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Editorial

Sleep and wakefulness processes in moderate to severe chronic traumatic brain injury are related to global trauma and intake of psychoactive medications

Adding to the large number of factors and potential mechanisms underlying changes in the regular maintenance of sleep and wakefulness after moderate to severe traumatic brain injury (TBI) [1–4]; a recent study published in this issue of Sleep Medicine specifically highlights three. They are acute global injury severity score, but not severity of the brain injury itself (as measured by duration of post-traumatic amnesia and Glasgow Coma Scale score), duration of hospital stay, and psychoactive medication intake at the time of assessment [5].

This study [5], led by El-Khatib and Gosselin at the Hôpital du Sacré-Cœur de Montréal (QC, Canada), featured 34 participants with moderate to severe TBI in the chronic stage post injury, of which 38% were taking psychoactive medications (initiated after the injury), as well as 34 healthy, age-, sex-, and relationship status-matched controls. To measure sleep and wakefulness patterns, all participants wore an actigraph device (Philips Respironics, Andover, MA) on their non-dominant wrist for seven consecutive days. In addition, participants completed a sleep diary; which included information on sleep schedules (bedtime and wake time) for nighttime sleep and daytime naps, daily medication intake and doses, and the need to wake-up in the morning to fulfill personal responsibilities. Researchers reported that, compared to controls, persons with TBI had earlier bedtimes, longer time spent in bed during the nighttime, and more frequent daytime naps. Thus, they accrued more sleep time over a 24 h period when all sleep episodes were considered. Furthermore, nocturnal sleep duration, number of naps, and time spent in bed over 24 h were significantly higher in medicated participants with TBI when compared to both non-medicated counterparts and healthy controls. The significance was that, despite equivalent sleep efficiency to healthy controls, and longer sleep duration over the course of 24 h, persons with TBI reported more severe daytime sleepiness, fatigue, and poorer sleep quality.

The Injury Severity Score (ISS), an anatomical scoring system that provides an overall score for patients with multiple injuries within six body regions (head, face, chest, abdomen, extremities (including pelvis), and external) [6], has been linked to mortality, morbidity, hospital stay, and long-term employability after TBI [7–9]. El-Khatib et al.'s study is the first to highlight the relationship between ISS, measured early after the injury and documented in patients' medical files, sleep (duration and phasic distribution over 24 h cycle), and wakefulness (fatigue and daytime sleepiness) months after the TBI. While the pathophysiological mechanisms underlying the relationships were not investigated, severe trauma has been shown to trigger a systemic inflammatory response that can contribute to secondary bodily organ and systems complications [10,11], and can manifest in disturbed sleep architecture in the chronic phase post injury [12].

The medication effect highlighted in the study [5] requires special attention. El- Khatib et al., commented “The use of psychoactive medication is rarely accounted for in TBI research on sleep”. They investigated daytime complaints, sleep duration, and napping behaviour in light of psychoactive medication intake. Five out of 13 persons with TBI were taking a single psychoactive medication over the course of the study, while the rest were taking a combination of medications. The discussion of medication effects in the study was limited to simple binary associations with outcomes of interest, and the dose–response effect, timing of administration, and the expectations that the persons with TBI had about the consequences of taking medications on sleep and wakefulness, highly relevant to the topic of sleep quantity and distribution, quality, and continuity over the 24 h cycle, were not investigated. Nevertheless, the reported results support the basic principle of neuropharmacology with respect to psychoactive medications that act on different brain and body targets simultaneously and therefore can have a plethora of effects on function and behaviour [13]. While the effects of psychoactive medications on sleep as reported in the study provides insight into the possible sites of action of these medications within the brain (ie, medications' ability to alter activity in the reticular activating system and thereby affect sleep), important questions concerning the patients’ compliance with their prescribed medication regime and timing of administration, as well as the potential effects on the results, remain and preclude a formation of a definitive conclusion. Such information is of great importance as removal of the psychoactive medication from the brain, as result of non-compliance or improper uptake, is expected to cause biological and behavioural changes that are opposite to those produced by the medication [13]. Likewise, long-term use of medications that cross the blood–brain barrier could lead to changes in receptors and ion channel functions, signal transduction, synaptic reorganization, and alter pathways in sleep and wakefulness [14,15].

The balance of sleep and wakefulness in moderate to severe TBI is subject to physiological processes modulated by the extent of global trauma, and external influences such as the intake of medications to support the injured brain by producing or suppressing cortical activation. Therefore, figuring out a way to correct neurochemical imbalances stemming from brain injury [16,17], while being mindful of how medications impact the processes initiated by severe trauma, is timely.

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Conflict of interest

Tatyana Mollayeva has no conflict of interest to disclose.

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