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Sleep and wake disturbances following traumatic brain injury

Perturbations du sommeil et de l'éveil à la suite d'un traumatisme craniocérébral

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ABSTRACT

Traumatic brain injury (TBI) is a major health concern in industrialised countries. Sleep and wake disturbances are among the most persistent and disabling sequelae after TBI. Yet, despite the widespread complaints of post-TBI sleep and wake disturbances, studies on their etiology, pathophysiology, and treatments remain inconclusive. This narrative review aims to summarise the current state of knowledge regarding the nature of sleep and wake disturbances following TBI, both subjective and objective, spanning all levels of severity and phases post-injury. A second goal is to outline the various causes of post-TBI sleep-wake disturbances. Globally, although sleep-wake complaints are reported in all studies and across all levels of severity, consensus regarding the objective nature of these disturbances is not unanimous and varies widely across studies. In order to optimise recovery in TBI survivors, further studies are required to shed light on the complexity and heterogeneity of post-TBI sleep and wake disturbances, and to fully grasp the best timing and approach for intervention.

Mots clés :
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RÉSUMÉ

L'occurrence d'un traumatisme craniocérébral (TCC) est un problème de santé publique majeure. Les troubles du sommeil et de l'éveil sont parmi les symptômes les plus persistants et les plus déshabilitants à la suite d'un TCC. Or, les études empiriques portant sur l'apparition de ces symptômes, leur chronicisation et leur traitement demeurent non concluantes. Cette revue narrative a comme but de recenser le niveau de connaissance actuel sur la nature (objective et subjective) des troubles du sommeil et de l'éveil chez les patients TCC, en tenant compte de la sévérité du traumatisme et de la phase de rétablissement. Un but secondaire est de cibler les causes potentielles de ses perturbations. En général, bien que la présence de troubles du sommeil et de l'éveil dans toutes les études conduites auprès de patients TCC soit observée indépendamment de la sévérité du traumatisme, des signes objectivables de la présence de telles perturbations ne sont pas rapportés de façon consistante dans ces études. Des études supplémentaires semblent être requises afin de mieux comprendre la complexité des troubles du sommeil et de l'éveil chez les patients TCC et d'optimiser la récupération à court et à long terme chez cette clientèle par l'entremise d'interventions ciblées.

1. Introduction

Traumatic brain injury (TBI) is the leading cause of mortality and invalidity among young adults in industrialized countries, with an incidence estimated at over 600 per 100,000 individuals [1,2]. This high incidence represents a major public health concern since TBI often results in long-term physical, cognitive and psychological sequelae that interfere with general functioning and return to work or school.

Sleep-wake disturbances, particularly fatigue, insomnia and hypersomnia, are among the most prevalent and persistent sequelae reported after TBI [3,4]. They have been consistently

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reported among TBI survivors across all levels of severity, from the acute stage to several years post-injury [5–7]. Yet, the pathophysiology of post-traumatic sleep-wake disturbances is still poorly understood.

The purpose of this narrative review is to describe and appraise the current state of knowledge regarding sleep-wake disturbances following TBI across all levels of severity, spanning the continuum of recovery from the acute stage (first weeks post-injury) to the chronic stage, including years post-injury. A second goal is also to describe the possible causes of sleep-wake disturbances following TBI, as well as pharmacologic and non-pharmacologic treatment options for the management of sleep-wake disturbances post-injury. Finally, the importance of sleep for cognitive and functional recovery will be discussed, and general directions for future study perspectives will be provided.

For the purpose of this literature review, the acute phase of TBI refers to the first 6 months post-injury, which constitutes the period immediately following TBI and the early phase of recovery. The chronic phase of TBI will refer to the period following the acute phase, spanning from 6 months to several years post-injury, regardless of the presence of symptoms.

2. Diagnosis and general consequences of TBI

Traumatic brain injury occurs when an external force causes an alteration in brain functions such as decreased level of consciousness, loss of memory, neurological deficits or any alteration in mental state at the time of the injury [8]. The diagnosis of TBI necessarily involves a severity assessment [9]. Globally, mild TBI (mTBI) is characterized by a short loss of consciousness ($<$ 30 min), and/or a short post-traumatic amnesia (PTA) ($<$ 24 h), a Glasgow Coma Scale (GCS) score [10] between 13 and 15 [1]. Sports-related brain injuries with an alteration in mental state are generally referred to as "concussion". Moderate and severe TBI are typically associated with a longer loss of consciousness, a GCS score equal or lower than 12, and PTA longer than 24 h. No hospital admission is generally required for mTBI, while moderate and severe TBI often necessitate hospitalisation in the intensive care unit (ICU) due to the presence of cerebral haemorrhages, contusions and intracranial hypertension [11].

