

Sleep and anxiety disorders

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Anxiety is an experience of everyday life. It typically functions as an internal alarm bell that warns of potential danger and, in mild degrees, anxiety is serviceable to the individual. In anxiety disorders, however, the individual is submitted to false alarms that may be intense, frequent, or even continuous. These false alarms may lead to a state of dysfunctional arousal that often leads to persistent sleep-wake difficulties. Indeed, population surveys indicate that the prevalence of anxiety disorder is about 24% to 36% in subjects with insomnia complaints and about 27% to 42% for those with hypersomnia.^{1,2} Another point further underpinning the relationship between anxiety and sleep is that sleep disturbance is a diagnostic symptom for some anxiety disorders, such as generalized anxiety disorder (GAD) and post-traumatic stress disorder (PTSD).

Anxiety states may be focused upon some particular situation or may be generalized. Usually, there is a combination and most people suffering from severe phobic disorder will have some degree of generalized anxiety. Likewise, patients with generalized anxiety often experi-

Sleep disturbances—particularly insomnia—are highly prevalent in anxiety disorders and complaints such as insomnia or nightmares have even been incorporated in some anxiety disorder definitions, such as generalized anxiety disorder and posttraumatic stress disorder. In the first part of this review, the relationship between sleep and anxiety is discussed in terms of adaptive response to stress. Recent studies suggested that the corticotropin-releasing hormone system and the locus ceruleus–autonomic nervous system may play major roles in the arousal response to stress. It has been suggested that these systems may be particularly vulnerable to prolonged or repeated stress, further leading to a dysfunctional arousal state and pathological anxiety states. Polysomnographic studies documented limited alteration of sleep in anxiety disorders. There is some indication for alteration in sleep maintenance in generalized anxiety disorder and for both sleep initiation and maintenance in panic disorder; no clear picture emerges for obsessive-compulsive disorder or posttraumatic stress disorder. Finally, an unequivocal sleep architecture profile that could specifically relate to a particular anxiety disorder could not be evidenced; in contrast, conflicting results are often found for the same disorder. Discrepancies between studies could have been related to illness severity, diagnostic comorbidity, and duration of illness. A brief treatment approach for each anxiety disorder is also suggested with a special focus on sleep.

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Selected abbreviations and acronyms

ACTH	<i>adrenocorticotrophic hormone</i>
AN	<i>autonomic nervous (system)</i>
BZD	<i>benzodiazepine</i>
CNA	<i>central nucleus of the amygdala</i>
CRH	<i>corticotropin-releasing hormone</i>
GAD	<i>generalized anxiety disorder</i>
HPA	<i>hypothalamic-pituitary-adrenal (axis)</i>
LC	<i>locus ceruleus</i>
NE	<i>norepinephrine</i>
NREM	<i>non-rapid eye movement</i>
OCD	<i>obsessive-compulsive disorder</i>
PTSD	<i>posttraumatic stress disorder</i>
PVN	<i>paraventricular nucleus</i>
REM	<i>rapid eye movement</i>
SSRI	<i>selective serotonin reuptake inhibitor</i>
SWS	<i>slow-wave sleep</i>
TCA	<i>tricyclic antidepressant</i>

ence increase in anxiety in certain situations. Moreover, the various anxiety disorders share many biological and clinical similarities, and are highly comorbid. Therefore, in this article, we will first discuss common features of the neurobiological basis of anxiety and its relationships with sleep physiology. Next, sleep disturbances and its treatment will be discussed; for clinical convenience, each of the different anxiety disorders will be discussed separately. Indeed, the treatment of the anxiety disorder significantly improves sleep; however, when the sleep disturbance predominates, its treatment may improve the management of the anxiety disorder.

