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ORIGINAL ARTICLE

Prospective Evaluation of the Nature, Course, and Impact of Acute Sleep Abnormality After Traumatic Brain Injury

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Abstract

Objective: To prospectively characterize the prevalence, course, and impact of acute sleep abnormality among traumatic brain injury (TBI) neurorehabilitation admissions.

Design: Prospective observational study.

Setting: Freestanding rehabilitation hospital.

Participants: Primarily severe TBI (median emergency department Glasgow Coma Scale [GCS] score = 7; N = 205) patients who were mostly men (71%) and white (68%) were evaluated during acute neurorehabilitation.

Interventions: None.

Main Outcome Measure: Delirium Rating Scale-Revised-98 (DelRS-R98) was administered weekly throughout rehabilitation hospitalization. DelRS-R98 item 1 was used to classify severity of sleep-wake cycle disturbance (SWCD) as none, mild, moderate, or severe. SWCD ratings were analyzed both serially and at 1 month postinjury.

Results: For the entire sample, 66% (mild to severe) had SWCD at 1 month postinjury. The course of the SWCD using a subset (n = 152) revealed that 84% had SWCD on rehabilitation admission, with 63% having moderate to severe ratings (median, 24d postinjury). By the third serial exam (median, 35d postinjury), 59% remained with SWCD, and 28% had moderate to severe ratings. Using general linear modeling and adjusting for age, emergency department GCS score, and days postinjury, presence of moderate to severe SWCD at 1 month postinjury made significant contributions in predicting duration of posttraumatic amnesia ($P<.01$) and rehabilitation hospital length of stay ($P<.01$).

Conclusions: Results suggest that sleep abnormalities after TBI are prevalent and decrease over time. However, a high percent remained with SWCD throughout the course of rehabilitation intervention. Given the brevity of inpatient neurorehabilitation, future studies may explore targeting SWCD to improve early outcomes, such as cognitive functioning and economic impact, after TBI.

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While sleep has been intensively investigated for decades, the actual purposes and mechanisms underlying sleep are still not fully understood. Healthy subjects experience cognitive impairment, behavioral changes, and emotional lability with disrupted sleep or disruption of the 24-hour sleep-wake cycle pattern.[1,2] Specific impairments include attentional abnormalities, cognitive performance variability/fluctuation, impaired judgment, and emotional reactivity.[3-8] Impairments resolve once normative sleep is restored.[9,10] However, chronic sleep dysfunction can result in

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persistent impairments in cognition, behavior, and emotional functioning.[3-8]

Sleep disturbance in traumatic brain injury: While 10% to 17% of the normative population experience sleep disturbance, the reported prevalence of sleep disturbance after traumatic brain injury (TBI) is significantly higher (46%−100%) among the small samples studied.[11-18] Prevalence rates of sleep disturbance have varied because of measurement methodology, type of sleep disturbance being studied, interval from injury to assessment, and patient's cognitive ability to self-report sleep difficulties.[18-23] Despite the high prevalence of sleep disturbance after TBI, the mechanisms leading to it are poorly understood. One possibility is the occurrence of focal lesions in sleep-wake control regions, such as the hypothalamus and brainstem, because of TBI.[24-26]

Most studies of the relations between sleep and TBI have examined subjects who were able to respond to paper and pencil testing in addition to objective sleep measurement in postacute phases of recovery.[20-26] Sleep assessments in acute neurorehabilitation settings have largely relied on clinician ratings on a nominal or ordinal scale based on staff observations or reports.[14,16-18] The lack of self-report measures of sleep is expected given that patients with altered consciousness, including posttraumatic confusion, are unable to report problems with sleep.