The most frequent causes of TBI are motor-vehicle accidents, falls, assault, recreational and sport-related injuries, and work accidents [12,13]. The principal factors known to increase the risk of sustaining a TBI are age (15–24 years old) and gender (male); other factors are alcohol or drug addiction, low socioeconomic status, and low education [14].

The extent of functional and cognitive deficits observed in the acute period is highly variable among TBI patients and depends on several factors, such as location of focal brain lesions [15,16], severity of diffuse axonal injury, length of PTA [15,17], age [16,18], education [16], and preexisting conditions [19]. Despite the variability of deficits, they can be categorized in relation to their influence on cognition, social behaviors, psychological status, and somatic symptoms.

Arousal and alertness impairments, reduced information processing speed, impaired memory, executive dysfunctions, impaired communication, and reduced self-awareness are among the most frequent cognitive deficits observed [20]. Neurobehavioral impairments such as impulsivity, irritability, disinhibition, mutism, confused and confabulatory communication, and apathy can be observed, particularly in those with more severe injuries and or in the acute stage of injury [21]. Psychological sequelae, such as irritability, anxiety, and depressed mood can be observed in $\geq$ 50% of individuals in the first 6 months following TBI [22]. These affective symptoms remain prevalent among 16–48% of patients over the two years post-injury, and are reported many years post-injury ($>$ 10 years) in those with chronic sleep-wake disorders [23]. Finally, somatic symptoms, such as headache, dizziness, and perturbation in sleep are often reported in the hours following TBI [22], and these symptoms remain present in 23–65% of patients two years after TBI.

Recovery from symptoms usually takes place within 1 to 3 months in mTBI, while 85% of improvements in functioning occur in the first six months and continue until one year after moderate to severe TBI [24]. Unfortunately, these impairments, including in those related to sleep disturbances, persist over one year in 50% of moderate-severe TBI patients [25], affecting their autonomy, productivity, and their quality of life [26].

3. Sleep disturbances following TBI

3.1. Changes in sleep quality and quantity

Complaints of sleep loss and poor sleep quality are common following TBI. These comprise complaints of difficulties initiating and maintaining sleep, frequent arousals, and early awakenings. In the following section, prevalence of poor sleep quality and related polysomnographic (PSG) findings will be described for mTBI and for the moderate-severe TBI population separately. For each TBI severity populations, results for the acute and chronic phases will be reported.

3.1.1. Acute stage of mTBI

According to Chaput et al. [27], sleep complaints are present in the first days and weeks following mTBI. In fact, 13.3% of the 443 patients included in their study reported sleep complaints on the Rivermead post-concussion symptom assessment questionnaire 10 days post-injury, while this proportion increased to 33.5% at 6 weeks post-injury. Interestingly, patients with sleep complaints at 10 days post-injury were 2.9 times more likely to experience sleep difficulties at 6 weeks post-injury and were more likely to suffer from irritability, depressive symptoms, and headaches at both 10 days and 6 weeks post-injury, suggesting that acute sleep complaints predict psychological and somatic symptoms among individuals with mTBI. Poor sleep quality was also reported after sports-related concussions where athletes who had suffered at least one concussion (4.4 $\pm$ 3.8 months since injury) complained of worst sleep quality, more severe sleep disturbances and poorer daytime functioning on the Pittsburgh Sleep Quality Index when compared with healthy control athletes [28].

Although a high proportion of patients have sleep complaints in the acute phase of their mTBI, heterogeneous results were obtained on objective measures of sleep such as PSG. In fact, several authors found no differences in sleep macroarchitecture between mTBI patients and controls in the acute stage of the injury [28–30].

Conversely, studies looking at sleep microarchitecture have found promising results. In fact, Rao et al. [29] showed that mTBI patients within 1 week of injury had abnormalities in sleep EEG power spectral analyses when compared to matched controls. More specifically, mTBI patients had lower delta power, but higher alpha and beta power in non-rapid eye movement (NREM) sleep. A more recent study conducted by Khoury et al. [31] compared 24 mTBI patients (45 $\pm$ 22.7 days post-injury) with post-traumatic sleep complaints to 18 controls on quantitative EEG during sleep. Overall, results showed that patients reported a worse sleep quality for their in-laboratory sleep recording compared with control subjects. Moreover, mTBI patients had significantly longer sleep