Sleep in psychiatric disorders
O sono em transtornos psiquiátricos

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Abstract

Altered sleep patterns are prominent in the majority of psychiatric disorders. This article examines the psychiatric disorders that are most often associated to sleep dysfunction as it is related in clinical practice and describes the polysomnographic findings. Patient's main complaints are related to difficulty in initiating and maintaining sleep (initial or middle insomnia, respectively) and poor quality of sleep. Early awakening or terminal insomnia is most described in the depressive conditions. Hypersomnia may be the main symptom in some depressive disorders, as seasonal depression, depression with atypical features or depressive episodes in bipolar disorder. Polysomnographic evaluation shows, in general, a significative reduction in the efficiency and total time of sleep, in detriment to the amount of slow wave sleep. The reduction of rapid eye movement (REM) sleep latency is mainly described for the depression, but has also been reported in other psychiatric disorders.

Keywords: *Sleep disorders; Sleep, REM/physiology; Depressive disorders; Attention deficit disorders with hyperactivity; Polysomnography; Sleep initiation and maintenance disorders*

Resumo

O achado de padrões alterados de sono é notável na maioria dos transtornos psiquiátricos. Neste artigo são abordados os transtornos psiquiátricos que mais freqüentemente apresentam alterações de sono na prática clínica e a descrição dos achados polissonográficos. As queixas mais freqüentes dos pacientes são relacionadas à dificuldade para iniciar e manter o sono (insônia inicial e de manutenção, respectivamente) e sono não reparador, observadas na maioria dos transtornos. A insônia terminal ou despertar precoce é mais relacionada a quadros depressivos. A hipersonia pode aparecer em alguns quadros de depressão como sazonal, atípica ou em transtornos bipolares. Em relação aos achados polissonográficos, temos, em geral, redução significativa da eficiência e do tempo total do sono à custa da redução do sono de ondas lentas. A redução da latência para o sono de movimentos oculares rápidos (REM) é descrita principalmente para os quadros depressivos, mas pode aparecer em outras patologias.

Descritores: *Distúrbios do sono; Sono REM/fisiologia; Transtornos depressivos; Transtorno da falta de atenção com hiperatividade; Polissonografia; Distúrbio do início e da manutenção do sono*

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Introduction

Sleep dysfunction is prominent in most psychiatric disorders.[1] In a survey carried out in various American cities, 40% of interviewees reporting insomnia and 46.5% of those reporting hypersomnia met the criteria for mental disease according to the DSM-III-R.[2]

In the international classification of sleep disorders (ICSD),[3] the third division refers to sleep dysfunction related to clinical and psychiatric disorders. Such mental disorders are subdivided into: psychoses, mood disorders, anxiety disorders, panic disorders and alcoholism. There is a discrepancy regarding the classification of mental disorders[4] in which panic disorder is part of an anxiety disorder. The justification for this separation in the ICSD is that some panic disorders may only present episodic manifestations during sleep.[3,5] Therefore, altered sleep patterns are used as diagnostic criteria for various psychiatric profiles, such as major depression, post-traumatic stress disorder and generalized anxiety disorder.[4]

This article addresses psychiatric disorders that most frequently present sleep dysfunction in clinical practice and the main polysomnographic findings described. Some studies evaluating the physiopathology of such alterations in certain sleep disorders and of those caused by the most common drug therapies will also be discussed. Sleep patterns and changes related to specific disorders of childhood and adolescence will be presented separately.

Mood disorders
1. Depression

Approximately 80% of patients with depression complain of changes in sleep patterns. Of these 80%, most present terminal insomnia, waking up hours before necessary (early awakening).[6] In cases of accompanying anxiety symptoms, initial insomnia, in which the patient presents difficulty in initiating sleep, is also common.[6] In longitudinal epidemiological studies, insomnia has been found to be an important predictor of increased risk of depression in one to three years of follow up.[7] In addition, persistent insomnia has been correlated with the onset of a new depressive episode.[8]

Specific complaints may include frequent nighttime awakenings, poor quality sleep, reduction in total sleep time, and nightmares.[9] Although complaints of excessive daytime sleepiness are rare in major depression, some patients with insomnia relate increased fatigue and try to compensate for their sleep loss with daytime naps.[10]

