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REVIEW

Sleep Disorders and Sleep Problems in Patients With Tourette Syndrome and Other Tic Disorders: Current Perspectives

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Abstract: Sleep disorders seem to be a frequent complaint of patients diagnosed with Tourette syndrome (TS) or chronic or persistent tic disorders (CTD or PTD). In this review, we expanded a previously used search using 4 well-known databases up to February 15, 2022, looking for the coexistence of global and/or specific sleep disorders and polysomnographic studies performed on patients with TS/CTD/PTD. The references of interest in the topic were selected by hand. Sleep disorders in general, insomnia, different arousal disorders, the persistence of tics during sleep, excessive daytime sleepiness, and periodic limb movements during sleep (PLMS) were very frequent in patients with TS, most of them being more frequent in patients with comorbid Attention Deficit Hyperactivity Disorder. The most frequent results from polysomnographic studies were decreased sleep efficiency and increased sleep onset latency. Many of these findings could be related to medication used for the treatment of tics and comorbid disorders.

Keywords: Tourette syndrome, sleep disorders, insomnia, hypersomnia, arousal disorders, periodic limb movements during sleep

Introduction

In 1884, Georges Gilles de la Tourette described 9 patients who presented with multiple tics, coprolalia, echolalia, and echopraxia. However in 1825, Itard had already made the first description of patients with a clinical picture consistent with what would nowadays be considered Tourette syndrome (TS).[1,2] TS is defined as a neuropsychiatric disorder of genetic origin mainly characterized by the presence of motor and vocal tics. Both attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) are very frequently associated with motor and vocal tics,[1,3–5] other well-established comorbidities being learning problems, anxiety, depression, disruptive behaviour disorders, and substance abuse.[1,5]

In his seminal work, Gilles de la Tourette described one patient who showed confusional pictures of violence after a sudden awakening from a profound sleep, which is probably the first description of a sleep disorder in a patient with TS.[6] Several recent reviews have shown that the presence of sleep disorders in TS should be considered as a frequent comorbidity of this condition.[7–11]

The current review, which updates previously reported information,[7–11] focuses on the main findings of studies addressing sleep features, including polysomnographic studies, of patients diagnosed with TS or persistent (chronic) tic disorder (CTD) according to the DSM-5,[2] by describing and discussing the reported data on this issue. Our search strategy, which used the terms of the international classification of sleep disorders (3rd edition)[13,14] and followed the methodology outlined in the PRISMA guidelines,[15] has been reported in detail elsewhere.[9] The time of the search was extended up to February 15, 2022.

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Studies on the Prevalence of Sleep Disorders in Tourette Syndrome

Table 1 summarizes the studies reporting on the frequency of sleep disorders in patients diagnosed with TS or CTD. Most of the studies were hospital-based series,[16–29] two were population-based studies,[31,39] and one study was a prospective follow-up.[31] The prevalence of sleep disorders described in these series ranges from 7.24% to 80%, although the definitions of sleep disorders, the age ranges, sex distribution, frequency of comorbidities, and the treatments used for TS and CTD show high variability between different studies. The lowest prevalence was found in a population study, although this was significantly higher than that found in a comparison control cohort, with a hazard ratio (95% confidence intervals) of 2.05 (1.43–2.95) ($p < 0.01$).[30]

Some authors reported a significantly higher "mean sleep problems score" in patients diagnosed with severe TS or with TS + ADHD when compared with controls,[22] and higher scores on the items related to "sleep disturbances" of the Child Behaviour Checklist in patients diagnosed with TS (especially if they had ADHD and/or OCD).[27] In addition, patients with TS/TD showed fewer nights with "sufficient sleep" than controls in a population-based study.[32]

According to several studies, sleep disturbances were more frequent in TS patients with comorbidities, such as ADHD,[22,23,27,29] OCD,[22,27,29] mood disorders-depression,[22,29] and anxiety disorders,[22,30] and in those with a family history of TS or tics.[17,18]

Association Between Specific Sleep Disorders and Tourette Syndrome

Insomnia

Table 2 summarizes the results of studies addressing the prevalence of insomnia and related symptoms in patients with TS/CTD, which was a frequent complaint. As was described in the studies on the global prevalence of sleep disorders, most of the studies on the prevalence of insomnia in these disorders were hospital-based series,[20–22,28,34–37] one was a population-based study[30] and the other a total population cohort study.[38] The prevalence of insomnia in these series ranged from 0.3% to 60%. The lowest prevalence, which was found in a population study in Taiwan, was similar to that found in a comparison control cohort (0.3 vs 0.2%).[30] TS patients with coexistent ADHD were more prone to developing insomnia, according to several series.[22,28,38]

The most consistent study, reported recently, was a total population cohort study carried out in Sweden[38] which described a prevalence of insomnia of 32.2%, a 6.7-fold increase compared to the general population. Insomnia was more frequent in TS/CTD patients than in their asymptomatic siblings, and was more frequent in patients with coexistent ADHD or those taking ADHD medication.[38]

Sleep-Related Breathing Disorders

Literature references to the presence of sleep breathing disorders in patients with TS or CTD are scarce. Some authors reported an increased risk of life-threatening sleep apnea in children carrying TS gene variations and described sudden infant death related to obstructive sleep apnea in children from TS families.[39] Apneic episodes with a relative increase in pCO2, which ceased after specific therapy, were reported in 3 out of 14 TS patients in a series.[18]

Other authors described the presence of *obstructive sleep apnea* confirmed by polysomnography, in 8 out of 34 TS patients.[21] A population study carried out in Taiwan, involving newly diagnosed TS patients, showed an estimated prevalence of sleep apnea of 0.2%, which was similar to that found in a control cohort (0.4%).[30]