A brief survey of sleep physiology

Human sleep consists of two qualitatively different brain states, non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep is further subdivided into stages 1 through 4, with stage 1 being the lightest and stage 4 being the deepest sleep. Since slow “delta” waves distinguish stages 3 and 4, the stages are often defined as delta sleep or slow-wave sleep (SWS). REM sleep is also called paradoxical sleep because of the close resemblance with the electroencephalogram (EEG) of active wakefulness combined with a “paradoxical” active inhibition of major muscle groups that seems to reflect a heavy sleep. Normal sleep is characterized electrographically as recurrent cycles of NREM and REM sleep of about 90 min. In the successive cycles during the night,

the duration of stages 3 and 4 decrease, and the proportion of the cycle occupied by REM sleep tends to increase with REM episodes occurring late in the night having more eye movement bursts than REM episodes occurring early in the night.³

Most models of sleep regulation have implicated the monoaminergic and cholinergic systems and the importance of inhibitory GABAergic (GABA, γ -aminobutyric acid) mechanisms in sleep regulation is well established.⁴ Since dysfunction of these neurotransmitter systems have been implicated in anxiety disorders,⁵ it is no wonder that one of the chief complaints of anxiety disorder patients relates to sleep alteration.

Sleep-wake regulation is classically viewed as resulting from the interaction of two regulating processes (circadian [C] and homeostatic [S]).⁶ The propensity to sleep or be awake at any given time is a consequence of a sleep debt (process S), and its interaction with signals coming from the circadian clock located in the suprachiasmatic nucleus (process C). Process S is supposed to reflect the activity of a somnogenic substance that progressively accumulates with prolonged wakefulness, with adenosine being one of the most cited candidates.⁷ Both homeostatic and circadian mechanisms are thought to influence the opposite action of neurons promoting wakefulness and neurons promoting sleep. Wake-active neurons are cholinergic (located in the basal forebrain and in the tegmentum) and monoaminergic (noradrenergic in the locus ceruleus, serotonergic in the dorsal raphe, and histaminergic in the tuberomammillary nucleus), whereas sleep-active neurons are GABAergic and located in the preoptic area of the hypothalamus.⁴

The discovery of the hypocretin (also called orexin) system has brought new inroads into understanding the sleep-regulatory neural circuit.⁸ Hypocretin neurons are located in the lateral hypothalamus and have dense excitatory projections to all monoaminergic and cholinergic cell groups. Recent studies suggested that monoaminergic and hypocretin neurons play a different and complementary role in wakefulness maintenance.⁴ For example, the dual effects of hypocretins on arousal and food intake (orexin from “appetite-stimulating”) suggest a more important role for hypocretins in the control of arousal maintenance related to energy homeostasis.⁸ In the same way, data summarized in the following section suggest a role for the norepinephrine (NE)-containing neurons of the locus ceruleus (LC) in stress-induced arousal and concomitant anxiety.

Interactions between stress, anxiety, and sleep

Anxiety and stress

Anxiety is a universal emotion and it would at times be maladaptive not to experience it; it is a necessary part of the response of the organism to a stress, ie, a threat to the psychological or the physiological integrity of an individual. Anxiety may be polarized between a state and a trait. It may supervene at some point in the course of life, in which case anxiety is referred as a state. Anxiety trait is a long-term feature of a person's experience, present throughout life and considered to be a key feature of the avoidant or anxious personality disorder. It probably reflects a lifetime maladaptive response to stress due to individual differences in biogenetic background, developmental influences, and early life experiences. There is no hard and fast distinction between anxiety that may be considered as a normal, acceptable accompaniment of stress and the pathological state that warrants classification as a psychiatric disorder. In the latter, the nature of the stress is not always clearly discernible. In other words, pathological anxiety could be characterized by a sense of fear, but it is differentiated from fear in that the threat is not immediate or always obvious. Whether normal or pathological, the constituent features of anxiety always comprise indices of increased arousal or alertness that could lead to sleep-wake alterations. Indeed, anxiety is only one part of the arousal response to stress, whether the stress is real, implied, or overvalued.

Arousal and stress

Response to stress implicates two systems that both play a key role in physiological responses to stressful situation by promoting arousal, the corticotropin-releasing hormone (CRH) system and the LC-autonomic nervous (AN) system. This topic has recently been reviewed by several authors⁹⁻¹¹ and will be only briefly described here. Before going further, it should be emphasized that promoting arousal is essential for identifying a given situation as important, as well as for maintaining the central nervous system (CNS) in states that most favor survival during stressful situations. Arousal response to stress comprises three components (hormonal, behavioral, and autonomic) in which CRH and LC-AN systems have been diversely implicated (*Figure 1*). Different stressors

activate different components of the stress system, eg, the LC-AN system will be more implicated in the response to physiological stressors such as hypoxia, while the CRH system will be recruited for more complex environmental dangers such as emotional stress. However, there are several connections between the two systems which are continuously in close interaction (see next section).