A small percentage of patients with major depression, the majority of whom are young adults,[10] complain of excessive sleepiness. Most patients with bipolar disorder also relate insomnia when in depression, but a significant percentage of patients relate hypersomnia symptoms with prolonged nighttime sleep, difficulty in awakening and excessive daytime sleepiness.[9] Patients with seasonal affective disorder and atypical depression also report hypersomnia.[4,9]

1) Polysomnographic findings

In patients with depression, polysomnographic findings can be divided into three main categories: sleep continuity, slow-wave sleep and rapid eye movement (REM) sleep. In the sleep continuity category, increased sleep latency, more frequent nighttime awakenings and early awakening are observed, resulting in sleep fragmentation and decreased sleep efficiency.[11] Studies comparing depressed patients to age-matched controls have confirmed these results.[1,9]

Slow-wave sleep deficit has been reported by various authors, although not all studies have shown this reduction.[1,9] Reduced slow-wave sleep seems to be more pronounced in the first non-rapid eye movement (NREM) period, which alters its distribution throughout the night.[12] Decrease in delta power has also been observed in quantitative electroencephalography studies carried out during sleep.[12]

The first finding regarding REM sleep was the reduction in REM latency (period of time from sleep onset to REM onset).[1,9-10] Over the years, this has been proven to be the most frequently described factor in patients with major depression, although it is as yet unknown whether REM latency is a specific indicator of current or past depression, perhaps linked to cholinergic hyperactivity.[9] Other findings refer to the increase in the first REM sleep period, in REM density (increase in the rate of rapid eye movements) and in REM percentage.[1,9-11]

In a study attempting to relate subjective sleep complaints to polysomnographic data in patients with depression, the patients were incapable of accurately estimating the number of awakenings during the night.[13] The subjective evaluation of sleep quality seemed to be associated with sleep continuity and the amount of slow-wave sleep.[13]

2. Mania

During episodes of mania, patients relate reduced total sleep time, with a subjective sensation of a decreased need for sleep. In various cases, the transition to the mania stage is preceded by periods of sleeplessness. It has also been suggested that the transition from euthymia or depression to the maniac stage occurs during sleep.[10]

1) Polysomnographic findings

The main characteristic of mania seems to be reduced total sleep time, since the maniac patient appears to have difficulty in falling asleep.[1,9-10] Two or three hours after falling asleep, the patient awakes, totally reinvigorated. As in depression, the duration of stages 3 and 4 may be curtailed, although the findings regarding REM sleep were less consistent.[1,9-10]

Anxiety disorders
1. Generalized anxiety disorder

Patients with generalized anxiety disorder (GAD) frequently complain they cannot relax or stop worrying about their problems when they are in bed.[5] The sleep dysfunctions most frequently associated with GAD profiles are sleep maintenance insomnia[14] and difficulty in initiating sleep (initial insomnia).[5,10,15] Poor quality sleep and interrupted sleep have also been reported.[5,10,14]

1) Polysomnographic findings

Patients with GAD present increased sleep latency (frequently more than one hour[15]), increased duration of the lightest sleep stages, lower percentages of REM sleep and, except for isolated cases, increased or normal REM sleep latency.[1,5,10]

2. Panic disorder

The most common sleep-related complaints of patients with panic disorder are initial or maintenance insomnia (approximately 70% of the patients) and poor quality or fragmented sleep.[5,10,16] Panic attacks may occur during sleep. In patients with nocturnal panic attacks, levels of anxiety seem to be higher and the duration of the attacks longer. In addition, there is increased presence of somatic symptoms and more comorbidity with other psychiatric disorders, especially depression.[17] Symptoms similar to those associated with panic attacks during sleep may be found in patients with arrhythmia, gastroesophageal reflux, sleep apnea, night terrors or REM

sleep behavioral disorders.[10] All of these factors have to be taken into consideration in the differential diagnostic evaluation.

Maybe the most important complication of nocturnal panic attacks is chronic sleep deprivation.[5,16] In fact, patients with this complication develop anticipation anxiety and avoidance behavior, as seen in daytime attacks. In the specific case of sleep panic attacks, many patients develop a fear of sleep and are reluctant to sleep.

