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ORIGINAL ARTICLE

Poor sleep is linked to impeded recovery from traumatic brain injury

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Abstract

Study Objectives: While disruptions in sleep are common after mild traumatic brain injury (TBI), the longitudinal relationships between sleep problems and global functioning after injury are poorly understood. Here, we prospectively investigate risk for functional impairment during the first 6 months of TBI recovery based on sleep onset insomnia symptoms and short sleep.

Methods: Patients presenting to the Emergency Department (ED) at Johns Hopkins Hospital within 24 hours of head injury and evaluated for TBI were eligible for our study. Demographic and injury-related information were collected in the ED. Patients then completed in-person surveys and phone interviews to provide follow-up data on global functioning, sleep, and depressive symptoms at 1, 3, and 6 months post-injury. A total of 238 patients provided sufficient data for analysis, and hypotheses were tested using mixed effects modeling.

Results: Sleep quality and global functioning improved over the 6 months of TBI recovery, but patients were at increased risk for functional impairment when sleeping poorly (odds ratio [OR] = 7.69, $p < .001$). Sleep onset insomnia symptoms and short sleep both independently corresponded to poor global functioning. Functional impairment was highest among those with both insomnia and short sleep (43%–79%) compared to good sleepers (15%–25%) and those with short sleep (29%–33%) or insomnia alone (33%–64%). A bidirectional relationship between sleep quality and functioning was observed.

Conclusions: Functionally impaired patients diagnosed predominantly with mild TBI exhibit high rates of insomnia and short sleep, which may impede TBI recovery. Monitoring sleep after head injury may identify patients with poor prognoses and allow for early intervention to improve functional outcomes.

Statement of Significance

Poor sleep is endemic to patients with traumatic brain injury (TBI) and may a represent critical threat to recovery from TBI. In our study, poorly sleeping TBI patients were more functionally impaired during the first 6 post-injury months than good sleepers. The highest rates of impairment were observed among patients with both sleep onset insomnia symptoms and concomitant short sleep. Critically, the relationship between sleep quality and global functioning was bidirectional, such that higher sleep disturbance predicted greater functional impairment months later, and vice versa. Given the roles of insomnia symptoms and short sleep in functional impairment during the post-acute recovery period, early detection of sleep problems may identify patients with poor prognosis, and intervention may improve recovery from TBI.

Key Words: TBI; insomnia; short sleep; functional impairment; global functioning; sleep latency

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Introduction

Traumatic brain injury (TBI) results in a physiological disruption of brain function as consequence of external force that often results in temporary loss of consciousness, loss of memory for events immediately before or after the head injury, alteration in mental state at time of injury, and focal neurological deficits that may or may not be temporary [1]. Recent estimates indicate that nearly 5 million patients seek treatment for TBI in emergency departments (EDs) annually [2]. Sleep disturbances are common TBI sequelae with 30%–70% of patients having difficulty sleeping after injury, which often last months or even years and often goes untreated [3–10].

Insomnia symptoms are among the most common sleep complaints reported by TBI patients [3, 10], with estimates suggesting 50% of TBI patients reporting symptoms and 29% meeting diagnostic criteria for insomnia disorder [8]. Sleep onset insomnia is especially prevalent among TBI patients [8, 11, 12], which is clinically concerning given that sleep initiation difficulties can portend insomnia persistence [13, 14]. Patient-reported difficulty falling and staying asleep [8, 15, 16], which can result in short or insufficient sleep duration, have been confirmed in TBI patients using objective polysomnographic and actigraphic measures [10, 16–19]. Moreover, TBI patients with aberrant sleep are more likely to suffer from headaches [20], neurobehavioral deficits [21, 22], and depression and other mood alterations [7, 15, 16, 20, 23–26]. Thus, post-injury sleep issues may reflect more severe pathology and warrant poorer prognosis.

A small but growing body of research suggests that sleep health is associated with recovery of function after TBI. In a sample of 31 inpatients with TBI, those who presented with sleep disturbance were more functionally impaired at admission and had longer stays in both acute and hospital settings [27]. A study utilizing continuous electroencephalography within 14 days of severe TBI showed that poor sleep predicted later readiness for rehabilitation and negative functional outcomes [28]. Other studies have shown that severity of sleep disturbances are associated with broad cognitive impairment [29], posttraumatic amnesia [30, 31], post-concussion symptoms [32], and global disability [33].