The stress system

During these last years, a series of studies in rodents established the role of CRH as a key neurotransmitter in the stress response, beside its stimulating effect on the hypothalamic-pituitary-adrenal (HPA) axis.^{9,11} It has been shown that hypothalamic CRH neurons activate the LC-AN system and inhibit a variety of neurovegetative functions, such as food intake, sexual activity, growth, and reproduction. CRH-containing neurons located in the central nucleus of the amygdala (CNA) play a key role by activating fear-related behavior, while inhibiting exploration behavior. Like the CRH system, the NE-containing neurons of the LC promote arousal, inhibit the parasympathetic system as well as several vegetative functions such as feeding and sleep, and contribute to HPA axis stimulation.¹² It has been shown that stress increases NE turnover in many terminal projections of the LC and that the activity of LC neurons is monotonically related to increased arousal.⁹

There is also evidence that NE stimulates the release of CRH in the paraventricular nucleus (PVN) of the hypothalamus and in the CNA.⁹ These NE-CRH influences suggest a potential feed-forward system between the

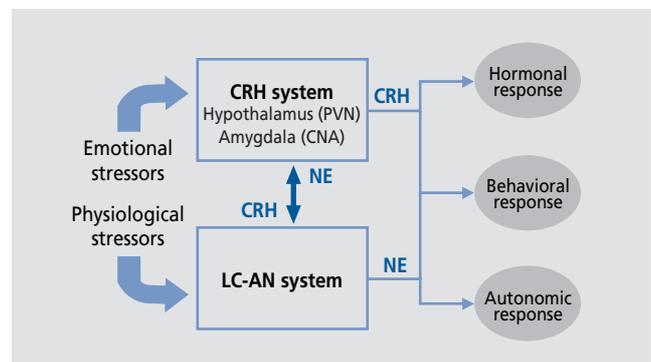


Figure 1. Arousal response to stress. CRH, corticotropin-releasing hormone; PVN, paraventricular nucleus; CNA, central nucleus of the amygdala; LC-AN, locus ceruleus-autonomic nervous; NE, norepinephrine.

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LC-AN system and the CRH system, and both systems have stimulating properties on its counterpart. It has been suggested that such a feed-forward mechanism may be particularly vulnerable to dysfunction during which the arousal reaction is maintained despite the removal of the stressful situation.^{9,10} The same authors have proposed that, if prolonged, such dysfunctional arousal state could lead to anxiety and depressive disorder.

Stress and sleep-wake regulation

Animal and human studies showed that both acute and chronic stress have pronounced effects on sleep that are mediated through the activation of the HPA axis and the sympathetic system.¹³ For instance, in rats, effects of acute stress on sleep are primarily manifested by changes in REM sleep. These alterations seem to involve CRH-mediated mechanisms: CRH acts as a neurotransmitter in the LC to increase activity of the NE neurons, which leads to an increase in REM sleep.¹⁴ Rats exposed to various models of chronic stress have shown sleep disruption, increase in REM sleep, and decrease in SWS.^{15,16} There are also indications that CRH could contribute to the regulation of spontaneous waking even in the absence of stressors.¹⁷ In humans, there is a close temporal relationship between HPA activity and sleep structure. The HPA axis is subject to a pronounced inhibition during the early phase of nocturnal sleep, during which SWS predominates. In contrast, during late sleep, when REM sleep predominates, HPA activity increases to reach a diurnal maximum shortly after morning awakening. During SWS, sympathetic activity is reduced and there is positive correlation among the amount of REM sleep and activities of the HPA axis and the sympathetic system.^{18,19} More generally, a close coupling has been shown between adrenocorticotrophic, autonomic, and EEG indices of arousal during the sleep-wake cycle.²⁰

	Insomnia alone	Hypersomnia alone	Both
GAD	7.0 (2.8–17.2)	4.5 (1.5–15.3)	4.8 (1.5–15.2)
Panic disorder	5.3 (2.0–13.6)	4.3 (1.3–14.8)	8.5 (3.1–23.5)
OCD	5.4 (2.0–14.8)	1.2 (0.1–9.7)	13.1 (4.8–35.7)
Phobic disorder	1.5 (1.0–2.3)	2.9 (1.8–4.8)	4.0 (2.5–6.5)
Any anxiety disorder	2.4 (1.6–3.5)	3.3 (2.0–5.4)	4.5 (2.8–7.3)

Table 1. Odds ratios for specific anxiety disorders associated with lifetime sleep disturbances (adapted from Breslau et al²). GAD, generalized anxiety disorder; OCD, obsessive-compulsive disorder.