Seven of 31 TS-only patients (two of them with obstructive sleep apnea and 2 with central sleep apnea), and 3 out of 48 patients diagnosed with TS + ADHD, showed sleep-related breathing disorders in a study by Ghosh et al.[28] Moddafferi et al[37] reported a non-significant higher frequency of sleep breathing difficulties in patients with CTD than in controls (11.1% vs 4.9%), although the differences only reached statistical significance when unmedicated CTD patients (16%) were considered, but did not find any CTD patients with sleep apnea in their series.[37]

Finally, the frequency of *snoring* as a respiratory disturbance in sleep was found to be similar in TS-only patients (36.8%), TS + ADHD patients (46.6%), and in controls (43.7%) according to one study,[40] while another described a significantly higher frequency in patients with CTD (32.0% in unmedicated patients, 27.8% in the whole sample) than in a control group (14.3%).[37]

Table 1 Studies on the Prevalence of Sleep Disorders in Tourette Syndrome

Authors, Year ReF	Country	Definition Criteria and Setting	Study Subjects and Treatment	Main Findings
Moldofski et al, 1974[16]	Canada	Sleep disturbances (difficulty in sleep onset and/or frequent nocturnal arousals) assessed using a specific questionnaire Hospital-based series	15 patients diagnosed with TS, most of these adults (14 male, mean age at onset of motor and vocal tics 7.7 and 10.3 years, all treated with haloperidol)	Prevalence of sleep disturbances: 80%
Nee et al, 1980[17]	United States of America	Sleep disturbances assessed by clinical interview Hospital-based series	50 patients diagnosed with TS (mean age at onset 7.0 years, sex not specified, 46 were treated with haloperidol)	Prevalence of sleep disturbances: 44% (53.1% in patients with a family history of TS or tics and 27.8% in those without a family history of TS or tics)
Glaze et al, 1983[18]	United States of America	Sleep disturbances (including enuresis, somnambulism, and frequent awakenings). Assessment of sleep disorders by PSG and video monitoring Hospital-based series	14 untreated patients diagnosed with TS (9 men; 7 aged 8–19 years and 2 aged 48 years)	Prevalence of sleep disturbances: 42.9% (60% in patients with a family history of TS or tics and 0% in those without a family history of TS or tics)
Barabas et al, 1984[19]	United States of America	Sleep disturbances Hospital-based series Assessment of sleep disorders using a standardized questionnaire	57 patients diagnosed with TS (50 boys, age 5–21 years, treatment not specified)	Prevalence of sleep disturbances: 38.6% (this was significantly higher than in 57 patients with seizure disorders −10.3%- and 53 with learning disabilities - 17%).
Erenberg, 1985[20]	United States of America	Sleep disturbances Hospital-based series Assessment of specific sleep disorders using a standardized sleep questionnaire	58 patients diagnosed with TS aged 15 to 25 years (average 17 years), sex and medication not specified	Prevalence of sleep disturbances: 22.4% (6 patients had nightmares. none of them had enuresis or somnambulism).
Jankovic & Rohaidy, 1987[21]	United States of America	Sleep complaints Hospital-based series Assessment of sleep disorders through an in-person interview and PSG	112 patients diagnosed with TS (male-to-female ratio 3.8, mean age at onset 7.3, average duration of the symptoms 15.2 years; most of them treated with neuroleptics or tetrabenazine, 27 with clonidine, and 13 with clonazepam)	Prevalence of sleep complaints: 61.6% (the most frequent were the persistence of tics during sleep −19.6%, and enuresis −17.0%).
Comings & Comings, 1987[22]	United States of America	Mean sleep problems score Hospital-based series Assessment of specific sleep disorders using a standardized sleep questionnaire	246 TS patients, 197 males, age ranges 2–75 years, mean age at onset 6.65 years; 39% have received treatment for ADHD or behavior problems	Significantly higher "mean sleep problems score" in patients with severe TS and TS + ADHD patients than in controls.
Freeman et al, 2000[23]	Canada	Sleep disorders assessed as a part of a global questionnaire of comorbidities International database from 64 hospitals	2846 males and 654 females diagnosed with TS, ADHD, or OCD (mean age at onset 6.4 years, treatment not specified)	Prevalence of sleep disorders: 25% in males and 26% in females Prevalence significantly higher for subjects with TS + ADHD + OCD, and TS + ADHD than in those with TS only and with TS + OCD Prevalence significantly higher for subjects with comorbid mood or anxiety disorders.

(*Continued*)

Table 1 (Continued).

