Sleep and psychiatry

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Psychiatric disorders constitute 15.4% of the disease burden in established market economies. Many psychiatric disorders are associated with sleep disturbances, and the relationship is often bidirectional. This paper reviews the prevalence of various psychiatric disorders, their clinical presentation, and their association with sleep disorders. Among the psychiatric disorders reviewed are affective disorders, psychosis, anxiety disorders (including post-traumatic stress disorder), substance abuse disorders, eating disorders, and attention deficit/hyperactivity disorders. The spectrum of associated sleep disorders includes insomnia, hypersomnia, nocturnal panic, sleep paralysis, hypnagogic hallucinations, restless legs/periodic limb movements of sleep, obstructive sleep apnea, and parasomnias. The effects on sleep of various psychotropic medications utilized to treat the above psychiatric disorders are summarized.

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Mental illness exacts a heavy toll on individuals, families, and society. In 1998, an estimated 44.3 million people in the USA suffered from a diagnosable mental disorder. Twenty-nine thousand three hundred and fifty people died from suicide in 2000, and suicide was the third leading cause of death in the 15- to 24-year age-group.[1] Using the Disability Adjusted Life Years measure, the Global Burden of Disease Study reported that psychiatric disorders constitute 15.4% of the total disease burden in established market economies.[2]

Psychiatric disorders are frequently associated with disturbances of sleep and circadian rhythms. The relationship between psychiatric disorders and sleep complaints is bidirectional. In a community survey of 7954 people in different major US cities from 1981 to 1985, Ford and Kamerow reported that more subjects met the criteria for mental illness among those with complaints of insomnia (40%) or hypersomnia (46.5%), compared with subjects without any sleep complaints (16.4%).[3] In a study of 14 915 subjects from the UK, Germany, Italy, and Portugal, aged 15 to 100 years, Ohayon and Roth reported that 28% of subjects with insomnia had a current diagnosis of mental disorders, and 25.6% had a prior psychiatric history. In most cases of mood disorders, insomnia appeared prior to (~40%) or simultaneously with (~22%) mood disorder symptoms.[4] However, when anxiety disorders were involved, insomnia appeared at the same time (~38%) or after (~34%) the onset of the anxiety disorder.[4] In another study, 21% of insomniacs had symptoms of major depression, while 13% had symptoms of generalized anxiety.[5] Persistent childhood sleep problems can herald adult anxiety disorders. In a prospective longitudinal study of 943 children (52% male), Gregory et al[6] found that persistent sleep problems in childhood predicted the development of anxiety disorders (odds ratio [OR] =1.60, 95% confidence inter-

Selected abbreviations and acronyms

ADHD	*attention-deficit/hyperactivity disorder*
HI	*hyperactivity-impulsivity*
MDD	*major depressive disorder*
MSLT	*mean sleep latency test*
NREM	*non–rapid eye movement*
PD	*panic disorder*
PTSD	*posttraumatic stress disorder*
REM	*rapid eye movement*
SRE	*sleep-related eating*
SWS	*slow-wave sleep*
TST	*total sleep time*
WASO	*wakefulness after sleep onset*

val [CI] 1.05-2.45, *P*=0.030), but not depressive disorders (OR=0.99, 95% CI 0.63-1.56, *P*=0.959), during adult life.[6] Our review will describe various psychiatric disorders, their associated sleep complaints, and polysomnographic findings.

Mood (affective) disorders

Mood disorders are mental disorders characterized by one or more episodes of depression or partial or full manic or hypomanic episodes. The spectrum of affective disorders includes major depressive disorder (MDD) (unipolar depression), bipolar disorder, cyclothymia (mild bipolar swings), or dysthymia (neurotic or reactive depression).

A seasonal pattern is common in patients with bipolar disorders, with onset of depressive episodes during the fall or winter, and remission during spring. The prevalence of winter-type seasonal pattern increases with higher latitudes. Seasonality is more frequently seen in younger individuals and in women. Major depressive episodes are associated with prominent anergy, hypersomnia, overeating, weight gain, and craving for carbohydrates.[7]

Approximately two-thirds of depressed patients complain of insomnia (sleep-onset insomnia, frequent awakenings, and early morning awakenings 2 to 4 hours earlier than desired, with difficulty returning to sleep), while 15% complain of hypersomnia.[8,9] Women who are depressed are more likely to report insomnia than men.[10] Subjects with persistent insomnia have a higher risk of developing new major depression (OR=39.8) compared with those whose insomnia symptoms resolve (OR=1.6).[3] Similar findings were reported in a 3-year longitudinal epidemiological study of 979 adults (aged 21 to 30 years), where the relative risk of developing major depression was four times that in subjects with insomnia, while subjects with hypersomnia had a 2.9 relative risk when compared to subjects without sleep complaints.[11] Moreover, history of prior insomnia remains a significant predictor of subsequent major depression, and a recurring complaint of insomnia for 2 weeks or more signals the onset of major depression.[11] Additionally, sleep disturbance may be a risk factor for suicide.