²² Exogenous administration of CRH, adrenocorticotrophic hormone (ACTH), or cortisol produces either prolonged sleep onset, reduced SWS, and increased sleep fragmentation.¹³ Accordingly, patients with complaints of insomnia show electrophysiological and psychomotor evidence of increased daytime arousal,^{23–25} as well as indications of increased HPA activity²⁶ and increased sympathetic tone.²⁷

Sleep complaints and anxiety disorder

Anxiety disorders are considered as the most frequently occurring category of mental disorder in the general population. Estimates of the lifetime prevalence of anxiety disorders have ranged between 10% and 25%.²⁸ Epidemiological studies have also demonstrated the high prevalence of sleep complaints. As much as one third of the adult population reports difficulty sleeping^{29–31} and sleep disturbance is considered as the second most common symptom of mental distress.³² Some epidemiological studies investigated the relationship between the occurrence of sleep disturbances and anxiety disorder in the general population.^{1,2,33} In a longitudinal study of young adults, Breslau et al² found that lifetime prevalence was 16.6% for insomnia alone, 8.2% for hypersomnia alone, and 8% for insomnia *plus* hypersomnia. Odds ratios for various anxiety disorder diagnoses associated with lifetime sleep disturbance varied from 1.2 to 13.1. *Table 1* shows that the odds ratios associated with insomnia alone varied little from those associated with hypersomnia alone. The three highest odds ratios were those for obsessive-compulsive disorder (OCD) and for panic disorder associated with both insomnia and hypersomnia, and that for GAD associated with insomnia alone.

These findings were replicated for chronic insomnia in a recent study,³³ which further showed that insomnia appeared before the anxiety disorder in 18% of cases, anxiety and insomnia appeared about in the same time in 38.6% of cases, and anxiety appeared before insomnia in 43.5% of cases. These authors concluded that psychiatric history, including anxiety disorder, is closely related to the severity and chronicity of current insomnia.

Panic disorder and agoraphobia

The essential features of panic disorder are recurrent attacks of severe anxiety (panic attacks), which are not restricted to any particular situation or set of circumstances and are therefore unpredictable. According to

the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*³⁴ criteria of panic disorder, unexpected panic attacks have to be followed by at least 1 month of persistent concern about having another panic attack. The dominant symptoms of a panic attack vary from individual to individual. Typically, it includes autonomic symptoms with marked psychic anxiety. The most prominent autonomic symptoms are palpitations, sweating, trembling, shortness of breath, dizziness, chest pain, nausea, and paresthesias. There is almost always a secondary fear of dying, losing control, or going mad. Most individual attacks last only for a few minutes, but a common complication is the development of anticipatory fear of helplessness or loss of control during a panic attack, so that the individual may progressively develop avoidant behavior leading to agoraphobia or specific phobias. In this respect, most, if not all, patients with agoraphobia also have a current diagnosis (or history) of panic disorder.³⁴ Accordingly, sleep disturbances of panic disorder and agoraphobia are discussed in the same section.

Subjective sleep

Sleep disturbances, predominantly insomnia, are extremely common in panic disorder. Sheehan et al³⁵ reported a prevalence of 68% for difficulties in falling asleep and of 77% for restless and disturbed sleep. In a self-report sleep survey, Mellman and Uhde³⁶ found that, compared with healthy subjects, patients with panic disorder reported more complaints of middle night insomnia (67% versus 23%) and late night insomnia (67% versus 31%); the two groups did not differ with regard to early night insomnia. Many patients with panic disorder experience occasional sleep panic attacks, but only about 20% to 45% of patients with panic disorder have repeated nocturnal panic attacks.³⁷⁻³⁹ Some evidence suggests that patients experiencing regular nocturnal panic attacks represent a specific version of panic disorder characterized by fearful associations with sleep and sleep-like states.⁴⁰ Therefore, nocturnal panic attacks will be discussed in a separate section.

