found significant sleep disruption reported in these patients. Other studies did not find significant difference from controls in patients with TD alone [5,36]. The hypersomnolence found in patients with TD is likely secondary to the sleep disruption associated with the disorder and comorbid ADHD, and it is unlikely to be a correlation with a primary central hypersomnolence condition.

**Sleep related movement disorders**

Sleep related movement disorders are primarily characterized by relatively simple, usually stereotyped, movements that disturb sleep or its onset [23]. There are several diagnosable movement disorders including periodic limb movement disorder, restless leg syndrome, restless sleep disorder (RSD), bruxism, sleep related rhythmic movement disorder and secondary sleep related movement disorders.

Early studies from 1980 have demonstrated that patients with Tourette syndrome exhibit more movements during sleep, across all sleep stages including REM sleep, showing poor sleep quality in patients with Tourette syndrome when compared to normal controls [1]. Polysomnography studies have confirmed the presence of movements and persistence of tics during both REM and NREM sleep [4].

PLM are characterized by repetitive, highly stereotyped limb movements that clinically disturb sleep. Some studies have found increased numbers of PLMs [20] while others have not confirmed this finding [37].

Restless legs syndrome (RLS) is a sensorimotor disorder characterized by an irresistible desire to move legs due to uncomfortable and unpleasant sensations that are worse at rest, symptom relief with movement and symptoms occurring/worsening in the evening/night prior to sleep. There is not significant evidence of increased RLS in TD. One study found increased prevalence of RLS in children with TD but the generalizability is limited [38]. There is also a potential reported genetic association with RLS and TD although evidence is limited [39].

The frequency of subjective “restless sleeper” has been shown to be significantly higher than controls (38.9% of 36 patients with TD vs 2.18% of 266 controls) [26]. The same study reported increased incidence of sleep-induced bruxism which is characterized by repetitive, stereotyped, and rhythmic motor behaviors (not tremors) that occur predominantly during drowsiness or sleep and involve large muscle groups [23].

Sleep-related rhythmic movements disorder (SRRMD) is characterized by repetitive, stereotyped, and rhythmic motor behaviors (not tremors) that occur predominantly during drowsiness or sleep and involve large muscle groups [23]. There are no studies reporting rhythmic movements in children with TD.

**Sleep related breathing disorders**

SRBD which include OSA, central sleep apnea, sleep-related hypoventilation, and sleep-related hypoxemia disorder [23] have been infrequently reported in patients diagnosed with TD [40]. Rare cases describing the presence of OSA and sudden infant death in children belonging to TD families led to the postulation of an increased risk of life-threatening apnea in infancy for TD gene carriers [41].
Circadian rhythm sleep-wake disorders

Circadian rhythm sleep-wake disorders are characterized by a chronic pattern of sleep and wake disturbance due to incongruence of the individual’s circadian sleep-wake propensity and the 24-h social and physical environment [23]. Presence of circadian rhythm sleep-wake disorders were reported in 3 of 31 (9.7%) of patients with TD-only and in 2 of 48 (4.2%) TD + ADHD patients [5]. There are no other reported associations found to date.

Treatment options

There are currently no guidelines on the approach to treatment of sleep complaints in children with Tourette syndrome. As described through this review, sleep disruptions and increased overnight arousals secondary to the underlying TD can elicit or exacerbate other sleep conditions such as symptoms of insomnia, parasomnias, and daytime somnolence. It is therefore of utmost importance to assess sleep habits and sleep behaviors in children with TD. Comorbidities can further worsen sleep disruption and exacerbate effects on cognition, executive function, emotional regulation, and other associated consequences. Fig. 2 illustrates a potential algorithm for evaluation of sleep in children with TD. As is seen with improvement of sleep with treatment of underlying OSA or ADHD, treatment of underlying TD is important for the improvement of sleep related TD manifestations.

In general, the interventions recommended for treatment of tics include neuropsychological interventions (habit reversal training, exposure and response prevention, and comprehensive behavioral intervention), and medications. Medical treatment should be considered when tics cause emotional, physical, or social problems and consists mainly of antipsychotics. Atypical antipsychotics have been used for their antidopaminergic activity and potential benefit in both symptoms of Tourette and sleep complaints. A single case report of a 12 year old treated with risperidone showed benefit in sleep latency and sleep efficiency [42]. Most recently aripiprazole has shown some promising results [43]. Interestingly, studies have shown that iron deficiency has been associated with more severe tics in children with TD with iron supplementation improving tic severity [44]. Iron supplementation poses an interesting potential pathophysiology of brain iron deficiency in TD [45], which is also present in children with ADHD and some sleep related movement disorders (RLS and RSD) [46–48].