Functional neuroimaging studies can differentiate between primary insomnia and depression, as demonstrated in a controlled clinical trial of 25 depressed subjects, 10 primary insomnia subjects, and 28 healthy controls.[12] Insomnia subjects demonstrated greater waking metabolism in the frontal pole and ventral prefrontal cortex, showing greater reductions in metabolism from waking to non–rapid eye movement (NREM) sleep than depressed patients.[12] During sleep, insomnia subjects showed increased metabolism in the brain stem, anterior cingulate, and midbrain arousal structures, while depressed subjects showed elevated metabolism in a ventral and posterior emotional neural network that persisted into sleep.[12]

Major depressive disorder

Sleep disturbances can be an early debilitating symptom of MDD. Nine million nine hundred adults in the USA suffer from MDD, and it is the leading cause of disability in the USA and other established markets worldwide.[1] Depression is more prevalent in women (6.5%) compared with men (3.3%).[1] The prevalence of depression is unaffected by ethnicity, education, income, or marital status.[7] First-degree relatives of depressed individuals have a higher probability of developing depression and also have a higher risk of alcohol dependence.[7] There is a higher risk of attention-deficit/hyperactivity disorder (ADHD) in children of depressed adults.[7]

Major depression consists of depressed mood or loss of interest lasting at least 2 weeks, accompanied by anhedonia, significant weight loss or change in appetite, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, decreased ability to concentrate or think, and suicidal ideation or attempt.[7,13] The typical course of untreated mood disorder is to gradually resolve over 6 to 18 months.

Circadian temperature rhythm may demonstrate low amplitude during untreated depression, with return to a normal rhythm following successful somatic therapy. Growth hormone secretion may be increased during the day and decreased at night. Cortisol secretion is increased, and there is loss of amplitude in the circadian cortisol pattern. In addition to abnormalities in circadian pattern, sleep disturbances in patients with major depression are associated with elevated levels of inflammatory markers, interleukin-6, and soluble intercellular adhesion molecules, which are not accounted for by other confounding factors, such as age and body weight.[14]

Sleep in depressed individuals is disturbed, and complaints of almost daily insomnia or hypersomnia are common. Depressed subjects report nocturnal restlessness, feeling tired, waking up too early, and being unable to return to sleep. Sleep-onset difficulties are more prominently seen with younger subjects, whereas problems with sleep continuity are more characteristic of older subjects. The characteristic insomnia associated with depression is a harbinger of the mood change, often beginning before the clinical depression has been clearly established.[13]

In addition to insomnia and hypersomnia, other sleep abnormalities have also been reported in association with depression. In the Wisconsin Sleep Cohort study of 812 participants from 1998 to 2002, depression was associated with a 2.0-fold increase in hypnagogic hallucinations (≥1/month), 2.1-fold increase in automatic behavior (≥1/month), 5.1-fold increase in sleep paralysis (≥1/month), and 1.3-fold increase in cataplexy (≥1/month).[15]

Polysomnographic abnormalities can be seen in 40% to 60% of outpatients and 90% of inpatients with a depressive episode.[7] Sleep continuity is impaired with prolongation of sleep latency in younger subjects, increase in intermittent wakefulness, and early morning awakenings. Slow-wave sleep (SWS) is reduced (decreased percentage of stage 3 to 4 NREM sleep), and delta activity is decreased, as demonstrated by period-amplitude or power spectral analysis. Quantitative electroencephalographic (EEG) studies may show a change in the delta sleep ratio between the first and second NREM period, reduced amplitude of slow-wave activity in the first NREM period, and decreased interhemispheric beta and theta coherence and intrahemispheric coherence between beta and delta rhythms.[16-20] Rapid eye movement (REM) sleep is enhanced, with increased percentage of REM sleep and phasic movements during REM sleep. Temporal characteristics of sleep are altered with shortened REM sleep latency, reduced delta activity in the first NREM period relative to the second (reduced "delta sleep ratio"), increased phasic eye movement activity, and increased REM sleep duration during the first REM period.[7,13,21,22] Analysis of the cyclic alternating pattern reveals an increase in phases A2 and A3 and a decrease in phase A1 during NREM sleep highlighting an instability of NREM sleep in depressed patients.[23]

Dysthymic disorder

Like MDD, sleep in other affective disorders, such as dysthymic disorder, is also disturbed. Approximately 5.4% of the US population aged 18 and older suffers dysthymia during their lifetime. In the USA, 10.9 million American adults are affected.[1] Women are affected two to three times more frequently than men. Dysthymia is characterized by at least 2 years of frequent depressed mood accompanied by various symptoms. In a study of 512 dysthymic patients, Serretti et al reported that the most frequent symptoms in depressed subjects were low energy or fatigue (96%), poor concentration or indecisiveness (88%), low self-esteem (80%), insomnia or hypersomnia (77%), poor appetite or overeating (69%), and feelings of hopelessness (42%).[24] Children or adolescents with dysthymic disorder are cranky, irritable, depressed, pessimistic, and have poor social skills. Individuals with a family history of major depression respond better to antidepressant medications than dysthymic individuals without this history.[7]

In about 25% to 50% of dysthymic adults, polysomnographic findings are similar to those seen in MDD subjects, with shortened first NREM period, shortened REM latency, and increased REM density.[7,13] In a study of 12 hypersomnic dysthymic subjects, Dolenc et al reported excess stage 1 NREM sleep and reduced stages 3 and 4 NREM sleep on polysomnography; mean sleep latency on the mean sleep latency test (MSLT) was normal at 13±1 min.[25] As in MDD, an unresolved issue is whether the sleep-related complaints are due to a circadian rhythm disturbance or to an intrinsic sleep dysfunction.