1) Polysomnographic findings

When compared with control individuals, patients with panic disorder present slightly increased sleep latency and reduced sleep efficiency.[5,16] There is an increase in time of movement during sleep, but there is no temporal relationship between moving and nocturnal panic attacks.[18] Sleep panic attacks generally take place at the end of stage 2 or onset of stage 3 of REM sleep.[5,10,16]

3. Post-traumatic stress disorder

The main sleep-related complaints in patients with post-traumatic stress disorder are insomnia and awakening due to anxiety or nightmares. It is common to find a state of autonomic hyperactivity, characterized by hypervigilance and insomnia.[5,10,16] Frequent nightmares are reported by 59% to 68% of patients and are a marker for this disease, involving relived experiences as well as imaginary scenarios with frightening or life-threatening content.[5,10,16] Awakening due to anxiety seems, in turn, to be more related to REM sleep.[5,16]

1) Polysomnographic findings

Post-traumatic stress disorder has been associated with increased sleep latency, decreased sleep efficiency, increase in time awake after sleep onset, reduction in total sleep time, decreased stage 2 sleep and increased stage 1 NREM sleep (sleep that is more superficial).[5,10,16] There is considerable controversy regarding the effects of post-traumatic stress disorder on REM sleep. Some authors report normal REM parameters, whereas others relate decreased latency of REM sleep and increased REM density.[1,10,16]

Schizophrenia

Although sleep disorders in schizophrenia are sufficiently severe to warrant clinical attention, they are seldom the predominant complaint.[19] In a state of psychotic agitation, there are prolonged periods of total sleeplessness; and when agitation subsides, expressive insomnia takes its place.[20] There are reports of near total inversion of the wake-sleep cycle, a situation in which the patient sleeps during the day and remains awake at night.[20] Severe insomnia is also described in exacerbations of the schizophrenic profile and might precede the onset of other symptoms during relapse.[19,20] Schizophrenic patients may experience terrifying hypnagogic hallucinations and nightmares.[20] These may be accompanied by several primary sleep disorders, such as poor sleep hygiene and increased periodic lower limb movements.[20] When present, sleep apnea comorbidity may aggravate schizophrenic symptoms.[10]

Various studies have related schizophrenia to specific polysomnographic findings, as we shall discuss herein. Slow-wave sleep, as well as sleep maintenance, seems to be inversely related to the size of the cerebral ventricles. It is suggested that decreased slow-wave sleep and increased schizophrenic negative symptoms may be related to reduced brain metabolism and accelerated ageing or brain atrophy.[21]

The first attempt to establish a connection between REM sleep abnormalities and schizophrenia was related by Dement, in 1955.[22] The study was carried out before the advent of the neuroleptics, and the author found decreased REM sleep latency but did not observe any difference in its density in schizophrenics.[22] Several studies followed, with distinct findings in REM parameters.[1,10,20] This variation may be explained by the different stages of the disease, by the imbalance of neurotransmitters and by the use of short- and long-term medication.[10] Despite these conflicts, the similarity between the hallucinatory activity that normally occurs in REM sleep and the hallucinations found in schizophrenia continue to intrigue researchers, and several theories have been suggested in the attempt to explain this similarity.[10,20]

1) Polysomnographic findings

Sleep continuity disturbance, decreased slow-wave sleep, decreased REM latency, increased REM percentage and decreased amount of time in NREM sleep (in minutes) have been observed.[1,10,19-20] Atypical antipsychotics such as olanzapine, risperidone and clozapine significantly increase total sleep time and stage 2 sleep. In addition, olanzapine and risperidone increase slow-wave sleep.[19] Typical antipsychotics such as haloperidol, thiothixene and flupentixol significantly decrease stage 2 sleep and increase sleep efficiency.[19]

Alcoholism

Among the general population, alcohol is probably the most commonly used sleep-inducing substance.[23] Acute administration of alcohol to normal volunteers before bedtime tends to curtail sleep latency, increase NREM sleep and decrease REM sleep within the first hours after intake.[23] However, alcohol is quickly metabolized. Within four to five hours after intake there is a decrease in concentration in the blood and the individual may present sleep interrupted by gastric irritation, headache, nightmares, tachycardia and profuse sweating. There may also be REM sleep rebound.[23]