Although sleep issues are common after TBI and are associated with poor outcomes, little work has examined association between sleep disturbance and longer term functional outcomes. In 2015, Chan *et al.* [34] found that patients with persistent sleep disturbance for 1 year after TBI also had poorer functioning during that first post-injury year. Although this study offers key preliminary evidence identifying problematic sleep as a potential risk factor for poor functional outcomes, these findings are limited by a lack of prospective analysis. Despite having repeated measures, prospective relationships between sleep and functional impairment were not tested. Moreover, the Chan *et al.* study assessed sleep with a single item from the Rivermead Post-Concussion Questionnaire [35] (*Compared with before the accident, do you now [i.e., over the last 24 hours] suffer from Sleep Disturbance?*). However, multiple dimensions of sleep health uniquely and aggregately impact health and function [36]. Thus, the findings of Chan *et al.* [34] highlight the need to determine which components of sleep disturbance impede TBI recovery. A recent and burgeoning literature has identified insomnia and short sleep (<6 hours/night) as two key sleep ingredients that are especially toxic when concomitant, that lead to negative health outcomes [37–39] and vocational impairment [40]. And while insomnia is associated with poor TBI outcomes, it remains unclear whether the short sleep augments the corrosiveness of insomnia during recovery.

The present study is a post hoc analysis of data from a 6-month prospective study following patients who presented to the Johns Hopkins ED and diagnosed with TBI. These patients provided data at study enrollment in the ED, then follow-up data at 1, 3, and 6 months after injury. We sought to address two important gaps in the literature on sleep and TBI: (1) identify prospective associations between sleep and functional impairment during TBI recovery, and (2) characterize the independent and combined influences of insomnia symptoms and short sleep on functional outcomes. We hypothesized that sleep and global functioning share a bidirectional relationship after TBI such that difficulty sleeping would predict poor global functioning in the future, and vice versa. We also predicted that insomnia symptoms and short sleep would independently associate with difficulty functioning, and that the highest rates of impairment would be observed among patients endorsing both sleep onset insomnia symptoms and short sleep.

Methods

Participants and procedure

We performed an analysis of subjects enrolled in the *Head* Injury Serum Markers for Assessing Response to Trauma (HeadSMART) study. Details of the HeadSMART study design and methods have been previously published [41]. This study was approved by the Johns Hopkins Institutional Review Board. Subjects were recruited from two academic EDs located in Baltimore, Maryland (one a designated level-1 trauma center and the other a level-2 trauma center). Patients transferred from other hospitals were eligible for enrollment if they were enrolled within 24 hours of injury. Written informed consent was obtained from subjects or legally authorized representatives (in cases where the subject lacked the capacity to provide informed consent).

Eligible TBI subjects were ≥18 years old and presented to the ED within 24 hours of blunt head injury and met the American College of Emergency Physicians'/Centers for Disease Control criteria for evaluation with a non-contrast head CT scan. Exclusionary criteria included: inability to communicate in English, no working telephone number, pregnancy, or had a past medical history of intracranial surgery, intracranial hemorrhage, brain tumor, seizure-induced head injury, and severe dementia. TBI was diagnosed according to the definition proposed by the Demographics and Clinical Assessment Working Group of the International and Interagency.

Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health, also referred to as the American Congress of Rehabilitation Medicine (ACRM) criteria [42].

Demographic and clinical data were collected by trained research coordinators using structured data collection tools recommended by the National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements [43]. Data were collected and managed using REDCap electronic data capture tools hosted at the Johns Hopkins Bloomberg School of Public Health. Head CT images were read by one board-certified neuro-radiologist.

Baseline assessments: data collected in ED

TBI severity was rated at first evaluation in the ED using the revised Glasgow Coma Scale (GCS) [44, 45], which ranges from 3 (deep coma) to 15 (awake, converses normally and following commands). GCS scores <13 indicate moderate or worse TBI. Higher GCS scores at the time of injury are associated with better recovery from TBI and overall long-term prognosis [46–48]. At study enrollment in the ED, patients reported demographic information (age, gender, and ethnicity) and whether or not consciousness was lost at the time of injury. Head injury severity was assessed using the first item on the Abbreviated Injury Scale (AIS) [49], with scores ranging from 1 (minor injury severity) to 6 (maximum severity). Injury ratings of >2 on the AIS are graded "serious" or worse.

Follow-up assessments: 1 to 6 months post-injury

Outcome data were collected at 1, 3, and 6 months post-injury either by telephone interview or in-person assessment by trained research coordinators. Global functioning was assessed using the Extended Glasgow Outcome Scale [50] (GOSE), which categorizes recovery on a scale of 1 (dead) to 8 (upper good recovery) and has been shown to have greater validity and sensitivity to change than the original Glasgow Outcome Scale [51]. A board-certified neuropsychologist reviewed all GOSE data for accuracy. Functional impairment was defined as GOSE ≤ 6. The 19-item Pittsburgh Sleep Quality Index [52] (PSQI) was used to assess parameters of sleep, including sleep duration, sleep latency, sleep efficiency, subjective sleep quality, and sleep interfering-behaviors. The data were obtained by a group of trained research assistants who were not blinded to subjects' clinical data. A global cutoff score of PSQI > 8 has been recommended for identifying poor sleepers in clinical populations [53], and a study validating the PSQI in TBI patients showed that a score of 8 differentiates between subjects with clinically diagnosed insomnia disorder versus non-insomniacs [12]. In addition to measuring overall sleep quality, we used the PSQI to classify patients as having sleep onset insomnia symptoms (item 5a: endorsing inability to fall asleep within 30 m on ≥ 3 nights/week) and short sleep (item 4a: <6 hours/night). This method of classifying sleep onset insomnia symptoms with the PSQI has been supported by prior TBI research [11, 12], and this short sleep cutoff is consistent with current practices [37, 39]. The Patient Health Questionnaire-9 [54] (PHQ) is a nine-item self-report measure of depressive symptoms. Higher PHQ scores indicate greater depression severity, with scores ≥ 10 having 93% sensitivity and 88% specificity for detecting clinical depression [55].