Bipolar disorder

Bipolar disorder affects 2.3 million Americans.[1] Bipolar I disorder consists of one or more manic or mixed episodes usually accompanied by a major depressive episode.[7,13] On the other hand, bipolar II disorder consists of one or more major depressive episodes accompanied by at least

one hypomanic episode.[7] Like dysthymia, bipolar II disorder is more frequent in women, while bipolar I disorder does not have a gender difference. Compared with manic subjects, bipolar depression is associated with higher sleep efficiency. Polysomnographic findings in the depressed phase are similar to those of MDD.
During the manic episode of either bipolar I or II disorder, a persistent and abnormally elevated, expansive mood lasting at least 1 week is noted. Accompanying symptoms include inflated self-esteem or grandiosity, increased talkativeness, flight of ideas, distractibility, psychomotor agitation, and an excess involvement in pleasurable activities that have a high potential for painful consequences. During the manic phase, there is decreased need for sleep (eg, subject feel rested after only 2 to 4 h of sleep). Polysomnography in manic subjects demonstrates markedly decreased total sleep time (TST), and short REM latency; stages 3 and 4 NREM sleep may be reduced.[13,22]

Cyclothymic disorder

The manic and depressed phases of bipolar disorder are more severe than the mood fluctuations of cyclothymic disorder. The essential feature of this disorder is a chronic (at least 2 years' duration in adults or at least 1 year's duration in children and adolescents) fluctuating mood disturbance, with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a major depressive episode.[7,13] During hypomanic episodes, there is a profound inability to fall asleep. Depressed subjects complain of nocturnal restlessness and tired feelings, and polysomnographic findings demonstrate abnormalities in sleep continuity and sleep architecture, with reduced delta sleep and short REM latency.

Anxiety disorders

Similar to depressed subjects, subjects with anxiety disorders also experience sleep difficulties. Over 19 million American adults aged 18 to 54 years (13.3% of this age group) suffer from anxiety disorders.[1] Common sleep disturbances associated with anxiety disorders are sleep-onset or sleep maintenance insomnia. Additionally, some subjects develop sedative or hypnotic abuse, further complicating their sleep disturbances. Anxiety disorders are mental disorders characterized by symptoms of anxiety and avoidance behavior. The spectrum of anxiety disorders encompasses generalized anxiety disorder, panic disorder (PD), and posttraumatic stress disorder (PTSD).

Generalized anxiety disorder

Four million American adults suffer from generalized anxiety disorder.[1] It is a chronic (≥6 months) condition of excessive worrying, which is difficult to control. The anxiety is frequently associated with three or more of the following: restlessness or feeling "keyed up," easy fatigability, difficulty concentrating or "the mind going blank," irritability, muscle tension, and difficulty initiating or maintaining sleep or restless unsatisfying sleep.[7,13] Polysomnography shows nonspecific findings of increased sleep latency, reduced sleep efficiency, increased amounts of stages 1 and 2 NREM sleep, reduced SWS, increased frequency and duration of awakenings, normal or increased REM sleep latency, and decreased REM sleep percentage.[26-28] Positive correlations have been reported between anxiety ratings and number of awakenings, latency to stage 1 NREM sleep, and percentage of stage 2 NREM sleep.[27]

Panic disorder

PD is another anxiety disorder associated with sleep problems. Two million four hundred thousand American adults aged 18 to 54 years have PD[1]; the average age of onset is in the late 20s.[13] Women are affected two to three times more frequently than men, and the disorder tends to run in families.[13] Adults with PD frequently have a history of childhood separation anxiety disorder. PD is characterized by discrete episodes of intense fear or terror of dying, accompanied by dizziness, choking, palpitations, trembling, chest pain or discomfort, and sweating. PD can be associated with secondary depressive symptoms, alcoholism, sedative or hypnotic abuse, and agoraphobia.
Nocturnal panic (NP) episodes occur in 44% to 71% of PD patients and are associated with sudden awakening with the onset of typical panic symptoms.[29,30] The subject is hyperaroused and has difficulty returning to sleep.[30] Comparing patients with NP (n=51) to patients with PD without a history of NP (n=41), Craske et al reported no evidence of more severe psychopathology on measures of PD severity, comorbidity, or interpersonal functioning, and only weak evidence for more sleep disturbance in patients with NP.[29]
In addition to insomnia, other sleep complaints may

include sleep paralysis and hypnagogic hallucinations. Recurrent sleep paralysis has been reported by 59% of African-Americans and 7% of whites with PD, compared with 23% of African-American and 6% of white community volunteers.[31] Among a psychiatric population of 100 Cambodian refugees, 42 subjects had panic attacks and sleep paralysis; of this subgroup, 91% (38/42) reported hypnagogic visual hallucinations.[32] Night terrors and somnambulism can also occur with PD.[33]

Patients with PD appear to differ in autonomic regulation when compared with normal subjects, and there are small differences between patients with daytime panic attacks and those with sleep-related panic attacks.[34] In a controlled trial comparing heart rate variability (HRV) in response to sodium lactate challenge in patients with PD (n=12 with daytime panic, n=12 with sleep-related panic) and normal subjects (n=12), a marked subjective response was noted in the PD patients, but not in control subjects. Although the 3 groups showed changes in HRV in response to sodium lactate challenge, HRV decrease was more pronounced in the group of PD patients compared with control subjects. During NREM sleep, the value for total power (TP) was significantly higher in the nocturnal panic patients. The PD patients as a group had higher values for TP and low-frequency power during REM sleep than control subjects. The PD patients had lower sleep efficiency and less stage 4 sleep than control subjects.[34] There were no significant differences between the two PD groups in sleep architecture.