Sleep EEG recording

Most polysomnographic studies indicate that patients with panic disorder have impaired sleep initiation and maintenance characterized by increased sleep latency

and increased time awake after sleep onset resulting in a reduced sleep efficiency (the ratio between total sleep time and time in bed),⁴¹⁻⁴⁷ but there are also negative reports showing no difference compared with controls in these variables.^{48,49} Concerning sleep architecture, NREM sleep was found differently affected across studies; some reported a decreased stage 2 sleep duration^{42,43} with a concomitant increase in SWS.⁴⁷ Time spent in SWS was found reduced by Arriaga et al⁴⁶ and Stein et al,⁴⁹ but unchanged by other authors.^{36,42,45} Controversial results were also obtained regarding REM sleep. Although most studies agreed on the fact that REM sleep time is unchanged in panic disorder, some authors found a shortening of REM sleep latency,^{36,48} while others did not.^{41,44} To summarize, most studies suggest that the subjective sleep continuity disturbances reported by patients with panic disorder could be objectively demonstrated by polysomnographic recordings. Findings regarding sleep architecture are more controversial (although REM sleep seems to be preserved). These discrepancies could relate to sampling differences (some studies having included patients with a comorbid depressive disorder) and to the influence of nocturnal panic attack during the sleep EEG recording.

Treatment

Sleep disturbances linked to panic disorder respond to a number of antipanic pharmacological agents including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), benzodiazepines (BZDs), and monoamine oxidase inhibitors (MAOIs). Some patients could have an initial increased anxiety or insomnia in response to antidepressant medications, which should alert the clinician to the need to increase the dosage quite slowly. A BZD can also be used to reduce anxiety and aid sleep in the early phases of treatment.

Nocturnal panic

The majority of patients with panic disorder experience nocturnal panic attacks. However, in a subgroup of patients, sleep-related panic is the predominant symptom,³⁸ with up to 18% of all panic attacks occurring during sleep.⁵⁰ Nocturnal panic refers to waking from sleep in a state of panic and should be distinguished from nighttime arousal induced by nightmares or environmental stimuli (such as unexpected noise). It has often been mistaken for

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sleep apnea, sleep terrors, and nocturnal epilepsy. Nocturnal panic generally occurs during late stage 2 to early stage 3 sleep, and can therefore be distinguished from sleep terrors, which mostly occur during stage 4 sleep, and from nightmares, which mostly occur during REM sleep.⁵¹ Moreover, nocturnal panic could be differentiated from nocturnal seizures by the fact that no EEG abnormality was demonstrated during nocturnal panic attacks and from sleep apnea because sleep apnea occurs mostly during stages 1 and 2, as well as during REM sleep, and is more repetitive than nocturnal panic.⁴⁰

There are limited indications that subjects with frequent sleep panic attacks have a severe form of panic disorder.^{37,38,52} More recent studies suggest that there are only few differences on measures of psychopathology and on sleep EEG between panic-disordered patients with and without sleep-related panic attacks.^{40,53} However, differences may be more subtle and evidenced by techniques such as measurement of the autonomic nervous system (ANS) activity. For instance, Sloan et al⁵⁴ used a lactate infusion panicogenic challenge and heart rate variability as a measurement of ANS activity to demonstrate that ANS dysregulation during sleep is more pronounced in nocturnal panic patients than in daytime panic patients. This suggests a more increased arousal level in nocturnal panic.

On the basis of several observations,^{38,40,51} it has been proposed that nocturnal panic is characterized by heightened distress to situations that involve loss of vigilance, such as sleep and relaxation, and that it may represent one particular version of panic disorder that responds just as well as other forms of panic disorder to usual antipanic treatment.⁴⁰ In this regard, the adjunction of cognitive-behavioral therapy to pharmacological agents will be particularly beneficial in patients with nocturnal panic, since some patients can develop a conditioned fear or even an avoidance of sleep, which may cause further sleep deprivation and thus aggravate the condition.