Authors, Year ReF	Country	Definition Criteria and Setting	Study Subjects and Treatment	Main Findings
Teive et al, 2001[24]	Brasil	Sleep disorders assessed by clinical interview Hospital-based series	44 patients diagnosed with TS or other tic disorders. Treatment not specified	Prevalence of sleep disturbances: 9.1%
Saccomani et al, 2005[25]	Italy	Sleep problems assessed with a specific questionnaire to parents (increased number of arousals, poor sleep efficiency, increased frequency of sleepwalking, night terrors, sleeptalking, and trouble falling asleep) Hospital-based series	48 patients with TS (36 male, mean age 11.2 years; 26 with OCD, 21 with ADHD), 48 with chronic tic disorder (33 male, mean age 12.1 years; 4 with OCD, 11 with ADHD). Treatment not specified	Prevalence of sleep disturbances: 27.1% in TS, 16.7% in chronic tic disorder, 0% in 30 healthy controls.
Storch et al, 2007[26]	United States of America	Sleep-related problems assessed by 6 specific items from a Child Behavior Checklist and 1 item from a Multidimensional Anxiety Scale for Children Hospital-based series	56 patients diagnosed with TS or other tic disorders. Treatment not specified	Prevalence of "sleep-related problems": 19.7% with four or more, and 19.6% with none
Mol Debes et al, 2008[27]	Denmark	Scores in the items related with "sleep disturbances" of the Child Behaviour Checklist Hospital based series	314 patients diagnosed with TS (89.1% males, mean age at onset 12.4 years, 21.7% TS + OCD, 21.4% TS + OCD, 18.2% TS + ADHD + OCD; treatment not clearly specified, although 24 were on methylphenidate and 5 used medications for OCD)	Prevalence of sleep disturbances: 17% (the order of frequency was TS + ADHD + OCD > TS + OCD > TS + ADHD > TS only)
Ghosh et al, 2014[28]	United States of America	Sleep disorders Hospital-based series Assessment of sleep disorders using a standardized questionnaire	123 patients diagnosed with TS (48 TS-only and 75 TS + ADHD; mean age 13.6 ± 3.8 years, range 6–21 years; male-to-female ratio 5:1 for TS-only and 3:1 for TS +ADHD). Treatment not specified	Prevalence of sleep disturbances: 64.2% (64.6% in patients with TS only and 64.0% for patients with TS + ADHD)
Sambrani et al, 2012[29]	Germany	Assessment with a clinician reviewed semi-structured questionnaire assessing several comorbidities including sleep problems Hospital-based series	1032 patients diagnosed with TS (978), chronic tics (40), or other tic disorders (529 children, 503 adults, median age 17 years, mean age at onset 6.97 years; male-to-female ratio 3.4/1) Treatment not specified	Prevalence of sleep problems: 26.7% (these showed a strong association with comorbid depression, and a lesser association with ADHD, OCD, and tic severity)
Lee et al, 2017[30]	Taiwan	Sleep disorders Population-based study Diagnosis of TS and specific sleep disorders in a Longitudinal Health Insurance Database	1124 under 18-year-old patients newly diagnosed with TS between 2001–2007 (76% male, most of them likely untreated).	Prevalence of sleep disorders: 7.24% (significantly higher than that found in a control cohort −3.53%-, the risk was highest in patients with a comorbid anxiety disorder)

(*Continued*)

Table 1 (Continued).

Authors, Year ReF	Country	Definition Criteria and Setting	Study Subjects and Treatment	Main Findings
Groth et al, 2017[31]	Denmark	Sleep disturbances, assessed by scores in the items related to "sleep disturbances" of the Child Behaviour Checklist Prospective follow-up study	146 patients diagnosed with TS followed during 4–8 years (median 5.6 years) interviewed at 18.2 years (SD 3.0, range 11.1–25.9). 17.2% of patients of the initial cohort used antipsychotics, 17.1 methylphenidate, 8.8 atomoxetine, 4.4% clonidine, 5.2 melatonin, and 4.8% SSRIs	Prevalence of sleep disorders: 11.1%
Ricketts et al, 2018[32]	United States of America	Telephone survey with a single question regarding nights per week with "sufficient sleep". Population-based study	298 patients with current diagnosis of Tourette disorder (TD), 122 with a history of TD, compared with 254 controls, aged 6 to 17 years (66.0%, 48.8%, and 17.3%, respectively, using medications other than vitamins)	Controls showed significantly more nights per week with "sufficient sleep" (6.59) that both TD groups (5.49 and 5.41, there were no significant differences between both TD groups) Early adolescent females with moderate/severe TD had lesser "sufficient sleep".

Abbreviations: TS, Tourette syndrome; ADHD, Attention Deficit Hyperactivity Disorder; OCD, Obsessive-Compulsive Disorder; EEG, Electroencephalogram; EMG, Electromyogram; EOG, Electrooculogram; ECG, Electrocardiogram; REM, Rapid Eye Movements; NREM, Non-Rapid Eye Movements; PLMS, Periodic Limb Movements during Sleep.

Central Disorders of Hypersomnolence

According to Allen et al,[40] patients with TS + ADHD showed significantly higher scores in items of "drowsiness during the day" and "irresistible daytime sleep", and significantly higher frequencies of "drowsiness during the day" and "irresistible daytime sleep" than controls (33.3% and 23.0% of 89, and 3.0% and 3.0% of 146, respectively). However, the frequencies of these items in patients with TS-only (10.7% and 10.7% of 57) and ADHD-only (15.0% and 15.8% of 21) did not reach significant differences compared to controls.

According to Ghosh et al,[28] the frequencies of "excessive daytime sleepiness" and "unrefreshed after sleep" did not differ significantly between TS-only (52% and 65%, respectively) and TS + ADHD patients (52% and 64%, respectively). According to the same group, only 3 of 31 TS-only patients and 2 of 48 TS + ADHD patients showed primary hypersomnia (one in each group was diagnosed with concomitant sleep apnea).[28]

"Daytime somnolence" and "falling asleep at school" were significantly more frequent in patients diagnosed with tic disorders (19.4% and 5.6%, respectively) than in healthy controls (5.6% and 0.4%, respectively).[37] In addition, in the tic disorder patient group, these two symptoms were more frequent in patients with higher severity of tics (according to the Yale Global Tic Severity Scale –YGTSS) and those medicated,[37] and 2.8% of patients (all of them unmedicated and with low YGTSS scores) and 1.5% of the controls reported "sleep attacks".[37]

Finally, a recent population-based study in a large cohort carried out in Taiwan showed a similar frequency of "hypersomnia" in patients with a recent diagnosis of TS (0.3%) than in healthy controls (0.1%).[30]

Ghosh et al[28] reported the presence of *narcolepsy* in 2 of 31 patients diagnosed with TS-only and in 2 of 48 with TS + ADHD. One of 70 patients diagnosed with TS, 2 of 28 patients with narcolepsy, and none of 110 control individuals, carried mutations in a gene implicated in an animal model of narcolepsy and some sporadic cases of human narcolepsy, called *orexin2/hypocretine2 receptor* gene (*HCRTR2*, chromosome 6p12.1, gene ID 3062).[41] In the literature search, we did not find any reports of co-occurrence of TS with Kleine-Levin syndrome.