Polysomnography in PD patients demonstrates marginally increased sleep, reduced sleep efficiency, and abrupt awakening with sensation of panic out of stage 2 NREM sleep toward the transition to SWS.[13] Rarely, panic episodes may occur at sleep onset. Specific treatment of the sleep disturbance may be needed, since Cervena et al reported that conventional therapy of PD in 20 subjects was not sufficient to treat the coexisting insomnia.[35]

Posttraumatic stress disorder

Similar to PDs, insomnia is also frequently seen in subjects with PTSD. In America, 5.2 million adults aged 18 to 54 years suffer from PTSD. PTSD results from exposure to a traumatic episode during which the subject experienced, witnessed, or was confronted with an event or events which involved actual or threatened death, serious injury, or threat to the physical integrity of self or others, and the subject responded with either intense fear, helplessness, or horror. The traumatic event is persistently reexperienced through recurrent and intrusive distressing recollections of the events, recurrent distressing dreams of the event, acting or feeling as if the traumatic event were recurring, or intense psychological distress or physiological reactivity on exposure to external or internal cues that symbolize or resemble an aspect of the traumatic event.[13] Consequently, there is numbing of general responsiveness and persistent avoidance of stimuli associated with the trauma. In addition, persistent symptoms of hyperarousal (not present before the traumatic event) occur, including difficulty falling or staying asleep, irritability or outbursts of anger, difficulty concentrating, hypervigilance, and exaggerated startle response.

In a study of 10 PTSD subjects (mean age 34.6 years old, SD=6.3 years, n=7 women) compared with 7 normal controls using Cohen's *d* effect sizes, PTSD subjects showed longer sleep latency (d=0.57), increased number and duration of nocturnal awakenings (d=1.06 and d=0.93, respectively), and reduced TST (d=1.42).[36] Quantitative EEG analysis demonstrated that PTSD subjects had greater beta activity (d=0.36) and reduced delta activity (d=1.45).[36] Preliminary heart period analyses comparing 4 PTSD subjects with 4 control subjects suggested that parasympathetic tone is lower in PTSD than healthy subjects during NREM (d=3.14) and REM (d=2.20) sleep. These findings indicate that sleep disruption occurs in PTSD, as demonstrated by visually scored sleep, EEG power spectrum, and heart period analysis.[36]

Among a group of 21 subjects with acute traumatic injury, the development of PTSD was associated with more periods of REM sleep and shorter average duration of REM sleep before stage shifts to either NREM sleep or wake.[37] Similar findings of increased arousals from REM sleep were noted in PTSD subjects who participated in a community-based cohort of young adults followed longitudinally over 10 years.[38] Polysomnographic findings in chronic PTSD are variable, with normal or reduced sleep efficiency, normal or increased nocturnal awakenings, increased REM density, and increased phasic muscle activation during REM sleep.[39-44]

Psychoses

Schizophrenia

Sleep disruption is also noted in psychotic disorders, such as schizophrenia. These disorders are characterized by

delusions, hallucinations, catatonic behavior, incoherence, or inappropriate affect that impair interpersonal relations, work or education, or self-care. There are 2.2 million American adults (1.1% of adults age 18 or older) who are schizophrenic.[1] Onset is usually between late teens and mid-30s, and both men and women are equally affected. Acute psychosis is often associated with significant sleep disruption and severe difficulty initiating sleep. Extreme anxiety and delusional preoccupation may result in motor hyperactivity. Partial or complete inversion of the day-night cycle or reversion to a polyphasic sleep pattern is observed. Reduced sleep efficiency may occur prior to psychotic decompensation.

Sleep patterns vary, and polysomnographic findings depend on whether the patient is experiencing the first episode and is neuroleptic-naive, or is chronically ill. The sleep disturbances of either never-medicated or previously treated schizophrenia patients are characterized by sleep-onset and maintenance insomnia.[45] In 11 first-episode and neuroleptic-naive patients with schizophrenia, Poulin et al reported prolonged sleep latency, decreased stage 4 duration, reduced REM sleep latency, normal sleep spindles, and normal REM densities, indicating difficulty initiating but not maintaining sleep.[46] However, others have reported decreased TST, significant disruption in sleep continuity, shortened REM latency, normal or increased REM density with variable REM time, and normal or decreased SWS.[13,45,47-50]

After REM sleep deprivation, acute schizophrenics have no REM sleep rebound, while chronic schizophrenics with no active symptoms have more rebound than normal.[51-53] With neuroleptic treatment and clinical improvement over 3.5 weeks, Maixner et al demonstrated improvements in sleep continuity (sleep latency decreased, time spent asleep increased, and sleep efficiency improved) and an increase in REM latency and SWS during follow-up polysomnography.[54] However, despite improvement in these measures during neuroleptic treatment, these parameters remained abnormal when compared to normative data.[54] In a longitudinal study of schizophrenic subjects comparing baseline sleep data to results at 4 weeks and 1 year after starting treatment, Keshavan et al reported significant improvement in sleep continuity measures and modest increase in REM latency, with no other changes in sleep architecture at 4 weeks, while at 1 year, REM latency, REM duration, and average automated REM counts increased without significant changes in SWS parameters.[55] These findings suggest that SWS parameters are relatively stable during follow-up, while REM parameters may vary in relation to the phase of illness and treatment. In addition to the sleep disturbances noted above, a study of psychiatric hospital inpatients referred for sleep evaluation reported higher rates of obstructive sleep apnea in schizophrenia patients.[56] However, the schizophrenia patients had history of chronic neuroleptic usage and were heavier than patients with other disorders.[56]