Generalized anxiety disorder

A persistent state of anxiety, ie, lasting for at least 6 months, characterizes GAD. Anxiety and apprehensive expectation (“worry”) need to relate to a certain number of events and to be accompanied by additional symptoms belonging to a motor tension cluster (muscle tension; restlessness; and easy fatigability) or to a vigilance and scanning cluster (difficulty falling or staying asleep; restless, unsatisfying sleep; difficulty concentrating; and irri-

tability). According to *DSM-IV*,³⁴ the diagnosis is not made if the symptoms exclusively relate to another Axis I disorder. As sleep disturbances are part of the diagnosis requirement, a high prevalence of these symptoms is expected in GAD. For instance, in mental health epidemiological surveys, Ohayon et al⁵⁵ found that, among subjects complaining of insomnia and having a primary diagnosis of mental disorder, GAD was the most prevalent diagnosis. It has been estimated that about 60% to 70% of patients with GAD have insomnia complaint, whose severity parallels that of the anxiety disorder,^{56,57} suggesting that insomnia could represent one of the core symptoms of GAD.

Sleep EEG recording

Monti and Monti⁵⁸ have extensively reviewed six selected studies investigating polysomnographic recording of patients with GAD. The sleep EEG recordings following an adaptation night of 130 patients were compared to those of 147 normal controls in the age range 20 to 65 years (mean 37 years). Regarding sleep continuity, the results indicate that GAD is mostly associated with sleep maintenance insomnia, and to a lesser extent with sleep initiation difficulties. Five studies found a significant decrease in total sleep time, four an increase of waking after sleep onset, while only two studies showed a significant prolongation of sleep onset latency. As regards NREM and REM sleep structures, results are inconsistent. Stage 4 was significantly decreased in three studies, all six studies showed nonsignificant decrease in REM sleep, and one study a significant shortening of REM latency.

Treatment

GAD is often responsive to BZDs, buspirone, and antidepressants. Anxiolytic BZDs provide a prompt relief of the GAD symptoms belonging to the motor and the vigilance-scanning clusters. However, psychic symptoms such as worry and ruminations are less affected by these compounds and respond better to antidepressants such as TCAs, SSRIs, or norepinephrine and serotonin selective antidepressant (NaSSA), such as venlafaxine.⁵⁸ Adjunctive psychotherapy with a cognitive focus can be beneficial. In this regard, studies have shown that cognitive-behavioral techniques are better than control conditions or to either cognitive or behavior therapy alone.⁵⁸

The alleviation of the sleep disturbance can often greatly improve the condition: therefore a low-dose, intermediate-acting BZD at bedtime may be temporarily indicated early in the treatment. Sedative antidepressant could also help improve sleep.

Obsessive-compulsive disorder

According to *DSM-IV*,³⁴ the essential features of the OCD are recurrent obsessions or compulsions that are sufficiently severe to cause a significant disruption of a person's daily routine. The most common obsessional thoughts are fears of contamination, of being aggressive, and of a sexual nature; the most common compulsions relate to checking, cleaning, and counting. The sufferer knows that it is his or her own thought (or act), that it arises from within him- or herself, and that it is subject to the sufferer's own will. Anxiety is provoked by the fear of what may happen if the compulsive rituals are disturbed, the need to both perform the action and preserve social acceptability, or the fearful nature of the obsessional thoughts themselves. The person usually functions satisfactorily in other areas of life not contaminated by the obsessional thoughts, but as the obsessions become more severe there is increasing social incapacity.

Patients often complain of disrupted sleep and sleep delay due to compulsive behaviors. In one epidemiological survey,⁵⁵ insomnia related to OCD had a prevalence of 0.2% (ie, insomnia complaints sufficiently severe to warrant an Axis I diagnosis in addition to OCD), while the prevalence of OCD with insomnia (not sufficiently severe to warrant a separate diagnosis) was 1.2%. These data should be compared with the 2.5% of OCD prevalence in the general population.³⁴

Sleep EEG recording

Studies comparing polysomnographic sleep EEG recordings from OCD patients with those of normal volunteers are scanty and bring divergent results. Most of these studies contained a large number of patients with a comorbid mood disorder, leaving doubt about the specificity of their findings.⁵⁹⁻⁶¹ The three studies found various degrees of sleep continuity disturbances, mainly regarding sleep maintenance. REM latency was found shortened in two out of the three studies. Robinson et al⁶² investigated a group of OCD patients free of major depression and could not evidence any significant difference in sleep

continuity and architecture variables between patients and healthy controls. However, slight negative correlations were found between severity of obsessive-compulsive symptoms and total sleep time or sleep efficiency. In summary, except for sleep maintenance disturbances, there is at yet no clear pattern of polysomnographic findings in OCD.

