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COMMENTARY

Why sleep matters after traumatic brain injury

Commentary on Castriotta RJ, Wilde MC, Lai JM, Atanasov S, Masel BE, Kuna ST. Prevalence and consequences of sleep disorders in traumatic brain injury. *J Clin Sleep Med.* 2007;3(4):349–356. doi:10.5664/jcsm.26855

Emerson M. Wickwire, PhD, FAASM

Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland; Sleep Disorders Center, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland

By any measure, traumatic brain injury (TBI) is a major public health concern. Each year in the United States, more than 2.5 million Americans experience a TBI.[1] TBI has been identified as a signature injury of the armed conflicts in Iraq and Afghanistan, impacting > 380,000 military service members and veterans.[2,3] In civilian and military samples of patients, the majority of TBIs are classified as mild (defined as a Glasgow Coma Scale score of 13–15 with normal imaging), and most sequelae resolve within 3 months after injury.[1] However, for an important minority of individuals, symptoms including poor cognitive function, fatigue, depressed mood, posttraumatic stress, chronic pain, diminished quality of life, and difficulties performing activities of daily living can persist for months and years. For mild TBI alone, the estimated health care costs exceed $23.2 billion per year ($16.7 billion in 2003 U.S. dollars[4]). Further, despite dozens of clinical trials, no effective TBI treatments have been identified, and clinical guidelines are lacking.

Notably, insufficient and disturbed sleep and circadian dysregulation are among the most common self-reported complaints after TBI.[5,6] Approximately half (range, 30%–85%) of individuals who have experienced a TBI report sleep disturbances.[7] In addition to self-reported complaints, relative to non-TBI control patients, those patients with a TBI show differences in objective sleep architecture[8] and alterations in melatonin secretion.[9] More important, data from laboratory studies among animals and clinical, epidemiological, and experimental studies among humans suggests that poor sleep can precede, exacerbate, or prolong many of the most common sequelae of TBI.[5,6] Further, poor sleep and TBI share neurological underpinnings that may impair glymphatic function,[10] reduce neurotoxin clearance, and accelerate neurodegeneration.

As a result, the past decade has seen an explosion of research and clinical interest in sleep after TBI. Indeed, insufficient and disturbed sleep have been identified as modifiable treatment targets to enhance outcomes after TBI. Because sleep-related treatments can improve many of the adverse outcomes of TBI, such as depression, posttraumatic stress disorder, and diminished quality of life, TBI researchers and clinicians alike have sought to advance understanding and leverage enhanced sleep to improve TBI outcomes.

In 2007, 2 years after the inception of the *Journal of Clinical Sleep Medicine,* Castriotta and colleagues[11] published a seminal article on sleep disorders after TBI in this journal. Their study is notable for several reasons. To begin with, the authors recruited prospective patients with a TBI (n = 87) from rehabilitation departments at 3 academic medical centers with level 1 trauma centers and sleep disorders centers. Given the heterogeneity of TBI, such multisite recruitment strategies are needed to ensure sufficiently large samples of TBI participants.[12] Participants completed overnight polysomnography and a daytime Multiple Sleep Latency Test, completed standardized questionnaires and neurocognitive assessment, and underwent clinical evaluation with a sleep specialist. All participants were at least 3 months post-TBI, ensuring that all sequelae could be considered chronic. Thus, their study provides insight into multiple measures of objective, self-reported, and clinical aspects of sleep in a typical sample of patients with TBI.