Current theory on schizophrenia proposes an imbalance between dopaminergic and acetylcholinergic influences on key central nervous system (CNS) structures, such that dopaminergic activity is increased during the psychotic phase, and a compensatory increase in muscarinic acetylcholinergic activity results in increased negative symptoms.[22,57] Tandon et al reported decreased REM sleep latency and increased REM density in association with the negative symptoms of schizophrenia and attributed these to increased CNS muscarinic activity.[50]

Treatment of schizophrenia and other psychoses may lead to use of new atypical antipsychotic medications. Some of these drugs have important metabolic effects associated with induction of insulin resistance and leptin resistance. These abnormalities are seen mostly during the nocturnal period and are associated with development of significant weight gain and obesity. Due to these metabolic and body mass index (BMI) changes, patients may develop obstructive sleep apnea and associated sleep disruption. With use of some of these atypical antipsychotic drugs, the BMI increase is rapid and treatment with nasal chronic positive airway pressure (CPAP) may be needed.

Substance-induced sleep disorder

As seen with mood disorders, anxiety disorders, and psychosis, sleep is also impaired in subjects with substance abuse. Sleep problems during childhood (ages 3 to 5 years) appear to be markers for increased risk of abuse of alcohol, marijuana, and illicit drugs later in life.[58]

Alcohol abuse

Acute alcohol ingestion during the first half of the night increases sleepiness, prolongs TST, reduces wakefulness after sleep onset (WASO) lasting for 3 to 4 h, increases SWS, and reduces REM sleep. During the second half of the night, alcohol leads to increased sleep fragmentation, increased WASO, restless sleep, reduced SWS, and increased REM sleep with vivid and anxiety-laden

dreams for the rest of the sleep period. With continued habitual use, the short-lived sedative effect of alcohol is followed by disruption of sleep continuity.[13] Insomnia is a common complaint, reported by 36% to 72% of alcoholics; this symptom may persist for weeks to months after initiation of abstinence.[59] Among patients entering treatment for alcoholism, insomnia has been significantly associated with subsequent alcoholic relapse.[59] During alcohol withdrawal, sleep is grossly disturbed with extremely disrupted sleep continuity, increased WASO, REM sleep rebound with an increase in the amount and intensity of REM sleep, vivid dreaming, and, occasionally, delirium. After acute withdrawal, subjects with chronic alcohol use may complain of light fragmented sleep lasting for months to years, and the EEG shows persistent deficit in SWS and persistent sleep continuity disturbances.[7]

Stimulant-dependent sleep disorder

Stimulant-dependent sleep disorder consists of reduction in sleepiness or suppression of sleep by central stimulants, with alterations in wakefulness following abstinence. Central stimulants include phenylethylamines (amphetamine, ephedrine), cocaine, thyroid hormone, and various xanthine derivatives (caffeine, theophylline). Individuals who abuse or self-administer central stimulants have sustained periods of total sleep suppression, often followed by periods of deep hypersomnolence. Drug administration is frequently associated with increased behavior activity progressing to states of hypomania, garrulousness, paranoid ideation, and repetitive behavior.[13] As tolerance to the alerting effect of the stimulant occurs, higher doses are utilized, and, later, periods of high-dosage drug administration are interrupted only by periods of somnolence that result from exhaustion, following a prolonged period of sleep suppression. Acute toxicity may result in cardiac arrhythmias, intracerebral hemorrhage, convulsions, and respiratory arrest. Withdrawal from chronic amphetamine use develops within a few hours and lasts for several days after cessation. Symptoms include dysphoria, fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation. "Crashing," resulting from acute withdrawal after periods of repetitive high-dose use of amphetamines or cocaine, is associated with intense lassitude and depression, and even suicidal ideation.

Polysomnographic recordings during acute intoxication with stimulants demonstrate increased sleep latency, decreased TST, increased spontaneous awakenings with increased body movements during sleep, prolonged REM latency, and reduced total REM time. Stimulant withdrawal is associated with reduced sleep latency and increased TST with hypersomnia and prolongation of nocturnal sleep duration.[7,13] REM and SWS may rebound to greater than baseline values. MSLT during the withdrawal phase shows increased sleepiness with mean sleep latency <10 min.

Sedative-, hypnotic-, and anxiolytic-dependent sleep disorder

The inverse of stimulant abuse is abuse of sedative-hypnotic agents. Hypnotic-dependent sleep disorder presents with excessive sleepiness or insomnia associated with tolerance to or withdrawal from sedative-hypnotic medications. Sleep complaints and objective measures of sleep are affected by the differences in duration of action and half-life of the various sedative-hypnotic agents.[7] During acute intoxication, sedative-hypnotic drugs produce hypersomnolence and decrease wakefulness.[7] Chronic usage, however, may lead to tolerance, with return of underlying insomnia, and, if the dose is increased, daytime hypersomnia, sluggishness, ataxia, slurred speech, and visual-motor problems with late-afternoon restlessness and nervousness, can occur.[13] Polysomnography in subjects using hypnotic agents demonstrates disrupted sleep architecture with an increase in stage 2 NREM sleep, reduction in stages 1, 3, and 4 NREM sleep, and reduction in REM sleep.[22] Both NREM and REM sleep are fragmented, with frequent sleep-stage transitions. Increased 14 to 18 Hz spindles are seen together with increased alpha and beta activity. Sedative-hypnotics can also aggravate underlying breathing disorders.