Treatment

Treatment is generally a combination of pharmacotherapy with serotonin-potentiating agents and behavioral therapy. In contrast to other anxiety disorder, only drugs inhibiting serotonin reuptake have proven their efficacy in OCD.⁶³ According to a recent meta-analysis, clomipramine has been demonstrated to be superior to the other drugs,⁶⁴ but poor tolerance and the lethal risk of overdose can limit their utilization. Accordingly, SSRIs are now considered to be first-line treatment for OCD.⁶⁵ Placebo-controlled studies have shown the efficacy of paroxetine, fluoxetine, fluvoxamine, citalopram, and sertraline.⁶⁶ Since SSRIs can act as stimulants, especially at the doses required to treat OCD, and induce insomnia, the concurrent use of trazodone or a low-dose sedative TCA is often prescribed, particularly for patients with a history of sleep complaints prior pharmacotherapy.

Posttraumatic stress disorder

Neuropsychological problems following experience of a traumatic event characterize patients suffering from PTSD. The stressful event must have been exceptionally threatening or catastrophic in nature, such as a natural disaster, combat, serious accident, witnessing the violent death of someone, or being the victim of torture or rape. The typical features of PTSD are commonly grouped into three categories³⁴: (i) reexperiencing the traumatic event (comprising preoccupation of reliving the trauma, intrusive memories or flashbacks, and vivid nightmares); (ii) persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness; and (iii) signs of increased arousal, such as hypervigilance, insomnia, and difficulty concentrating. Patients with PTSD may become socially isolated and, at times, may resort the use of drugs or alcohol to suppress the traumatic memories and tormented wakefulness. The lifetime prevalence of the disorder is between 1% and 9%.⁶⁷ Sleep disturbances in terms of nightmares and insomnia are a very promi-

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ment complaint of subjects who have undergone trauma; for instance, it has been estimated that 96% of Holocaust survivors complained of insomnia and 83% reported recurrent nightmares.⁶⁸ Pillar et al⁶⁷ reported that patients with PTSD frequently described very prolonged sleep latencies (ie, more than 2 h), and estimate being awake more than half of the time in bed during the night (ie, a subjective sleep efficiency of less than 50%). More generally, it must be underlined that recurrent distressing dreams of a traumatic event are pathognomonic of PTSD, in the sense that they are not observed in other disorders, contrary to complaints such as insomnia.

Sleep EEG recording

Results of studies investigating polysomnographic recordings of patients with PTSD have been previously reviewed⁶⁷ and contrast somewhat with the prevalence of subjective sleep complaints. Pillar et al⁶⁷ concluded that PTSD itself does not dramatically adversely affect objective sleep. Some studies found longer sleep latencies, reduced total sleep time, and lower efficiencies among patients with PTSD, but numerous other studies failed to replicate this finding. SWS did not seem to be affected during PTSD, while inconsistent results have been reported for REM sleep: both shortening and prolongation of REM latency and lower and higher time spent in REM were reported in PTSD. Most relevant studies in PTSD reported on increased REM density, ie, more rapid eye movements per REM time, a finding that could relate to the hostile and threatening characteristics of a dream. Some of the positive findings could be related to comorbid psychiatric illness, such as major depression.⁶⁷

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Treatment

Patients with PTSD generally benefit from some form of individual or group psychotherapy, especially early in the course of the disorder. With regard to pharmacotherapy, SSRIs appear to be the treatment of choice and their efficacy and safety have been demonstrated by meta-analysis, while TCAs have a more modest effect on PTSD symptoms.⁶⁶ Early in treatment, for severe cases, sedative antidepressant could bring relief to night terror activity. BZDs may be helpful, but tolerance may develop because of the chronicity of the disorder and it should be kept in mind that the risk of associated dependence is high in these patients.