Table 2 Studies on the Prevalence of Insomnia in Tourette Syndrome

Authors, Year Ref	Country	Definition Criteria and Setting	Study Subjects and Treatment	Main Findings
Erenberg, 1985[20]	United States of America	Difficulty falling asleep Hospital-based series Assessment of specific sleep disorders using a standardized sleep questionnaire	58 patients diagnosed with TS aged 15 to 25 years (average 17 years), sex and medication not specified	Prevalence of difficulty falling asleep: 5.4%
Jankovic & Rohaidy, 1987[21]	United States of America	Sleep complaints Hospital-based series Assessment of sleep disorders through in-person interview and PSG	112 patients diagnosed with TS (male-to-female ratio 3.8, mean age at onset 7.3, average duration of the symptoms 15.2 years; most of them treated with neuroleptics or tetrabenazine, 27 with clonidine, and 13 with clonazepam)	Prevalence of insomnia: 10.7%
Comings & Comings, 1987[22]	United States of America	Difficulty falling asleep or early awakening Hospital-based series Assessment of specific sleep disorders using a standardized sleep questionnaire	246 TS patients, 197 males, age ranges 2–75 years, mean age at onset 6.65 years; 39% have received treatment for ADHD or behavior problems	Prevalence of difficulty falling asleep: 49.6% (65.5% in severe TS) Prevalence of early awakening; 32.5% (42.5% in severe TS and 47% in ADHD only)
Champion et al, 1988[33]	Canada	Problems getting to sleep Assessment of sleep disorders using a standardized questionnaire sent to the parents Hospital-based series	210 patients diagnosed with TS. Age, sex, and treatments not specified	Prevalence of problems getting to sleep: 66%
Drake et al, 1992[34]	United States of America	Difficulty falling asleep. Clinical assessment and nocturnal sleep cassette EEG recording Hospital-based series	20 drug-free TS patients (8 treated previously; 14 males, age not specified, 7 had ADHD and 5 OCD) and 7 controls (6 males, age not specified)	Prevalence of difficulty falling asleep: in 45%
Wand et al, 1993[35]	Canada	Difficulty falling asleep Problems staying asleep Hospital-based series Assessment of sleep disorders using a standardized questionnaire sent to the parents	422 TS patients (245 aged 6–17 years and 177 aged >17 years, male-to-female ratio 4:1, treatments not specified)	Prevalence of difficulty falling asleep: 29.7% for the two groups of age Prevalence of problems staying asleep: 9.3% in patients aged 6–17 and 12.9% in patients aged ≥18 years

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Romano et al, 2004[36]		Assessment of sleep disorders using a standardized questionnaire including difficulty or refusal to go to sleep, difficulty falling asleep, distress, anxiety, or fear during drowsiness, startle episodes during drowsiness, rhythmic swing movements during drowsiness, and sweating episodes during drowsiness. Hospital-based series	40 children and 9 teenagers with tic disorders (TD) and in 893 age- and sex-matched controls. Treatment not specified	Difficulty or refusal to go to sleep (TD 54.1%, controls 29.7%) Difficulty falling asleep (TD 24.3%, controls 8.9%) Distress, anxiety, or fear during drowsiness (TD 45.9%, controls 8.2%) Startle episodes during drowsiness (TD 40.5%, controls 5.0%) Rhythmic swing movements during drowsiness (TD 10.8%, controls 2.7%) Sweating episodes during drowsiness (TD 10.3%) controls 24.5%
Ghosh et al, 2014[28]	United States of America	Insomnia Problems in sleep initiation Problems in sleep maintenance Hospital-based series Assessment of sleep disorders using a standardized questionnaire	123 patients diagnosed with TS (48 TS-only and 75 TS + ADHD; mean age 13.6 ± 3.8 years, range 6–21 years; male-to-female ratio 5:1 for TS-only and 3:1 for TS +ADHD). Treatment not specified	Prevalence of insomnia: 48.0% in TS-only patients and 77.1% in TS + ADHD (in 33.3% insomnia was related to drugs used for ADHD, specially methylphenidate and atomoxetine) Prevalence of problems in sleep initiation: 48.0% in TS-only patients and 56.0% in TS + ADHD Prevalence of problems in sleep maintenance: 26.7% in TS-only patients and 46.7% in TS + ADHD
Moddafferi et al, 2016[37]		Assessment of sleep disorders using a standardized questionnaire including going to bed reluctantly, difficulty falling asleep at night, anxiety or fear when falling asleep, need for a transitional object, need for fluids or drugs to facilitate sleep, and myoclonic jerks on falling asleep. Hospital-based series	36 patients with TS (n=28) and chronic tic disorders (n=8) (30 males aged 8–16.3 years, mean 11.7 years, age at onset 3–10.5 years, mean 6.3 years; treatments not specified) and 266 age and sex-matched controls	Prevalence of going to bed reluctantly: 44.4% Prevalence of difficulty falling asleep at night: 30.6% Prevalence of anxiety or fear when falling asleep: 36.1% Prevalence of need for a transitional object: 30.6% Prevalence of need for fluids or drugs to facilitate sleep: 13.9% Presence of myoclonic jerks on falling asleep: 27.8%. All these variables were significantly more frequent than in controls and most of them in non-medicated patients and those with lower severity assessed with the Yale Global Tic Severity Scale (YGTSS)

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Table 2 (Continued).