Abrupt discontinuation of chronic sedative-hypnotic use can result in withdrawal insomnia, decreased sleep duration, increased anxiety, tremulousness, and ataxia.[7] Although sleep architecture rapidly improves, subjective complaints of sleep quality and quantity will be deemed greater than before hypnotic therapy commenced.[13] Abrupt discontinuation of chronic use of barbiturates and the older nonbarbiturate, nonbenzodiazepine drugs is associated with a higher incidence of withdrawal seizures compared to benzodiazepines. Shorter-duration sedative-hypnotic drugs can result in withdrawal insom-

nia, while longer-duration sedative-hypnotic agents can cause daytime hypersomnia during active use. However, any sedative-hypnotic agent can produce either withdrawal insomnia or daytime sedation. Polysomnography during withdrawal demonstrates reduced sleep duration, increased sleep disruption, and REM sleep rebound.

Eating disorders

As with substance abuse disorders, patients with eating disorders also go through phases of indulgence and withdrawal, and have associated sleep-related problems. Eating disorders consist of severe disturbances in eating behavior, and the spectrum encompasses anorexia nervosa, bulimia, and sleep-related eating disorder.[60-66]

Anorexia nervosa

About 90% of anorexia nervosa occurs in females, and the prevalence of this condition among women in late adolescence and early adulthood is approximately 0.5% to 1.0%.[13] Peak onset occurs bimodally at ages 14 and 18 years. Essential features include refusal by the individual to maintain a minimally normal body weight, intense fear of gaining weight, and a significant disturbance in body perception (shape or size). Subsets include restricting type (weight loss is induced by fasting, dieting, or vigorous and excessive exercise) and binge-eating/purging type. In anorexia nervosa individuals, insomnia together with other depressive symptoms, such as depressed mood, irritability, and decreased libido, can also be present.[7] Long-term mortality is over 10% due to starvation, suicide, or electrolyte imbalance.[7]

Bulimia nervosa

This eating disorder occurs in 1% to 3% of adolescent and young female adults, and is characterized by binge-eating and inappropriate compensatory methods to prevent weight gain. These behaviors must occur on the average at least twice a week for 3 months. Subsets include the purging type (use of self-induced vomiting or misuse of laxatives, diuretics, or enemas during the current episode) or the nonpurging type in which abnormal behaviors, such as fasting or excessive exercise, are utilized. Bulimic individuals are usually within the normal weight range, although some are slightly underweight or overweight. Anxiety or depressive symptoms frequently occur. Sleepwalking has also been reported in bulimic individuals.

Nocturnal eating (drinking) syndrome

Like sleepwalking, nocturnal eating/drinking syndrome represents a parasomnia. This sleep disorder is characterized by recurrent awakenings with inability to return to sleep without eating or drinking. This problem occurs primarily during infancy and early childhood, with a prevalence of 5% in children between ages 6 months to 3 years. Nighttime waking can become conditioned to hunger and eating. After consuming the expected amount of food or drink, return to sleep is rapid. The prevalence in adults is unknown, but appears more common in women. Manni et al reported 5.8% prevalence among 120 adult subjects (51 males, 69 females, mean age 42.6 years) referred for insomnia complaints.[60]
Schenck et al described 19 adults with sleep-related eating (SRE), with mean age of onset of 24.7±9.1 years, and reported that psychiatric disorders affected 47.4% (9/19) of these patients; 31.6% (6/19) were diagnosed with affective disorders, while 21.0% (4/19) had anxiety disorders.[61] Winkelman reported that 35% (8/23) of their patients with SRE had a lifetime eating disorder diagnosis.[63] Symptoms in SRE include eating almost on a nightly basis (1-6 times per night), preferential consumption of high-caloric foods, binging or "out of control" eating, food preparation/consumption ranging from elaborate to sloppy, associated injuries from cooking/eating, including sustaining burns, dreamlike mentation with descriptions of being "half-awake," "half-asleep," and "asleep" associated with "consistent" or "occasional" amnesia for the event.[61-63] Patients complained of weight gain, concerns about choking while eating, starting fires from cooking, and sleep disruption.[61] Polysomnographic recordings documented complex behaviors arising abruptly from NREM sleep (stages 2 and 3 to 4) and occasionally also from REM sleep. Excessive numbers of arousals from NREM sleep were documented. Complex behaviors during polysomnographic recording ranged from moaning to somniloquy (logical or nonsensical), yelling, disorganized limb movements and thrashing, gesturing and finger pointing, throwing punches, sitting up abruptly, looking around in a confused manner with open eyes, grabbing at either hallucinated or actual bedside objects, picking up and handling the electrode jack box with perplexity, and kicking and attempting to leave the bed.[61] Accompanying EEG changes with SRE ranged from persistence of stage 2 or 3 to 4 to rapid complete arousal.[61,62] Two forms of disordered arousals, each with

multiple precipitants, can result in SRE: confusional-amnestic arousals associated with somnambulism, triazolam abuse, narcolepsy, sleep apnea, and psychotropic medications, or alert arousals associated with periodic movements of sleep or autoimmune hepatitis.[61]

Attention-deficit/hyperactivity disorder

Like the eating disorders, ADHD can impair quality of life and can be associated with sleep problems. ADHD consists of a persistent pattern (≥6 months) of inattention and/or hyperactivity-impulsivity (HI) that is maladaptive and inconsistent with an individual's developmental level.[7,13] The prevalence is estimated at 3% to 5% of school-age children in the USA.[7] The disorder is more frequent in males, with male to female ratio of 4:1 to 9:1.[7] Three subtypes occur: combined, predominantly inattentive (attention-deficient), and predominantly hyperactive-impulsive (HI).