Sleep and neuroplasticity: Animal and human studies have shown that sleep-wake cycle disturbances (SWCDs) or sleep deprivation may alter neurotransmitters and receptor systems, neuronal activation, related signaling molecules, as well as cognition and behavior.[27-30] Data from clinical populations with focal lesions (ie, stroke) suggest a modulating role of sleep in recovery processes and neuroplasticity. Studies of stroke populations found that 20% to 40% of participants had SWCDs.[31] Those with SWCDs had worse outcomes, including cognition and psychiatric disturbances.[32,33] The duration of slow-wave sleep, rapid eye movement, and sleep efficiency have been found to correlate with cognitive outcome among neurologic patients in both acute and chronic stages of recovery.[34]

Recently, Zunzunegui et al[35] demonstrated the moderating effects of sleep on several endogenous brain repair mechanisms in an animal model. After lesion placement, an experimental group was deprived of sleep during recovery and performed significantly worse on behavioral tasks (inferring cognition/memory) compared with a control group allowed to sleep during recovery. After autopsy, the experimental group (deprived of sleep) demonstrated significantly lower amounts of pathophysiologic indices of brain repair, including axonal sprouting, synaptogenesis, and vasogenesis compared with the control group.[35]

List of abbreviations:

DelRS-R98	**Delirium Rating Scale-Revised-98**
DPI	**days postinjury**
ED	**emergency department**
EEG	**electroencephalogram**
GCS	**Glasgow Coma Scale**
GLM	**general linear model**
GOAT	**Galveston Orientation and Amnesia Test**
LOS	**length of stay**
PTA	**posttraumatic amnesia**
SWCD	**sleep-wake cycle disturbance**
TBI	**traumatic brain injury**

Human investigations of acute sleep abnormalities have been small studies that do not characterize the nature and course of early sleep disturbance. Given the role of sleep in promoting neuroplastic mechanisms, this study proposes to (1) characterize the prevalence and nature of acute sleep abnormality in a large consecutive series of TBI inpatients, (2) characterize the course of acute sleep abnormality in a large consecutive series of TBI patients, and (3) evaluate differences in cognition and rehabilitation course for those with greater sleep abnormality at 1 month postinjury.

Methods

Participants

The study population was comprised of all TBI Model Systems participants admitted to a freestanding neurorehabilitation hospital from January 1999 through December 2003 and approved by the local institutional review board. Criteria for the National Institute on Disability and Rehabilitation Research TBI Model Systems program includes: (1) medically documented TBI; (2) treatment at an affiliated level I trauma center within 24 hours of injury; (3) receipt of inpatient rehabilitation within the TBI Model Systems; (4) admission to inpatient rehabilitation within 72 hours of discharge from acute care; (5) aged at least 16 years at the time of injury; and (6) provision of informed consent by the person with injury or a legal proxy.[36] Because these data came from another study examining acute confusion phenomenology and late outcome, additional exclusion criteria included (1) diagnosis of a minimally conscious state[37] or vegetative state at 1 month postinjury and (2) severe premorbid neurologic disorder.

Measures

Delirium Rating Scale-Revised-98

The Delirium Rating Scale-Revised-98[38] (DelRS-R98) is a 16-item clinician rating scale, which includes 13 severity items and 3 diagnostic items of delirium. Individual items assess temporal onset of symptoms, perceptual disturbance, delusions, psychomotor behavior, aspects of cognition (attention, language, visuospatial disturbance, and short- and long-term memory), presence of a physical disorder accounting for symptoms, SWCD (see fig 1 for SWCD ratings), thought process abnormalities, lability of mood, and fluctuation of symptoms. Ratings are determined by presence and severity of symptoms. Item scores are summed to obtain a total score that may range from 0 to 46 (severity and diagnostic items summed) or 0 to 39 for the severity items only. The DelRS-R98 has excellent reliability with a Cronbach coefficient alpha of .90. Interrater reliability is excellent with intraclass correlation coefficients ranging from .98 to .99.[38]

SWCD rating

For this study, participant sleep was rated on a scale of 0 to 3 on DelRS-R98 item 1 (SWCD) (see fig 1) based on nursing logs, clinicians, and family report. Participants without sleep-wake disturbances were rated as 0 (none present). Participants who experienced mild sleep discontinuity (awakened but able to return to sleep) or drowsiness during the day were rated a 1. Participants who had moderate disorganization of sleep (ie, several awakenings at night with confusion and difficulty returning to sleep