Authors, Year Ref	Country	Definition Criteria and Setting	Study Subjects and Treatment	Main Findings
Lee et al, 2017[30]	Taiwan	Sleep disorders Population-based study Diagnosis of TS and specific sleep disorders in a Longitudinal Health Insurance Database	1124 under 18-year-old patients newly diagnosed with TS between 2001–2007 (76% male, most of them likely untreated)	Prevalence of insomnia: 0.3% (similar to that found in a control cohort −0.2%)
Isomura et al, 2021[38]	Sweden	Insomnia A total population cohort study Registered diagnostic of TS/CTD, and diagnostic of insomnia, including those subjects using medications with a specific indication for insomnia, in a National Registry	10.444.702 individuals aged 3 years or older living in Sweden between January 1, 1997, and December 31, 2013, excluding those with an organic brain disorder and/or epilepsy (5.877 with TS/CTD)	Prevalence of insomnia: 32.2% (30.8% in men, 37.1% in women) significantly higher than that found in subjects without TS/CTD (13.7%, 10.6% in men, 16.8% in women), with OR (95% CI) 6.82 (6.44–7.22), 7.23 (6.78–7.71), and 5.33 (4–74–5.99), respectively. Prevalence of insomnia in individuals with TS/CTD with unaffected siblings (n=1218): 30.8%, significantly higher than that in their unaffected siblings (11.4%) Comorbid ADHD and use of ADHD medication increased considerably the likelihood of insomnia

Abbreviations: TS, Tourette syndrome; ADHD, Attention Deficit Hyperactivity Disorder; OCD, Obsessive-Compulsive Disorder; EEG, Electroencephalogram; EMG, Electromyogram; EOG, Electrooculogram; ECG, Electrocardiogram; REM, Rapid Eye Movements; NREM, Non-Rapid Eye Movements; PLMS, Periodic Limb Movements during Sleep; YGTCS, Yale Global Tic Severity Scale.

Circadian Rhythm Sleep-Wake Disorders

Ghosh et al[28] reported the presence of circadian rhythm sleep-wake disorders in 3 of 31 (9.7%) of their patients with TS-only and in 2 of 48 (4.2%) of the TS + ADHD patients in their series. We found no clinical descriptions of these disorders in TS.

Parasomnias

Data from studies addressing the frequency of both NREM-related parasomnias (confusional arousals, sleeptalking, sleepwalking or somnambulism, and sleep night terrors) and REM-related parasomnias in TS patients (REM sleep behaviour disorder, sleep paralysis, night terrors, and sleep enuresis) are summarized in Table 3.

Confusional arousals, resembling those described in the seminal work by Gilles de la Tourette,[6] have been described in 50% of TS patients in a short clinical series.[18]

The frequency of *sleepwalking (somnambulism)* in patients with TS found in several clinical series shows high variability, ranging from 8% to 46.0%.[19,21–24,27,35,40,42] Moreover, Erenberg et al[20] did not find any patients suffering from this parasomnia among 58 patients aged 15–25 years, and Modafferi et al[37] reported a frequency of 5.6% in patients with tic disorders. Some authors report a 3-fold higher frequency of *sleepwalking* in TS patients compared with controls,[22,52] and others report a significantly higher frequency in patients with TS + ADHD than in those with TS-only,[28,40] in healthy controls,[40] and in patients with co-occurrence migraine.[43] Similarly, high variability was reported regarding the frequency of *sleeptalking*, which ranged from 1.7% to 47.9%,[20,22,28,37,40] was significantly higher[40] or did not differ significantly from that found in controls[37] in two clinical series, and was higher in patients diagnosed with ADHD-only and TS + ADHD than in those with TS-only according to Allen et al.[40] Finally, according to Storch et al,[26] 14.3% of 56 young patients with CTD or TS walked or talked during sleep.

The frequency of *sleep terrors* in patients with TS, which ranged from 15.8% to 49%,[19,22,23,40] was significantly higher than that reported in controls[37] and patients with learning disabilities or seizure disorders,[19] and was even higher in patients with comorbid migraine[43] and ADHD.[40] Moddaferi et al[37] described sleep terrors in 2.8% of patients with tic disorders and 1.1% of controls. To our knowledge, the association between *sleep-related eating disorder* and TS has not been reported to date.

Despite the fact that *REM behaviour disorder* is a very infrequent condition in children,[44] Trajanovic et al[45] described a boy diagnosed with TS who developed a clinical picture compatible with this disease aged 7 years. Modafferi et al[37] reported a frequency of 5.6% of *sleep paralysis* in patients with tic disorders and 2.6% in controls, although the difference did not reach statistical significance. The frequency of *nightmare disorders* in TS or tic disorders, which was higher in patients with TS + ADHD,[28,40] ranged from 5.4% to 46.2%.[20,21,24,28,37,40] Finally, although *sleep enuresis* was not found in any of the 58 TS patients of a clinical series,[20] other authors have reported this comorbidity in 10–20% of patients with TS or tic disorders,[19,21,23,24,40] being more frequent in patients with TS + ADHD.[40]

Sleep-Related Movement Disorders

Alonso-Navarro et al[46] recently reviewed the relationship between TS and *restless legs syndrome* (RLS), which were first described as coexistent disorders, together with akathisia, in a German family.[47] Walters et al[48] found a frequency of TS of 1.7% (similar to that described in the general population) in 118 adult patients referred with a diagnosis of RLS to a Sleep Disorders Unit. On the other hand, 10% of 144 probands diagnosed with TS or CTD chronic tics, and 23% of their parents, fulfilled diagnostic criteria for RLS, most of them being linked to paternal RLS.[49] A recent study found an association between TS without concomitant OCD and 3 intronic variants in the *BTB domain containing 9* gene (*BTB9*, chromosome 6p21.2, gene ID 114781, MIM 611237; related to the risk for RLS according to Genome-Wide Association Studies).[50]

Periodic limb movements during sleep (PLMS) have been reported as a frequent finding in TS patients (even more frequent in patients with TS + ADHD −32.0% than in patients with TS-only – 20.8%) in a clinical series.[28] In addition, PLMS have been a frequent finding in polysomnographic studies in patients with TS,[51–54] especially in those with comorbid ADHD,[53] are most frequently seen in sleep stages I/II,[51,52] and in many cases cause arousals.[41]