Various sleep disorders have been reported as associated with ADHD. In a prospective controlled study of adults with restless legs syndrome (n=62) or insomnia (n=32) and adult controls (n=77), ADHD symptoms were more common in restless legs syndrome patients (26%) than insomnia patients (6%) or controls (5%) (P<0.01).[67] Restless legs and periodic leg movements of sleep were also correlated in children with ADHD. In a cross-sectional survey of 866 children aged 2.0 to 13.9 years (mean 6.8±3.2 years), Chervin et al reported that positive HI scores (>60) were found in 13% of all subjects, 18% of children with restless legs, and 11% of children without restless legs (chi-square P<0.05).[68] ORs between HI>60 and each of the following were: a 1-SD increase in the overall PLMS score, OR=1.6; restless legs, OR=1.9; and growing pains, OR=1.9 (all age- and sex-adjusted). Poor sleep quality and increased sleepiness associated with ADHD children can be due to either periodic leg movements of sleep or sleep-disordered breathing.[68,69]

Habitual snoring is more common in ADHD children (33%) compared with 11% in a psychiatry clinic and 9% in a general pediatric clinic.[70] Another cross-sectional study of 45 ADHD children reported that only the HI subtype of ADHD correlated with chronic snoring.[71] In a cross-sectional survey of 866 children aged 2.0 to 13.9 years (mean 6.8±3.2 years), the OR between HI>60 and a 1-SD increase in the overall sleep disordered breathing score was 1.7.[68,69] In two other studies, sleep-disordered breathing occurred in 50% (17/34) to 76% (67/88) of ADHD children, and periodic limb movements of sleep were reported in 10% (9/88) to 15% (5/34).[72,73] Polysomnographic recordings of ADHD children compared with normal controls demonstrate an increase in the percentage of phase 3 of sleep.[74] Epileptic paroxysms have also been reported in 16.7% of ADHD children.[74] In addition to behavioral measures, medications have been utilized in ADHD; like other psychotropic medications, these can also affect sleep.

Sleep effects of medications and substances of abuse

Sleep architecture can be affected by acute or chronic ingestion of medications or substances of abuse, as well as by abrupt withdrawal of these agents. Antidepressant drugs consist of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), and noradrenaline reuptake inhibitors (NARIs). Acute intake of TCAs, except trimipramine, decreases WASO, increases stage 2 NREM sleep, increases delta sleep, and reduces REM sleep with varying degrees of residual daytime sedation. During withdrawal, WASO is increased and REM sleep rebound occurs. Trimipramine ingestion increases SWS, but has no effect on REM sleep. MAOIs, such as moclobemide, phenelzine, and trancylpromine, increase sleep continuity, increase REM sleep latency, and reduce REM sleep amount, but do not affect SWS. However, moclobemide can result in insomnia.[75,76] Acute ingestion of SSRIs may cause insomnia or hypersomnia. WASO may be normal or increased, but SWS is not affected. REM latency is increased and REM sleep is reduced. SSRI agents, such as fluoxetine, sertraline, and paroxetine, may induce sleep bruxism, which may improve with buspirone.[75,77-79] Acute ingestion of trazodone decreases WASO, increases or has no effect on SWS, and decreases or has no effect on REM sleep. Buproprion reduces REM latency, increases REM sleep, and normalizes a propensity for sleep-onset REM periods on multiple sleep latency testing.[75] Mirtazapine increases SWS, but does not affect stage 2 NREM sleep, nor does it affect REM latency or REM percentage of total sleep. NARIs increase the duration of stage 2 NREM sleep, lengthen REM latency, and shorten REM sleep.

Mood stabilizers are used for bipolar disorders and include lithium and anticonvulsant drugs. Lithium ingestion acutely decreases REM sleep and increases delta sleep. Anticonvulsant drugs utilized in bipolar disorders include

sodium valproate (VPA), carbamazepine, topiramate, gabapentin, lamotrigine, tiagabine, and zonisamide. Valproic acid disrupts sleep by increasing stage 1 sleep.[80] Carbamazepine increases sleep efficiency, shortens sleep latency, decreases REM percentage of TST, and decreases REM density.[75,80] Gabapentin increases REM sleep percentage, increases mean duration of REM periods, reduces number of awakenings, reduces stage 1 sleep percentage, and increases SWS.[80-82] Lamotrigine increases REM sleep, reduces the number of entries into REM sleep, decreases the number of phase shifts, and decreases the percentage of SWS.[81] Tiagabine significantly increases sleep efficiency, decreases wakefulness, and increases SWS and low-frequency activity during NREM sleep.[83] Zonisamide is associated with daytime somnolence and fatigue.