Conclusions

Although sleep disturbances, and particularly severe insomnia complaints, are often encountered in patients with anxiety disorders, polysomnographic studies documented limited alteration of sleep continuity, ie, sleep initiation and sleep maintenance. Regarding sleep architecture, no clear picture emerges for specific anxiety disorders. Discrepancies between studies could have been related to illness severity, diagnostic comorbidity, and duration of illness. It should be stressed that anxiety in itself is present in many psychiatric disorders and that therefore the assessment of anxiety as a single influence on sleep is quite difficult. Our current preclinical understanding of arousal responses to aversive stress and some confirmation that similar mechanisms may play a role in human stress, should open the way to the development of more specific therapeutic tools in sleep medicine, particularly for anxiety-induced sleep alterations. □

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Sueño y trastornos de ansiedad

Los trastornos del sueño particularmente el insomnio son altamente prevalentes en los trastornos de ansiedad, e incluso molestias como el insomnio o las pesadillas han sido incorporadas en las definiciones de algunos trastornos de ansiedad, como el trastorno de ansiedad generalizada y el trastorno por estrés postraumático. En la primera parte de esta revisión se discute la relación entre el sueño y la ansiedad en términos de una respuesta de adaptación al estrés. Estudios recientes sugieren que el sistema que implica la hormona liberadora de corticotrofina y el sistema que implica el locus ceruleus y el sistema nervioso autónomo pueden jugar un papel importante en la respuesta de alerta al estrés. Se ha sugerido que estos sistemas pueden ser particularmente vulnerables al estrés prolongado o repetido, lo que conduciría a un estado de alerta disfuncional y estados de ansiedad patológica. Los estudios polisomnográficos han documentado pocas alteraciones del sueño en los trastornos de ansiedad. Hay ciertos elementos a favor de una alteración del sueño en el trastorno de ansiedad generalizada, y del inicio y en el mantenimiento del sueño en el trastorno de pánico; en cambio, los datos son contradictorios en el trastorno obsesivo compulsivo o en el trastorno por estrés postraumático. Finalmente, no se ha podido determinar que alguna anomalía del sueño se relacione de manera específica con algún trastorno ansioso, y a la inversa, se han encontrado resultados contradictorios para el mismo trastorno. Las discrepancias entre los estudios pudieran deberse a la severidad de la enfermedad, la comorbilidad diagnóstica o la duración de la enfermedad. Además se sugiere una breve aproximación terapéutica para cada trastorno ansioso con especial atención sobre el sueño.

Sommeil et troubles anxieux

Les perturbations du sommeil, et en particulier l'insomnie, sont très fréquentes dans les troubles anxieux, et les plaintes comme l'insomnie et les cauchemars font même partie de la définition de certains troubles anxieux, comme le trouble anxieux généralisé et l'état de stress posttraumatique. Dans la première partie de cette revue de la littérature, les relations entre sommeil et anxiété sont présentées dans un contexte de réaction d'adaptation au stress. Des études récentes suggèrent que le système impliquant la corticolibérine et le système impliquant le locus ceruleus et le système nerveux autonome joueraient un rôle majeur dans la réaction d'activation suite à un stress. Ces systèmes pourraient être particulièrement vulnérables à des stress prolongés ou répétés, ce qui serait à l'origine d'un état d'activation dysfonctionnel et d'états anxieux pathologiques. Les études polysomnographiques n'identifient que peu d'anomalies du sommeil dans les troubles anxieux. Certains éléments sont en faveur d'une perturbation du maintien du sommeil dans le trouble anxieux généralisé et d'une perturbation de l'endormissement et du maintien du sommeil dans le trouble panique ; les données sont contradictoires pour le trouble obsessionnel-compulsif et l'état de stress posttraumatique. Enfin, les études n'ont pu mettre en évidence des anomalies de l'architecture du sommeil spécifiques d'un trouble anxieux particulier et, inversement, des résultats contradictoires ont été rapportés pour un même trouble anxieux. Ces discordances entre les études proviennent probablement de différents niveaux de sévérité de la maladie, de la comorbidité psychiatrique et de la durée de la maladie. Une brève approche thérapeutique est également proposée pour chaque trouble anxieux avec une attention particulière au sommeil.

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