Table 3 Summary of Frequency of Parasomnias in Patients Diagnosed with Tourette Syndrome

Authors, Year Ref	Country	Study Subjects and Treatment	Confusional Arousals	Sleep Walking (Somnam-Bulism)	Sleep Talking	Sleep (Night) Terrors	Rem Sleep Behavior Disorder	Sleep Paralysis	Nightmare Disorder	Sleep Enuresis
Glaze et al, 1983[18]	United States of America	14 untreated TS patients (9 men; 7 aged 8–19 years and 2 aged 48 years) and 11 healthy controls (10 men, 8 aged 8–16 years, and 3 adult men). Assessment of sleep disorders by PSG and video monitoring	7/14 (50%)	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA
Barabas et al, 1984[19]	United States of America	57 patients with TS (50 boys, age 5–21 years, treatment not specified), 58 with seizures disorders, and 53 with learning disabilities. Assessment of sleep disorders using a standardized questionnaire	NS	10/57 (17.5%) Significantly higher than in patients with seizure disorders and learning disabilities	NS/NA	9/57 (15.8%) Significantly higher than in patients with seizure disorders and learning disabilities	NS/NA	NS/NA	NS/NA	10/53 (18.9%) Significantly higher than in patients with seizure disorders
Barabas et al, 1984[42]	United States of America	57 patients with TS (50 boys, age 5–21 years, treatment not specified), 57 with seizures disorders, and 57 with learning disabilities. Assessment of somnambulism using a standardized questionnaire	NS/NA	10/57 (17.5%) Significantly higher than in patients with seizure disorders and learning disabilities	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA

Erenberg et al, 1985[20]	United States of America	58 patients with TS aged 15 to 25 years (average 17 years), sex and medication used were not specified. Assessment of specific sleep disorders using a standardized sleep questionnaire	NS/NA	0/58 (0%)	1/58 (1.7%)	NS/NA	NS/NA	NS/NA	6/58 (46.2%)	0/58 (10.3%)
Jankovic & Rohaidy, 1987[21]	United States of America	34 TS patients recruited from a sample of 112 TZ patients with male-to-female ratio of 3.8, mean age at onset of 7.3, and an average duration of the symptoms of 15.2 years. Most of them were in treatment with neuroleptics or tetrabenazine, 27 with clonidine, and 13 with clonazepam. Assessment of sleep disorders through in-person interview and PSG	NS/NA	9/112 (8%)	NS/NA	NS/NA	NS/NA	NS/NA	6/112 (5.4%)	19/112 (17%)
Comings & Comings, 1987[22]	United States of America	246 TS patients, 197 males, age ranges 2–75 years, mean age at onset 6.65 years; 39% have received treatment for ADHD or behavior problems Assessment of specific sleep disorders using a standardized sleep questionnaire	NS/NA	116/247 (46.9%) often or occasionally (14.9% in 47 controls)	114/247 (46.2%) often or occasionally (56.9 in severe TS; 51.1% in 47 controls)	112/247 (45.5%) often or occasionally (21.2% in 47 controls)	NS/NA	NS/NA	NS/NA	NS/NA

(*Continued*)

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Table 3 (Continued).

Authors, Year Ref	Country	Study Subjects and Treatment	Confusional Arousals	Sleep Walking (Somnam-Bulism)	Sleep Talking	Sleep (Night) Terrors	Rem Sleep Behavior Disorder	Sleep Paralysis	Nightmare Disorder	Sleep Enuresis
Champion et al, 1988[23]	Canada	Age, sex, and treatments not specified. Assessment of sleep disorders using a standardized question-naire sent to the parents	NS/NA	42/210 (20%)	NS	103/210 (49%)	NS/NA	NS/NA	NS/NA	42/210 (20%)
Allen et al, 1992[40]	United States of America	57 boys diagnosed with TS-only (mean age 11.6 ± 2.0 years, 47.4% under specific therapy); 89 boys with TS + ADHD (mean age 10.9 ± 1.9 years; 64.0% under specific therapy); 21 diagnosed with ADHD-only (mean age 10.4 ± 2.0; and 146 controls (mean age 10.8 ± 1.8). Assessment of specific sleep disorders using a standardized sleep behaviour questionnaire	NS/NA	Higher frequency in TS+ ADHD (23.9% of 89) than in controls (8.2% of 146). TS-only (20.0% of 57) and ADHD-only (25.0% of 21) similar to controls	Frequency significantly higher for TS + ADHD (52.3% of 89), TS-only (45.6% of 57), and ADHD-only (58.5% of 21) than for controls (22.8% of 146)	Frequency significantly higher in TS +ADHD (19.8% of 89) and in ADHD-only (20.0% of 21) than in TS-only (9.1% of 57) and controls (9.8% of 146)	NS/NA	NS/NA	Higher frequency in TS+ ADHD (40.2% of 89) than in controls (17.0% of 146). TS-only (29.8% of 57) and ADHD-only (20.0% of 21) showed similar frequency to controls	Higher frequency in TS+ ADHD (25.6% of 89) than in controls (11.3% of 146). TS-only (7.0% of 57) and ADHD-only (15.8% of 21) showed similar frequency to controls
Drake et al, 1992[24]	United States of America	20 drug-free TS patients (8 treated previously; 14 males, age not specified, 7 had ADHD and 5 OCD) and 7 controls (6 males, age not specified). Clinical assessment and nocturnal sleep cassette EEG recording	NS/NA	5/20 (25%)	2/20 (10%)	NS/NA	NS/NA	NS/NA	1/20 (5%)	1/20 (10%)

