

Sleep, Sleeplessness & Neuropsychiatric Conditions

Sleep disturbances are symptoms of psychiatric conditions that can worsen prognosis; however, nonpharmacologic treatments are available and effective.

By Fiona Barwick, PhD



Introduction

Sleep disturbance is so common in neuropsychiatric conditions, it is considered a cross-cutting symptom.¹ It often manifests as insomnia, hypersomnia, nightmares, or circadian dysregulation. Sleep disturbance can be a precipitant

or a prodrome, likely through multiple interconnected pathways, and it can also exacerbate symptoms and increase the risk of relapse. Brief screening instruments help assess for the various types of sleep disturbance common in neuropsychiatric conditions. Although appropriate medications are essential for effective management of the neuropsychiatric condition, nonpharmacologic approaches such as cognitive-behavioral therapy (CBT) offer highly effective evidence-based treatments for insomnia and adjunctive treatments for hypersomnia, nightmares, and circadian dysregulation.

Frequency of Sleep Disturbance in Psychiatry

Sleep disturbance is pervasive in almost all neuropsychiatric conditions.^{2,3} It occurs so frequently in major depressive disorder (MDD), bipolar disorder (BPD), generalized anxiety disorder (GAD), and posttraumatic stress disorder (PTSD) that it is included in diagnostic criteria. It disappeared from early editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) as a criterion for attention-deficit/hyperactivity disorder (ADHD) but has now reappeared in informal guidelines.⁴ It also commonly occurs in schizophrenic spectrum disorders (SSD), autism spectrum disorders (ASD), and neurocognitive disorders due to dementia, cerebrovascular accident, or traumatic brain injury. Not surprisingly, disrupted sleep occurs in all substance-use disorders (SUD).¹

Types of Sleep Disturbances

In neuropsychiatric conditions, sleep disturbance most commonly manifests as insomnia, hypersomnia, nightmares, or circadian dysregulation, although some conditions are associated with increased risk for other sleep disorders (eg, sleep apnea in PTSD, restless legs in ADHD).

Insomnia—problems falling or staying asleep despite adequate opportunity for sleep—occurs in all neuropsychiatric disorders, with sleep-onset problems occurring more frequently in GAD and ASD, and sleep maintenance problems, especially early morning awakenings, more common in MDD. Hypersomnia, which is excessive sleepiness despite a sleep period of 7 hours or more, appears in seasonal affective disorder (SAD) and SSD. Individuals with BPD have reduced sleep need during manic phases and insomnia or hypersomnia during depressive phases. Nightmares and associated fear of going to sleep reflect the re-experiencing symptoms and hypervigilance seen in PTSD.¹ Circadian dysregulation, which reflects changes in the timing of sleep-wake and other behavioral rhythms, occurs in BPD, SSD, ADHD, ASD, and neurodegenerative conditions. It often results from irregular, inappropriate, or inadequate timing of *zeitgebers* (“timegivers”) that regulate circadian rhythms, such as exposure to light, engagement in activities, and scheduling of meals and social events.⁵

The effect of substances on sleep varies depending on the substance. Sedatives such as alcohol, benzodiazepines, and narcotics can shorten sleep onset in the first half of the night but disrupt sleep and cause insomnia due to rebound effects in the second half of the night. Stimulants promote wakefulness by altering neurochemicals, leading to insomnia at night and sleepiness during the day (eg, caffeine blocks adenosine, which prevents the build-up of sleep drive, and amphetamines increase the release of dopamine, which promotes wakefulness). Substances with a short half-life, such as tobacco, are especially disruptive of sleep because cravings due to withdrawal are more frequent and intense. Many substances, including cannabis, suppress rapid-eye-movement (REM) sleep and cause REM-sleep rebound when they are discontinued. The effects of cannabis on sleep, especially the more potent strains currently cultivated, are still unclear.⁶

Pathophysiology

Mechanisms of action for sleep disturbance in neuropsychiatric disorders are multifactorial and poorly understood. The

causal relationship is almost certainly bidirectional and complex, as neuropsychiatric disorders can cause or contribute to disturbed sleep, while disrupted sleep exacerbates symptoms, worsens coping skills, impairs daily functioning, and increases risk for onset of, and relapse to, neuropsychiatric problems.