Alcoholic patients generally report insomnia, hypersomnia, disruption of circadian rhythms and parasomnias. Alcohol withdrawal symptoms may be confused with those related to panic attacks, and the differential diagnosis must be carried out.[24]

Alcohol increases the probability of snoring, respiratory resistance and the occurrence of apneic episodes, even in the individuals with no history of sleep apnea or snoring.[23]

1) Polysomnographic findings

Polysomnographic findings include increased sleep latency and decreased sleep efficiency, as well as a reduction in total sleep time, slow-wave sleep and REM sleep.[23] Alcohol inhibits REM sleep in a dose-dependent way, even in the presence of physiological REM sleep debt, such as sleep deprivation.[25]

Dementias

Dementias are not homogeneous regarding sleep. However, in dementia with Lewy bodies and frontotemporal dementia there is also a deficit in cholinergic transmission, with a consequent reduction in the percentage of REM sleep, similar to that seen in Alzheimer's disease.[26] A peculiarity of dementia with Lewy bodies is that it presents a higher frequency of REM sleep behavior disorder. This occurs because, in this dementia, there is an early onset of the loss of cholinergic neurons in the magnocellular part of the pontine reticular nucleus, damaging the excitatory connection between this nucleus and the locus coeruleus, which is responsible for the atony in REM sleep.[26]

In vascular dementia, sleep alterations are quite heterogeneous, depending on the distribution of the cortical

and subcortical lesions, but there is an important reduction in the percentage of slow-wave sleep.[27] However, more in-depth studies of sleep in dementias other than Alzheimer's are needed.

1. Alzheimer's disease

Alzheimer's disease is the most studied of all dementias. Many of the sleep dysfunctions present in normal ageing also occur in the patient with this disease, but with more intensity. In view of this, there is a reduction in total sleep time and in sleep efficiency,[28] as well as advanced sleep phase (trending toward early sleep onset and early awakening),[29] lower amplitude of circadian cycles (such as hormonal secretion, activity and temperature),[30-31] reduction in slow-wave sleep (stages 3 and 4), reduction in REM sleep and increased stage 1 sleep.[28,32] In addition, patients with Alzheimer's present episodes of nighttime agitation, hypnagogic hallucinations and aimless sleepwalking.[33]

Some of the dysfunctions present in Alzheimer's disease may be attributed to the growing disruption of circadian cycles, possibly accompanied by atrophy of the suprachiasmatic nucleus.[34] This disruption increases in parallel with disease severity.[35] It has also been observed that the lack of a rhythmic pattern in the secretion of melatonin affects the sleep of these patients, and that the administration of exogenous melatonin, or the stimulation of its production through morning phototherapy, help correct it partially.[36] In Alzheimer's disease, dysfunctions that affect REM sleep are especially important due to their physiopathology since one of the most affected structures at the onset of Alzheimer's is precisely a cholinergic nucleus involved in cortical activity during this stage, the basal nucleus of Meynert.[37] Therefore, it has been speculated that the relationship between REM sleep and Alzheimer's is functional since REM sleep is related to learning processes, severely impaired by this disease.[37] In fact, when patients are given drugs that enhance cholinergic conduction, there is an increase in the percentage of REM sleep, as well as an improvement in cognition.[38]

1) Polysomnographic findings

As previously discussed, polysomnographic findings include a significant reduction in the percentage of REM sleep, lower frequency of rapid eye movements during REM sleep (decreased REM density) and decreased sleep efficiency due to the increase in the number of awakenings after sleep onset.[28] A decrease in the basal rhythm has been observed in the spectral analysis of electroencephalogram during REM sleep.[39] According to some authors, the decrease in the basal rhythm of REM sleep in the spectral analysis is a sensitive marker for differentiating Alzheimer's disease from normal aging.[40] The presence of diffuse delta and theta rhythms is also noticed, in both sleep and wake, with general slowing on electroencephalogram in frontal and temporal abnormalities.[28,38]

