Psychiatric Disorders and Sleep Issues

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KEYWORDS

• Anxiety • Cognitive-behavioral therapy for insomnia • Depression • Insomnia
• Restless leg syndrome • Circadian rhythm disorders • Obstructive sleep apnea

KEY POINTS

- Sleep issues and psychiatric disorders commonly coexist and can influence each other (eg, insomnia and depression).
- Medications for psychiatric disorders can affect sleep and sleep disorders, particularly restless legs syndrome, positively or negatively.
- Medications for sleep disorders can cause or affect psychiatric symptoms (eg, dopamine agonists given for treatment of restless legs syndrome can cause gambling or other compulsive behaviors).
- Cognitive-behavioral therapy for insomnia in 4 to 8 sessions is the preferred treatment of chronic insomnia if acceptable to the patient and accessible.
- For depressed patients with insomnia, a sleep-promoting medication may be useful as adjunct therapy (zolpidem, eszopiclone, trazodone, or amitriptyline) or as monotherapy (mirtazapine, nefazodone, or trazodone).

INTRODUCTION

Psychiatric disorders and sleep problems are both common, with an estimated prevalence in 12 months of about 30% for any of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) disorders[1] and about 30% for insomnia experienced at least a few days a week for at least a month (as part of a greater but less well-determined prevalence for all types of sleep issues).[2] Psychiatric and sleep problems overlap significantly and are related. Insomnia, for example, correlates with likelihood of having at least 1 psychiatric diagnosis with an odds ratio of 5.0 for severe insomnia, 2.6 for moderate insomnia, and 1.7 for mild insomnia.[3]

In this review article, the neurobiology of the sleep/wake states and mental health and observed associations between selected psychiatric disorders and sleep issues

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(Table 1) are described, and treatment considerations relevant to primary care (Tables 2 and 3) are presented.

NEUROBIOLOGY COMMON TO SLEEP, WAKEFULNESS, AND MENTAL HEALTH

Although the purposes and mechanisms of sleep are not truly known, sleep is clearly crucial to optimal functioning of the brain. Insufficient quantity or quality of sleep affects alertness, hormone regulation, memory formation, emotional regulation, executive function, and multiple facets of behavior. Multiple experiments subjecting small groups of healthy people to total sleep deprivation for a night or 2 have shown myriad specific impairments. In the area of emotional regulation, those findings include increase in symptoms of psychopathology (depression, anxiety, paranoia, and somatic complaints),[69] reduction in the physical expression of emotion,[70] and impairment in the ability to recognize emotion in others.[71]

In observational studies, psychiatric conditions are associated with alterations in sleep architecture,[72] although the direction of the effect and its importance are not known. However, there is increasing evidence that basic brain functions regulating sleep and wake play a role in psychiatric disorders. For example, alterations in the circadian pattern of release of the wake-promoting neurotransmitter orexin may contribute to hypersomnia and insomnia in depression.[73] Narcolepsy, well known as *the* condition of orexin deficiency, is associated with a roughly 2.5-fold higher risk of psychiatric disorder, including major depressive disorder (MDD) and social anxiety disorder.[12]

The association between sleep problems and affective disorders may be rooted at the genetic level. Circadian clock gene polymorphisms seem to be associated with mood regulation and affective disorders,[74,75] with blunting of the normal circadian pattern of gene expression in certain areas of the brain, including the limbic system, in people with MDD.[76] An orexin receptor antagonist is currently in phase 3 trials for treatment of insomnia, and other orexin receptor antagonists are being studied in animals for potential therapeutic effect in anxiety disorders and in compulsive behaviors, including eating and addiction.[77]

The remainder of this review focuses on observations in populations and in clinical studies, beginning with insomnia as the most common sleep issue and the one most commonly associated with psychiatric disorders, then considering specific types of psychiatric disorders in more depth.

INSOMNIA: STATE OF THE ART

Insomnia, the most common sleep problem, has been the target of research and reconsideration. In the most recent sleep medicine and psychiatric clinical diagnostic manuals, the distinction of persistent insomnia as primary versus secondary (eg, secondary to psychiatric or medical conditions) has largely been removed. DSM-5, released in 2013, gives "insomnia disorder" for persistent insomnia not completely explained by any coexisting mental disorders.[78] Similarly, the *International Classification of Sleep Disorders, Third Edition*,[79] released in 2014, introduced "chronic insomnia disorder" to replace the multiple subtypes of chronic insomnia described in previous classifications, including insomnia coexisting with psychiatric conditions. In each case, an important criterion is that another sleep disorder such as restless legs syndrome (RLS), sleep apnea, or a circadian rhythm disorder does not better explain the sleep impairment; those conditions, although often experienced as insomnia by the patient, are distinct sleep disorders, each with specific treatment approaches.[80]

For chronic insomnia not explained by another sleep disorder, cognitive-behavioral therapy for insomnia (CBTI) is considered to be the preferred treatment. CBTI has