Factors influencing sleep disruption can be direct or indirect. Direct factors are intrinsic to the overlapping pathobiology of sleep disorders and psychiatric conditions. In sleep loss, emotion dysregulation and attention dyscontrol may exacerbate MDD or BPD. Neurohormonal dysregulation has been implicated in a variety of neuropsychiatric conditions, most notably serotonergic and dopaminergic dysfunction and is involved, at least partially, in the pathogenesis of most psychiatric disorders (MDD, GAD, SSD, SUD). Given the critical role of monoamines in wakefulness, sleep dysfunction in these disorders is not surprising. The imbalance between monoaminergic and cholinergic tone may lie at the core of the characteristically reduced REM-sleep latency and increased REM sleep and density in patients with MDD.^{3,7,8} Similar REM-sleep abnormalities have been noted in other conditions (SSD, SUD) but are somewhat inconsistent between individuals, disorders, and studies.

Abnormalities in the circadian regulating hormone melatonin occur in ASD and are even a target of certain therapies in MDD (eg, triple chronotherapy or agomelatine). Finally, cortisol is among the most characteristically circadian hormones, having a peak secretion that precedes habitual wake time. The circadian nature of cortisol might be related to reports of early morning awakenings in those with depression, considering the chronic elevation of corticotropin releasing hormone (CRH), increased secretion of cortisol, and/or an abnormal cortisol suppression on the dexamethasone challenge test seen in individuals with depression.⁹ Similarly, hypothalamic-pituitary-adrenal (HPA) axis dysregulation may be at the root of stress responses in other conditions (eg, PTSD). Beyond neurohormonal abnormalities, the neurotoxic accumulation of excessive CNS proteins and consequent destruction of neurons that characterize brain injuries and various dementias may predispose to both sleep disorders and psychiatric illness.^{5,10}

Indirect factors include behavior changes, such as excessive time in bed for MDD; increased activities, electronics usage, and light exposure at night for BPD; avoidance of bedtime in PTSD; and social and physical isolation, limited mobility and activity, and reduced light exposure in neurodegenerative conditions. Medications used to treat neuropsychiatric conditions are also indirect factors that can have sedating effects (eg, trazodone and quetiapine), stimulating effects (eg, sertraline and venlafaxine), or circadian effects (eg, lamotrigine). Furthermore, medications can alter sleep patterns (eg, SSRIs suppress REM sleep, and benzodiazepines suppress not only REM sleep but N3 or slow-wave sleep) and lead to other sleep disorders (eg, atypical antipsychotics and serotonergic antidepressants can precipitate restless legs and opioids can worsen sleep apnea).¹¹

Screening

Given the ubiquity of sleep disturbance in neuropsychiatric conditions, initial evaluation should always screen for specific sleep disorders. Table 1 includes a list of brief subjective screening measures that assess for common sleep disorders including sleep tracking (Consensus Sleep Diary),

TABLE 1. SLEEP SCREENING MEASURES.

Measurement Tool	Useful in
Consensus Sleep Diary Daily log allows patients to record specific sleep parameters and can be used for assessment and intervention	ADHD, ASD, BPD, GAD, MDD, Neurocognition, PTSD, SSD, and SUD
Insomnia Severity Index 7-item self-report assesses for insomnia symptoms and effect on daytime functioning	ADHD, ASD, BPD, GAD, MDD, Neurocognition, PTSD, SSD, and SUD
Pittsburgh Sleep Quality Index 10-item self-report evaluates sleep quality, including insomnia symptoms	ADHD, ASD, BPD, GAD, MDD, PTSD, SSD, and SUD
Epworth Sleepiness Scale 8-item self-report assesses for degree of daytime sleepiness in different situations	ADHD, BPD, MDD, Neurocognition, and SSD
Stanford Sleepiness Scale Single-item self-report assesses perceived sleepiness at a specific moment in time; can be administered repeatedly	ADHD, BPD, MDD, Neurocognition, and SSD
Horne-Ostberg Morningness-Eveningness Questionnaire: RS 5-item self-report assesses preferred timing of sleep, wake, and other behaviors	ADHD, ASD, BPD, and SSD
Munich Chronotype Questionnaire 15-item self-report assesses actual timing of sleep, wake, and other behaviors on work/school vs free days	ADHD, ASD, BPD, and SSD
Sleep Hygiene Index 13-item self-report assesses specific behavioral and lifestyle factors that interfere with sleep	ADHD, ASD, BPD, MDD, Neurocognition, SSD, and SUD
Trauma Related Nightmare Survey 16-item self-report assesses nightmare frequency, severity, content, and impact on aspects of sleep	PTSD

Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; BPD, bipolar disorder; GAD, generalized anxiety disorder; MDD, major depressive disorder; PTSD, posttraumatic stress disorder; RS, reduced scale; SSD, schizophrenic spectrum disorders; SUD, substance-use disorder.

insomnia (Insomnia Severity Scale and Pittsburgh Sleep Quality Index), hypersomnia (Epworth Sleepiness Scale and Stanford Sleepiness Scale), chronotype (Horne-Ostberg Morningness-Eveningness Questionnaire: Reduced Scale and Munich Chronotype Questionnaire), sleep hygiene (Sleep Hygiene Index), and nightmares (Trauma Related Nightmare Survey).¹²⁻¹⁹

However, clinicians seeing individuals with any variety of primary medical, neurologic, or psychiatric conditions will likely not have the time or resources to screen broadly for sleep disorders in most patients. Tiered approaches, such as an electronic health record (EHR) sleep-screening questionnaire²⁰ or starting conversations by asking patients if they are satisfied with their sleep can often point the clinician in the right direction. As mentioned above, certain sleep disorders tend to associate more commonly with some conditions than others. As such, targeted questionnaires may be appropriately applied in certain contexts: sleep diaries and the morningness-eveningness questionnaire (MEQ) might reveal circadian dysfunction in neurodegenerative and neurodevelopmental disorders; whereas, sleepiness scales and fatigue measures (like the fatigue severity scale) may be more appropriate in assessing individuals with neurologic injury (eg, traumatic brain injury, stroke, multiple sclerosis) and/or depression.

Treatment

Appropriate medications, including proper timing to minimize impact on healthy sleep-wake patterns, are critical for effective management of neuropsychiatric conditions. However, cognitive-behavioral therapy (CBT) is the recommended, evidence-based treatment for insomnia and can be an important adjunctive treatment for hypersomnia, nightmares, and circadian dysregulation.²¹⁻²³ Techniques of CBT are based on the demonstrated interconnection between thoughts, feelings, behaviors, and physiology, so that effecting change in any one of these domains can catalyze change in one or more of the other domains.

Whereas predisposing factors (eg, age, gender, personality type, trauma history, etc.) can create an underlying vulnerability to insomnia and other sleep problems, and precipitating stressors can provoke an acute episode, CBT targets the perpetuating factors that lead to more chronic sleep problems. Perpetuating factors include beliefs, behaviors, and physiology that dysregulate circadian rhythms, interfere with sleep, and exacerbate wakefulness at night (Figure).²⁴ Use of CBT for insomnia can lead to sustained improvements in sleep even for individuals with neuropsychiatric conditions. Specific CBT techniques for sleep problems often overlap with similar techniques used to treat neuropsychiatric conditions (behavioral activation in MDD, relaxation in GAD, bright light therapy in SAD), and evidence increasingly suggests that improving sleep can also enhance psychiatric outcomes.^{25,26}

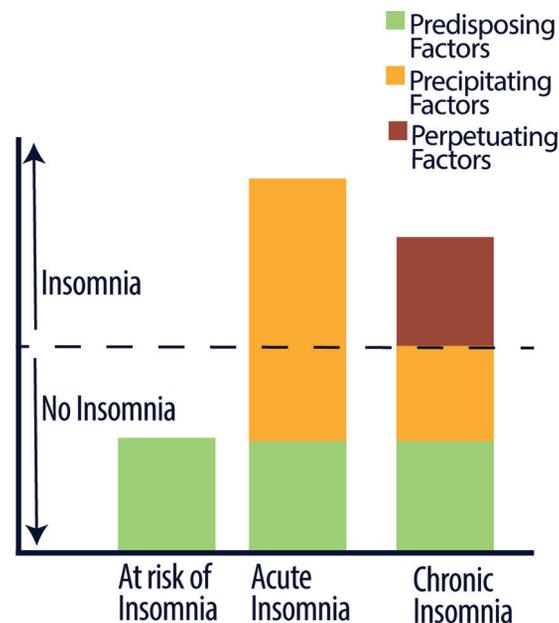


Figure. Three Factors Contributing to the Development of Chronic Insomnia. Factors that contribute to insomnia may be predisposing (green), precipitating (gold), or perpetuating (red). Insomnia occurs only when the sum of these factors goes above a certain threshold (dashed line).