Forty-six percent of individuals in Castriotta et al[11] were diagnosed with a sleep disorder, including OSA (23%), posttraumatic hypersomnia (11%), narcolepsy (6%), and periodic limb movement disorder (7%). Compared to rates among the general population, these prevalence rates were notably high. In particular, the rates of hypersomnolence were elevated and raise important questions about sleep/wake characteristics after TBI.[13] Indeed, the study found 1 in 4 (25%) participants to be sleepy (ie, mean sleep latency < 5 minutes), and sleepiness was associated with worsened cognitive outcomes in domains directly relevant to TBI. Relative to patients with TBI who were not sleepy (mean sleep latency > 10 minutes), individuals who were sleepy performed worse on 2 outcomes of the psychomotor vigilance task (fastest reaction time and lapses, both $P < .05$), and a nearly significant trend was observed ($P = .05$) for differences in mean reaction time. Of course, even at the time of publication, it was perhaps not surprising that sleepiness was associated with poor cognitive performance.

The most important and novel finding from this study, then published for the first time, is that sleep disorders are associated with worsened cognitive performance after TBI. Relative to patients with TBI without sleep disorders, individuals with sleep disorders showed lower fastest reaction times, slower overall reaction times, and more mental errors (lapses) on the psychomotor vigilance task (all $P < .05$).[11] Cognition is a key TBI outcome and is associated with multiple aspects of TBI

rehabilitation, including disability and difficulty completing activities of daily living. Thus, the importance of this discovery cannot be overstated; the findings of Castriotta and colleagues[11] included TBI in the very long list of medical, psychiatric, and neurodegenerative disease states that are demonstrably worsened by comorbid sleep disorders. Additional strengths of their study include self-reported and objective measures of sleep and cognitive functioning, attempts to characterize the cause of TBI, and efforts to control for time since injury.

At the same time, the study by Castriotta and colleagues[11] is not without limitations. For example, although the study provides important insight into the prevalence and consequences of sleep disorders after TBI, this cross-sectional design does not provide insight into changes over time. Missing data were common, and many statistical tests were performed without adjustment for multiple comparisons. Other missed opportunities were that neither injury severity nor history of multiple TBIs was consistently documented, and both have been associated with adverse outcomes post TBI.

The study by Castriotta and colleagues[11] is among the most highly referenced articles ever published in the *Journal of Clinical Sleep Medicine*. Indeed, excepting scoring reviews, clinical guidelines, and other American Academy of Sleep Medicine–related publications, the study by Castriotta and colleagues[11] has arguably had a greater scientific impact than all but a very few empirical articles in the 15-year history of the journal.

Finally, in terms of the advancement of the field of sleep medicine, this study is important because it highlights an important role for sleep and sleep disorders in a key outcome (cognition) that matters not only to sleep specialists but also to a constituency group of TBI professionals. For sleep medicine to realize its full potential, professionals in the field must improve our ability to adopt multiple perspectives and emphasize outcomes that matter to those whom we serve.[14]

TBI represents a major public health concern in the United States and worldwide. Effective treatments have not yet been identified, and clinical guidelines are lacking. It is thus especially important that insufficient and disturbed sleep are among the most common complaints after TBI and have been identified as modifiable treatment targets to enhance outcomes after TBI. To realize this vision, several steps will be required.[5,6] First, serial assessment of sleep after TBI is necessary to understand the natural history of sleep and sleep disturbances post TBI and how changes in sleep impact changes in TBI symptoms. Second, to advance precision medicine initiatives, it is necessary to identify which individuals are at greatest risk of developing sleep and circadian disorders post TBI and when to intervene to optimize outcomes. Given the heterogeneity of TBI, this project will require large, well-characterized samples of individuals with TBI, including the serial assessment of clinical characteristics, neuroimaging findings, sleep, and TBI outcomes. Finally, there is a dramatic need to adapt, tailor, refine, and test sleep-focused treatments among individuals with TBI. Given the lack of sleep specialty care in most TBI centers, telehealth and remote monitoring are likely to increase access to care and help ensure accurate outcome assessment. Our group and others are currently pursuing such initiatives, thus building upon the seminal findings of Castriotta and colleagues.

CITATION

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Address correspondence to: Emerson M. Wickwire, PhD, FAASM, University of Maryland School of Medicine, Baltimore, MD; Tel: (410) 706-4771; Email: ewickwire@som.umaryland.edu

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