Like the antidepressants, antipsychotic medications have different effects on sleep. Traditional neuroleptic agents (dopamine [D_2/D_3] antagonists, such as thorazine, haloperidol) increase sleep onset, sleep efficiency, and stage 3 NREM sleep; reduce REM sleep; increase periodic limb movements of sleep; and may induce restless legs syndrome–like akathisia. The newer non-D_2 neuroleptics, such as clozapine, olanzapine, and risperidone, increase sedation, reduce SWS, and increase restless legs syndrome and periodic leg movements. Use of quetiapine fumarate can result in insomnia. Withdrawal of narcoleptics results in reduction in sleep continuity and REM sleep. As mentioned previously, some of the atypical antipsychotic drugs have important metabolic effects, with development of obesity and subsequent obstructive sleep apnea. Atypical antipsychotics vary in their potential to cause metabolic abnormalities: olanzapine and clozapine carry the highest risks; risperidone and quetiapine have lower risks; and ziprasidone and aripiprazole have minimal metabolic risks.[84,85] Psychotic patients who relapse have greater reductions in TST, sleep efficiency, total NREM sleep, and stage 2 NREM sleep compared to nonrelapsers.[75]

Antianxiety drugs and hypnotic drugs, such as barbiturates and benzodiazepines, also affect sleep. Acute ingestion of barbiturates leads to increased TST, decreased WASO, increased stage 2 NREM sleep with increased spindles, variable effects on SWS, and reduced REM sleep. Tolerance to barbiturates rapidly develops, and withdrawal leads to insomnia and reduced TST. Acute ingestion of benzodiazepines decreases sleep latency (agents vary in onset), increases TST, increases stage 2 NREM sleep and spindles, decreases WASO and REM sleep, and usually suppresses stages 3 and 4 NREM sleep.[22] Withdrawal from benzodiazepines reduces TST. Rebound insomnia lasting for one to two nights occurs following withdrawal from short-acting benzodiazepines. Benzodiazepine receptor agents, such as zolpidem or zaleplon, reduce sleep latency and increase TST, but do not affect either SWS or REM sleep. Withdrawal from these agents leads to increased WASO.

Substances of abuse also impact sleep. Acute and chronic alcohol ingestion and withdrawal from alcohol affect sleep, as has been described above under substance-induced sleep disorder. Acute ingestion of opioids, such as heroin or methadone, profoundly disrupts sleep continuity and staging with increased brief arousals, reduces TST, decreases stages 3 and 4 NREM sleep, and reduces REM sleep.[86-88] Withdrawal from methadone can produce nocturnal insomnia lasting for 3 to 5 weeks. After methadone withdrawal, REM sleep and delta sleep increase.[88]

Amphetamines and methylphenidate are utilized to treat ADHD, but also have high abuse liability. Acute ingestion of amphetamines increases sleep latency, reduces sleep efficiency, reduces REM latency, and suppresses REM sleep. Withdrawal from amphetamines leads to increased TST and increased REM sleep, which can remain elevated for three to five nights. Methamphetamines increase average daily sleep latency on the MSLT in a dose-dependent manner for both normal subjects and narcoleptics.[75] Methlyphenidate reduces TST, increases REM latency, and reduces REM sleep duration. Nicotine produces a dose-dependent increase in wakefulness and reduction in REM sleep. Discontinuation of chronic nicotine use leads to increased number of arousals, awakenings, and sleep stage changes during the week of cessation.

Conclusions

Sleep problems and psychiatric disorders are codependent conditions that exacerbate each other and lead to impaired quality of life and increased disability. Recognition of the symptoms of these various psychiatric problems and their associated sleep issues has important therapeutic implications. ❑

Sueño y psiquiatría

Los trastornos psiquiátricos constituyen el 15,4% de los costos de las enfermedades en las economías de mercado. Muchos trastornos psiquiátricos están asociados con alteraciones del sueño y la relación a menudo es bidireccional. Este artículo revisa la prevalencia de varios trastornos psiquiátricos, su presentación clínica y su asociación con los trastornos del sueño. Entre los trastornos psiquiátricos revisados están los trastornos afectivos, las psicosis, los trastornos de ansiedad (incluyendo el trastorno por estrés postraumático), trastornos por abuso de sustancias, trastornos del comer y trastornos por déficit de atención con hiperactividad. El espectro de los trastornos del sueño asociados incluye insomnio, hipersomnia, terror nocturno, parálisis del sueño, alucinaciones hipnagógicas, síndrome de las piernas inquietas y de los movimientos periódicos del sueño, apneas obstructivas del sueño y parasomnias. También se resumen los efectos sobre el sueño de diversos psicofármacos utilizados para tratar los trastornos psiquiátricos mencionados anteriormente.

Sommeil et psychiatrie

Les troubles psychiatriques constituent 15,4 % du poids médical des économies de marché patentes. De nombreux troubles psychiatriques sont associés à des perturbations du sommeil, et le lien est souvent bidirectionnel. Cet article passe en revue la prévalence de troubles psychiatriques variés, leur présentation clinique, et leur association aux troubles du sommeil. Les troubles psychiatriques examinés comprennent les troubles affectifs, les psychoses, les troubles anxieux (y compris les troubles du stress posttraumatique), les troubles liés à l'abus d'une substance, les troubles des conduites alimentaires et les troubles du déficit de l'attention/hyperactivité. Le spectre des troubles du sommeil associés comprennent l'insomnie, l'hypersomnie, la terreur nocturne, la paralysie du sommeil, les hallucinations hypnagogiques, le syndrome des jambes sans repos/mouvements périodiques du sommeil, les apnées obstructives du sommeil et les parasomnies. Nous résumons ici les effets sur le sommeil de divers traitements psychotropes utilisés pour traiter les troubles psychiatriques ci-dessus.

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