In the elderly, depression can simulate Alzheimer's disease. However, in depression, the polysomnographic profile indicates cholinergic hyperactivity, with increase in percentage and reduction of latency of REM sleep.[41]

Sleep in children and adolescents and sleep dysfunctions in the most frequent psychiatric disorders

Sleep, seen in its various aspects, suffers modifications over the individual's life and these are more significant in the first years of life. A baby, right after birth, sleeps approximately 16 to 20 hours a day, whereas a two-year-old child sleeps approximately 12 hours.[42] In pre-adolescence, the waking period is at a maximum, and the need for a daily nap is very rare. The lack of daily sleepiness may disguise primary sleep dysfunctions such as sleep apnea and narcolepsy. During puberty, there is an increase in daily sleepiness, as assessed through the multiple sleep latency test, possibly accompanied by an increased need for sleep. Whether there is alteration of the biological (circadian) clock has been questioned, although some authors suggest that there is a trend toward a delay in its phase.[43-46]

The most frequent psychiatric disorders that may affect sleep in children and adolescents are depression, anxiety, and attention deficit hyperactivity disorder (ADHD). The anxiety profiles present sleep complaints and polysomnographic findings similar to those of adults. However, the occurrence of multiple awakenings during the night is relevant, when the patient reports a sensation of fear and imminent danger.[47]

1. Childhood depression

The symptoms of childhood depression are similar to those observed in the adult population, although with some peculiarities such as exaggerated fears and refusal to go to school.[48] It has been shown that, among children presenting altered sleep patterns, 75% complain of insomnia, and 25% report excessive sleepiness.[45] Those with insomnia mainly complain of difficulty in initiating sleep and have the impression that their sleep is superficial and of poor quality, consequently experiencing difficulty in waking up early to go to school, together with daytime tiredness.[45]

1) Polysomnographic findings

Findings have been inconsistent and hardly specific: in childhood (Tanner stages 1 and 2), there is increased sleep latency and decreased latency for the first episode of REM sleep. In adolescents (Tanner stages 3, 4 and 5), in addition to these findings, there is increased REM density.[47]

2. Attention deficit hyperactivity disorder

Children with ADHD complain of difficulty in waking up in the morning (perhaps due to sleeping too little), fragmented sleep, poor quality sleep and increased movement during sleep. It has been observed that children with obstructive sleep apnea syndrome, with periodic limb movements or narcolepsy, present more ADHD-related symptoms.[49]

1) Polysomnographic findings

In ADHD, increased physical activity during sleep, increased frequency of periodic limb movements and reduction in REM sleep have been observed.[49]

The treatment of ADHD, combined with careful orientation regarding appropriate sleep rhythm, has proven effective. Patients, when untreated, can present increased daytime sleepiness (observed in the multiple sleep latency test). Nevertheless, re-assessment of the treatment with stimulants - better scheduling, reduction of total dosage, etc - when carried out, propitiates better quality sleep and a consequent improvement in daytime behavior.[49]

Final considerations

The sleep alterations most frequently observed in most psychiatric disorders refer to difficulty in initiating sleep (initial insomnia), difficulty in maintaining sleep (middle insomnia), poor quality sleep and interrupted sleep. Terminal insomnia or early awakening is more often related to depressive profiles.

In describing polysomnographic findings in psychiatric patients, we principally observe significant reductions in sleep efficiency and total sleep time, which are consequences of the reduction of NREM sleep. In affective disorders, the

percentage of REM sleep is increased. Reduction of REM sleep latency is principally described for depression but may occur in other pathologies. Although no specific finding is pathognomonic, patterns of sleep dysfunction have been observed in certain psychiatric disorders. Even though a specific psychiatric diagnosis cannot be made based on polysomnographic data alone, sleep studies can help answer specific questions such as how to differentiate depression from dementia in the elderly.

There may still be a strong correlation between psychiatric disorders and primary sleep disorders. Therefore, patients with sleep apnea or narcolepsy seem to present high levels of anxiety, depression and alcoholism. More relevant still is the direct relation between poor sleep hygiene and various other psychiatric profiles. This relationship must be taken into consideration by psychiatrists in clinical practice since instructing patients in sleep hygiene can reduce the amount of medication administered, improving symptomatology and patient quality of life.

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