Although not studied specifically for sleep complaints in children with TD, some medicines commonly used for improvement of tics can potentially improve sleep complaints (clonidine, clonazepam, iron, among other). Table 2 lists a review of treatment options in TD with medicines potentially improving sleep marked with (*).

Illustrative case:

A 12 year old boy with TD presents for evaluation of sleep disruption and daytime sleepiness. The child does not have any comorbidities. Tics are frequent and brief presenting as both motor and vocal, but he does not feel they interfere with daytime activities, school, or interactions. The child does not snore, does not have symptoms of RLS, and does not report difficulty falling asleep, however during sleep the parents report he is restless, with bed sheets very disrupted in the morning. His bedtime is 9 PM and wake up time is 7 AM. He also reports waking up at least 3–4 times each night without any apparent precipitant. In the morning he wakes up sleepy and has difficulty focusing during school. When he comes home, he feels like taking a nap but is not able to fall asleep. The child does not take any medication.

A sleep study is performed to identify the unknown causes for frequent nocturnal awakening. A segment of the sleep study is shown in Fig. 3. Frequent tics were found throughout the night in all sleep stages; some associated with awakenings and sleep disruption.

Treatment of tics was recommended and discussed with the family. Ferritin levels were found to be low and iron supplementation started with improvement in tic frequency and improvement in sleep quality with subsequent resolution in daytime symptoms.
| Treatment | Subjects | Methods | Findings | Cite |
|-----------|----------|---------|----------|------|
| **Alpha Agonists** | | | | |
| Clonidine* | N = 27 | Retrospective uncontrolled open-label study | 9 (33%): Excellent Response | [49] |
| | | Expert Opinion from National Guideline of Traditional Chinese Medicine | 9 (33%): Moderate Response | |
| | | | 9 (33%): Poor Response | |
| | | First Line Therapy | | [50] |
| **Antiepileptics** | | | | |
| Topiramate * | Expert Opinion from National Guideline of Traditional Chinese Medicine | | | [50] |
| **Dopamine Depletors** | | | | |
| Tetrabenazine | 9 patients | Retrospective uncontrolled open-label study | 4 (44%): Marked/Lasting improvement | [21] |
| | N = 15 | Retrospective uncontrolled open-label study | 3 (33%): Mild/Transient improvement | |
| | | | 2 (22%): Minimal/No response | |
| | | | 7 (47%): Excellent Response | |
| | | | 5 (33%): Moderate Response | |
| | | | 3 (20%): Poor Response | |
| **D2 Blocker** | Expert Opinion from National Guideline of Traditional Chinese Medicine | | | [50] |
| Tiapride | | Multisite, double-blind, double-dummy, randomized, placebo-controlled trial | 68.3% in the tiapride arm had clinical response and these rates of response were significantly higher than those on placebo | [51] |
| **Dopamine Precursor** | | | | |
| Very-low-dose levodopa therapy (VLDT) | | Questionnaire to providers | 14 providers reported treating with VLDT for tics. VLDT was 30–50% effective for all types of tics | [52] |
| Benzodiazepine | Japanese pediatric neurologists | | | |
| Clonazepam * | N = 13 | Retrospective uncontrolled open-label study | 5 (38%): Excellent Response | [49] |
| | | | 5 (38%): Moderate Response | |
| | | | 3 (24%): Poor Response | |
| **Monoamine Oxidase Inhibitor** | | | | |
| Selegiline (Deprenyl) | 25 boys, 4 girls with mean age 11.2 years old (range 6–18) with ADHD + TD | Open Trial | 26 patients reported improvement of ADHD with 2 patients reporting exacerbation of tics | [53] |
| **Antipsychotic** | | | | |
| Aripiprazole * | 44 patients aged 18–58 Mean dose 12.2 mg | Prospective uncontrolled open-label study | Results suggest that aripiprazole may improve associated comorbid conditions in addition to tics in patients with TD | [54] |
| | 78 Patients | Expert Opinion from National Guideline of Traditional Chinese Medicine | First Line Therapy | |
| | Case Series | | | [50] |
| Sulpiride | 114 patients reviewed | Retrospective analysis | Worthwhile beneficial effects occurred in 59% of patients | [56] |
| Fluphenazine | N = 28 | Retrospective uncontrolled open-label study | 15 (54%): Excellent Response | [49] |
| | | | 9 (32%): Moderate Response | |
| | | | 4 (14%): Poor Response | |
| Haloperidol | N = 24 | | 11 (32%): Excellent Response | [49] |
| | | | 19 (56%): Moderate Response | |
| | | | 4 (12%): Poor Response | |
| | | | Second Line Therapy | [50] |
| Pimozide | | | | |
| N = 9 | | | | |
| Risperidone * | 12 year old boy | Pre & Post PSG | Blockage of dopaminergic systems with antipsychotic risperidone reverts both TD symptoms and disturbances | [42] |