Wand et al, 1993[35]	Canada	422 TS patients (245 aged 6–17 years and 177 aged >17 years, male-to-female ratio 4:1, treatments not specified). Assessment of sleep disorders using a standardized questionnaire sent to the parents	NS/NA	58/245 (23.7%) in TS aged 6–17 years 15/177 (8.5%) in <18 years	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA	NS/NA
Ghosh et al, 2014[28]	United States of America	123 TS patients (48 TS-only and 75 TS + ADHD; mean age 13.6 ± 3.8 years, range 6–21 years; male-to-female ratio 5:1 for TS-only and 3:1 for TS +ADHD; treatments not specified. Assessment of sleep disorders using a standardized questionnaire	NS/NA	11/48 (22.9%) in TS-only 14/75 (18.7%) in TS + ADHD	23/48 (47.9%) in TS-only 50/75 (66.7%) in TS + ADHD	NS/NA	NS/NA	NS/NA	8/48 (16.7%) in TS-only 28/75 (37.3%) in TS + ADHD	NS/NA
Modafferi et al, 2016[37]	Italy	36 patients with TS (n=28) and chronic tic disorders (n=8) (30 males aged 8–16.3 years, mean 11.7 years, age at onset 3–10.5 years, mean 6.3 years; treatments not specified) and 266 age and sex-matched controls. Assessment of specific sleep disorders using a standardized sleep behaviour questionnaire	NS/NA	2/36 (5.6%) in tic disorders vs 9/266 (3.4%) in controls (p =n.s.)	8/36 (22.2%) in tic disorders vs 35/266 (13.1%) in controls (p=n.s,)	1/36 (2.8%) in tic disorders vs 3/266 (1.1%) in controls (p= n.s.)	NS/NA	2/36 (5.6%) in tic disorders vs 7/266 (2.6%) in controls (p=n.s.)	3/36 (8.3%) in tic disorders vs 6/266 (2.3%) in controls (p=n.s.), 3/20 in tics disorders with low scores in the YGTSS (p>0.01 compared with controls)	NS/NA

Notes: Adapted from Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG. Sleep Disorders in Tourette Syndrome. *Sleep Med Rev.* 2020 Oct;53:101335.[8] With Permission from Elsevier.
Abbreviations: TS, Tourette syndrome; ADHD, Attention Deficit Hyperactivity Disorder; NREM, Non-Rapid Eye Movements; NS, Not Specified; NA, Not Assessed; REM, Rapid Eye Movements.

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Restless sleep was reported in 10.7% of patients with TS[21] and 38.9% of patients with tic disorders,[35] this frequency being significantly higher than that found in controls.[35] Another group described a significantly higher frequency of the presence of continuous movements of legs in TS patients (40.5%) than in controls (5.9%).[36] Finally, according to another clinical series, "moving a lot during sleep", which was a very frequent finding in patients with TS-only (47.4%) and in controls (44.4%), was significantly more frequent in patients with ADHD-only (84.1%) and with TS + ADHD (62.1%).[40]

The reported frequency of *sleep-induced bruxism* in TS was 2.7–10% in two clinical series,[21,34] while other authors reported this symptom in 19.4% of patients with tic disorders (most of them with lower severity), a frequency that was significantly higher than that found in controls (4.1%).[37] Jankovic & Rohaidy[21] reported *sleep-induced myoclonus* in 5.4% of their patients diagnosed with TS.

Several authors reported the *persistence of tics during sleep* in patients with TS, with wide variability in frequency that ranged from 13.8% to 100%.[18,20,21,34,52,54–56] The presence of tics during sleep has been documented in all sleep stages, having a predominance in I and II stages,[52,55,56] and in the REM stage.[42]

Other symptoms, such as "rocking during sleep"[20] and "unusual movements during sleep",[37] have been reported, respectively, in 1.72% of patients with TS and 22.2% of patients with tic disorders.

Polysomnographic Features of Sleep in Tourette Syndrome

The results of studies addressing the polysomnographic features of TS[18,21,34,51–62] have been one of the aims of a recently reported review.[9] In summary, the data reported with the highest consistency regarding this issue were the following:[9]

(A) Total sleep time[51,56] and sleep efficiency[51,53,56,61] were found to be decreased.
(B) Percentage in REM sleep was found to be decreased in 3 studies,[18,53,56] whereas another study reported an increase of this value.[54]
(C) Four studies described a decrease in the percentage of delta sleep,[34,52,57,60] while the other two studies found this value to be increased.[18,56]
(D) Six studies described an increase in nocturnal awakenings,[18,34,52,53,56,61] while another involving 2 patients did not report this finding.[59]
(E) Patients with TS showed an increase in periodic limb movements during sleep (PLMS),[51,52] periodic limb movements index (PLMI),[51,52] and PLMS with arousal,[51] this finding being more marked in patients with comorbid ADHD.[54]

Keenan et al[10] performed a meta-analysis of 20 studies combining data from polysomnographic studies of patients with persistent tic disorders (PTD)-only (n = 198), persistent tic disorders + ADHD (n = 79), ADHD-only (n = 316), and controls (n = 336), and found the following results in comparison with controls:

(A) Patients with PTD + ADHD showed significantly increased time in bed, increased total sleep time, decreased sleep efficiency, increased sleep onset latency, and similar REM sleep and slow-wave sleep percentages.
(B) Patients with PTD-only showed significantly decreased sleep efficiency, increased sleep onset latency, and similar time in bed, total sleep time, and similar REM sleep and slow-wave sleep percentages.
(C) Patients with ADHD-only showed similar time in bed, total sleep time, sleep efficiency, sleep onset latency, and REM sleep and slow-wave sleep percentages.

However, the results from many of these studies could be related to the medications used.