Techniques used in CBT leverage an understanding of sleep-wake science and circadian biology to correct misconceptions and modify unhelpful beliefs about sleep, promote behaviors that improve sleep quality, provide strategies for reducing worry at bedtime or during the night (if awakened), teach techniques that enhance relaxation, and educate regarding habits and routines that support healthy sleep. These techniques can be adapted for specific neuropsychiatric conditions. For example, motivational interviewing can be used to more fully engage patients in treatment (SSD, ADHD), sleep restriction can be implemented more gradually (“compression”) to reduce risk of precipitating a manic episode (BPD), and behavioral techniques can be emphasized for patients with mild cognitive impairment from neurodegenerative conditions. Table 2 briefly describes CBT techniques for treating and managing insomnia, hypersomnia, nightmares, and circadian dysregulation.²⁷⁻³⁶

Conclusion

Given the ubiquity of sleep disturbance in neuropsychiatric conditions and the sleep-disruptive effects of psychiatric medications, it is fortunate that nonpharmacological approaches employing CBT can treat insomnia successfully and provide helpful adjunctive treatments for hypersomnia, nightmares, and circadian dysregulation. These techniques, which often overlap with CBT techniques used to treat neuropsychiatric

TABLE 2. MULTICOMPONENT COGNITIVE BEHAVIORAL THERAPY AND SPECIFIC TECHNIQUES FOR INSOMNIA, HYPERSOMNIA, NIGHTMARES, AND CIRCADIAN DYSREGULATION

Technique (Level of evidence)	Instruction	Purpose
Multicomponent CBT (Standard)	Intervention combining CBT techniques below (eg, sleep restriction, stimulus control, relaxation training, cognitive therapy, and sleep education)	Increase sleep drive, improve sleep quality, reassociate bed with sleep, enhance relaxation, and correct unhelpful beliefs to reduce worry about and efforts to control sleep
Sleep restriction (Guideline)	Restrict time in bed to match actual time asleep as closely as possible before gradually increasing	Increase homeostatic sleep drive to decrease wakefulness at night and improve sleep quality
Stimulus control (Standard)	Use the bed only for sleep, go to bed when sleepy, get up if unable to sleep, do wakeful activities outside bed	Reinforce association between bed and sleep and extinguish association between bed and worried wakefulness
Relaxation training (Standard)	Reduce autonomic, physiologic, cognitive, and emotional activation using guided relaxation	Calm mind and relax body through daily practice to reduce time to fall asleep or return to sleep
Cognitive therapy (Insufficient evidence)	Change inaccurate and unhelpful beliefs about sleep through education, cognitive reframing, and behavioral experiments	Decrease anxiety at bedtime, efforts to control sleep, and worry about insomnia and daytime consequences
Sleep hygiene (Insufficient evidence)	Create a protected sleep environment (dark, cool, and quiet) and healthy lifestyle practices (exercise, diet, and substances)	Establish environmental and lifestyle factors that support rather than interfere with sleep
Sleep education (Not evaluated)	Provide basic information about normal variability in adult sleep and changes in sleep patterns over the lifespan	Correct misconceptions that exacerbate worry about sleep patterns and circadian sleep-wake rhythms.
Mindfulness based intervention (Not evaluated)	Promote nonjudgmental acceptance of present moment experience through regular meditation practice	Reduce negative thoughts and emotions about, as well as efforts to control, sleep and wakefulness at night.
Imagery rehearsal therapy (Recommended)	“Rescript” nightmares into more positive or neutral dreams with daily visualization practice	Reduce nightmare frequency and/or severity by incorporating more positive imagery into dreams.
Social rhythm therapy (Not evaluated)	Establish healthy patterns in habitual daily behaviors (sleep-wake, rest-activity, fasting-feeding, dark-light)	Improve mood and optimize daily functioning with consistent behavioral routines reflecting important circadian rhythms.
Light therapy/melatonin (None/weak recommendations)	Use strategic light exposure (dim light in evening, bright light in morning) and timed oral administration of melatonin	Stabilize and/or shift timing of circadian sleep-wake phase.

conditions, target cognitive, emotional, behavioral, and physiologic factors that perpetuate insomnia and other sleep disturbances. They can be delivered in a flexible format—online, by phone, or in individual or group settings—and modified to fit the preferences and needs of specific patients and populations. While treatment guidelines for hypersomnia, nightmares, and circadian rhythm disorders are currently limited by insufficient research, guidelines for multicomponent CBT for insomnia are well validated and highly effective. ■

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