(continued on next page)
| Treatment | Subjects | Methods | Findings | Cite |
|-----------|----------|---------|----------|------|
| SSRI (Selective Serotonin Reuptake Inhibitor) | | | | [50] |
| Fluoxetine | 21 year old 32 year old | Observational study | Significant reduction (at least 50%) of abnormal movements and objective improvements | [52] |
| Nonpharmacologic Therapy | | | | |
| Comprehensive Behavioral Intervention for Tics (CBIT) * | 126 children aged 9–17 from Dec 2004–May 2007 randomized to CBIT or supportive therapy and education. | RCT Observer Blind | Behavioral intervention led to a significantly greater decrease on the Yale Global Tic Severity Scale | [58] |
| Morning Light Therapy * | 34 Adults with tic disorder | Scoping Review | Study in Progress | [59] |
| Alternate Therapy | | | | |
| Cannabis/Cannabidiol (CBD)/Cannabimovone (CBM) | 10,000 Abstracts | Systematic Review | The evidence supporting improvement Tourette syndrome was described as limited, insufficient, or absent. | [61] |
| | 98 patients | Retrospective analysis | CBM resulted in a subjective improvement of tics (of about 60% in 85% of treated cases), comorbidities (55% of treated cases, most often OCB/OCD, ADHD, and sleeping disorders), and quality of life (93%). | [62] |
| | 42 patients | Interview | MC seems to hold promise in the treatment of TD as it demonstrated high subjective satisfaction by most patients however not without side effects and should be further investigated as a treatment option for this syndrome. | [63] |
| Nicotine | Expert opinion | | When chronically taken, nicotine may result in protection against TD | [64] |
| Procedural Intervention | | | | |
| Botulinum toxin | Expert Opinion | | Botulinum toxin may be helpful in the treatment of focal motor tics and in some simple and complex phonic tics (including coprolalia) | [65] |
| Deep Brain Stimulation (DBS) | Expert Opinion | | DBS for TD is a valid option for medically intractable patients | [66] |
| Iron Replacement * | Children <18 year old diagnosed with TD during 2009–2015 with recorded ferritin levels | Retrospective analysis | Iron supplementation showed a trend towards improvement of tic severity upon follow-up. | [44] |
| Changma Xifeng Tablets | Expert Opinion from National Guideline of Traditional Chinese Medicine | | First Line Therapy | [50] |
| Jiuwei Xifeng Granules | Expert Opinion from National Guideline of Traditional Chinese Medicine | | First Line Therapy | [50] |
| 5-Ling Granule | 603 Patients age 5-18 | Multisite, double-blind, double-dummy, randomized, placebo-controlled trial | The clinical efficacy of 5-LGr is comparable to tiapride in reducing tics. Its safety profile is better than tiapride. 5-LGr can be considered a safe and effective therapy for TD. | [51] |
Conclusion

As we have reviewed in this manuscript, children with TD are at high risk of sleep disruption and increase prevalence of some sleep disorders such as movement disorders during sleep. It is very important to remember that tics can persist in all stages of sleep and contribute to sleep disruption.

There is compelling need for the diagnosis and treatment of any sleep disorders in children with TD and/or ADHD to facilitate better management of problem behaviors. Through the review, we have also identified areas of that remain under further investigation with limited and inconclusive data to date.

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There is no conflicts of interest to report for any of the authors.

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