Discussion and Conclusions

This and other reviews regarding sleep disorders[7–11] and polysomnographic studies[9,66] in patients with TS have important limitations due to the relatively small size of the samples studied, differences in comorbid conditions, the age of the patients included, and the medications used by the patients. While in several studies the patients were not taking any

drugs for the treatment of TS at the time of evaluation,[18,34,51,53,55–57,61,62] in other studies many patients used stimulants or other specific therapies for tics, which could have an important influence on the results,[21,23,27,28,37,52] and in others, the treatment was not clearly specified.[19,20,24–26,30,32,33,35–37,59]

Patients diagnosed with TS or CTD, especially children, and those who have comorbidities such as ADHD or ADHD + OCD, suffer from one or more types of sleep disorders with a high frequency. Although the frequency of sleep disorders in patients with TS is widely variable among different studies, the most frequently reported are insomnia, excessive daytime sleepiness, the persistence of tics during sleep, different disorders of arousal, and the presence of PLMS.[9] Decreased sleep efficiency and increased sleep onset latency are the most frequent findings in TS patients with or without comorbid ADHD according to a recent meta-analysis.[10]

While the severity of TS or tic disorders has been assessed by several of the studies included in this review,[12,23,26,27,32,35,37,53,62] the possible relationship between sleep disorders and the severity of the disease has been addressed by few of them.[22,25,27,32,37] A negative correlation between the number of sleep-related problems and the severity of motor tics, assessed with the YGTSS, was reported by Storch et al.[26] Other authors reported that the interaction between age, sex, and severity of tic disorders could be a reliable predictor of the presence of sleep insufficiency.[32] Two reports described that patients with higher severity of TS have shown both higher total sleep scores,[22,27] and higher frequency of sleep problems according to Comings & Commings,[22] while another found that patients with lower severity of tic disorders, assessed by the YGTSS, showed more frequent difficulty in initiating sleep, nightmares, night awakenings, sleeptalking, bruxism, and unusual movement disorders compared with patients with higher severity of tics.

The contribution of anxiety to sleep disorders in TS has been addressed by 3 studies,[26,30,37] despite the fact that these and many others have shown a high frequency of anxiety as a comorbid condition in TS (11%–70%).[22–24,26,27,30,32,33,35–37] Patients with CTD with comorbid anxiety have shown a higher frequency of sleep-related problems when compared with those without this comorbidity, according to Storch et al.[26] TS or CTD patients with higher scores on an anxiety scale were more prone to present abnormal movements during or before sleep, according to Modafferi et al.[37] Finally, in a population-based study, patients recently diagnosed with TS showed a significant association between anxiety disorders and sleep disorders.[30]

Although it is beyond the scope of this review to analyze sleep disorders in patients with ADHD-only, and taking into account that ADHD is a frequent comorbidity of TS and CTD, it is reasonable to think that ADHD could contribute to sleep disorders/problems in TS/CTD. According to sleep questionnaires, patients with ADHD-only showed a wide range of frequent sleep disturbances.[40,63,64] Several case–control studies reported a higher frequency of PLMS in patients with ADHD than in controls,[65,66] a finding that was not confirmed by others,[67] and patients with RLS have shown a higher frequency of ADHD symptoms using DSM-IV ADHD scores.[68] Bioulac et al[69] described higher ESS and Maintenance of Wakefulness Test scores in patients with ADHD-only. Large population studies have shown that patients with ADHD symptoms report slower sleep duration, longer sleep latency and nocturnal wake time, longer sleep efficiency,[70] increased odds of insomnia,[70,71] poorer sleep quality,[72] and higher odds of suffering probable obstructive sleep apnea syndrome, RLS, and PLMS.[71] Despite the fact that many PSG and actigraphy studies have shown different alterations in patients with ADHD-only,[53,54,64–66,73–75] other studies do not show significant alterations.[63,67,76] Moreover, a meta-analysis of studies using PSG or actigraphy showed that ADHD-only patients spent more time in stage 1 than controls as the only finding,[77] while another found no differences in PSG parameters between the two groups.[10]

To our knowledge, neither formal specific studies nor guidelines on the approach to the treatment of sleep disorders/problems exist for TS. As was suggested in a recent review, treatment of tics and comorbid conditions that can worsen sleep in patients with TS/CTD, such as obstructive sleep apnea syndrome, ADHD, RLS, and so on, could result in an improvement of sleep complaints, and several drugs used for the improvement of tics such as clonidine, clonazepam, topiramate, aripiprazole, risperidone, or others could potentially improve sleep.[11]

To our knowledge, despite the fact that Modafferi et al[40] used a validated global sleep questionnaire, studies addressing the quality of sleep (which could be assessed with the Pittsburgh sleep quality index –PSQI-,[78] or other well-validated

scales), and/or looking for the presence of excessive daytime somnolence (for example, the Epworth Sleepiness Scale or ESS[79]) in patients diagnosed with TS or CTD, are still lacking.

Future assessments of sleep disorders in TS/CTD should ideally be multicenter, prospective, with long-term follow-up and multicenter studies, involving large samples of drug-free TS/CTD patients (at least at the time of recruitment) and age- and sex-matched controls without a family history of tics, using multiple sleep disorders screening questionnaires,[80–83] the PSQI,[78] the ESS,[79] and questionnaires on the presence of RLS[84] and REM sleep behaviour disorders,[85] together with objective assessment using nocturnal polysomnographic studies and/or actigraphy.

Abbreviations

ADHD, attention deficit hyperactivity disorder; BTBD9, BTB domain containing 9 gene; HCRTR2, orexin2/hypocretine 2 receptor gene; ECG, electrocardiogram; EEG, electroencephalogram; EMG, electromyogram; EOG, electrooculogram; NREM, non-rapid eye movements; OCD, obsessive-compulsive disorder; PLMI, periodic limb movements index; PLMS, periodic limb movements during sleep; REM, rapid eye movements; RLS, restless legs syndrome; TD, Tourette disorder; TS, Tourette syndrome; YGTSS, Yale global tic severity scale.

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Disclosure

The authors declare no conflicts of interest in relation to this work.

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