Analysis plan

Analyses were conducted using SPSS 24 and STATA IC 11.1. First, we presented demographic and injury-related information gathered at study enrollment. Next, we conducted a series of linear and logistic mixed effects models to examine changes in and associations among global functioning/functional impairment, depressive symptoms, and sleep parameters across the first 6 months of TBI recovery; mixed effects models allow for simultaneous examination of between-subjects factors (baseline assessments) and within-subjects factors (repeated follow-up assessments). Important to note: global functioning was represented by GOSE scores in linear models, whereas functional impairment was represented by GOSE ≤ 6 in logistic models. To test our substantive hypotheses, we first used linear mixed effects modeling to identify which demographic and injury-related factors corresponded to changes in global functioning across the first 6 post-injury months. Next, we used linear (continuous outcomes) and logit (binary outcomes) mixed effects models to evaluate the association between sleep and global functioning across the 6 months of follow-up assessment. This involved constructing the following models: (1) a concurrent model examining whether sleep quality (PSQI) and functional impairment (GOSE) were associated at 1, 3, and 6 months post-injury; (2) a lagged sleep model testing whether sleep parameters predicted future functional impairment during TBI recovery; (3) a lagged functional impairment model testing whether functional impairment predicts future poor sleep. The concurrent model tested whether sleep and functional impairment are associated during TBI recovery, and the two lagged models examined the directionality of effects. All three models controlled for time effects and relevant demographic and injury-related factors. Lastly, we presented rates of functional impairment among patients with and without sleep onset insomnia and short sleep.

Results

Sample characteristics

Data were collected from 554 TBI patients in the ED. We excluded from analysis all subjects who were unable to complete an in-person follow-up and thus were unable to provide sleep data at all follow-up time points (1, 3 and 6 months). Thus, 316 patients were excluded from analysis, resulting in 238 subjects in the present study. Comparisons of sociodemographic and baseline characteristics and global function ratings across follow-up assessments revealed no differences between included versus excluded TBI patients, except that included patients were younger than those who were excluded ($t = 5.72$, $p < .001$). Refer to Table 1 for sample characteristics and injury ratings for the 238 TBI patients in the present study. Our sample was largely comprised of non-Hispanic black and

Table 1. Sample Characteristics at Study Enrollment ($n = 238$)

Age ($M \pm SD$)	40.56 years ± 17.18
Female sex (n, %)	88/238; 37.0%
Hispanic or Latino (n, %)	14, 5.88%
Race (n, %)	
Black or African American	116, 48.74%
White or Caucasian	108, 45.38%
Asian	3, 1.26%
Native American	1, 0.42%
Hawaiian or Pacific Islander	2, 0.84%
Multi-racial	5, 2.10%
Unknown or Unreported	3, 1.26%
Glasgow Coma Scale ($M \pm SD$, % <13)	14.78 ± 0.97, 1.3%
Mild (13–15; n, %)	235; 98.74%
Moderate (9–12; n, %)	1; 0.42%
Severe (3–8; n, %)	2; 0.84%
Head injury severity ($M \pm SD$, % moderate or worse)	1.47 ± 0.97, 5.5%
Loss of consciousness (n, %)	140/238, 58.8%

Age, female sex, ethnicity, race, and loss of consciousness were self-reported. Head injury severity measured by the AIS, item #1. AIS > 2 indicates moderate or worse head injury.

white Americans of middle-age. Men (n = 150) were over-represented in the sample. At ED presentation, TBI severity was rated at moderate or worse per the GCS in 1.3% of the sample, and 5.5% of the head injuries were rated as "serious" or worse per the AIS. Over half (58.8%) of the patients reported losing consciousness at time of injury.

Using mixed effects modeling, we examined whether global functioning, depressive symptoms, and sleep ratings changed across the 6-month recovery period (regressing outcome variables onto time as a within-subjects factor); see Table 2 for descriptives and model results. As expected, global functioning improved over the 6 post-injury months with functional impairment rates (GOSE ≤ 6) decreasing from 43.5% to 26.6%. Similarly, rates of positive depression screens decreased slightly from 22.7% to 19.4%. Multiple indices suggested slightly reduced rates of sleep issues particularly regarding the quality and ease of falling asleep in the first 6 months of TBI recovery. These data indicate that, although patients with mild TBI exhibit slight decreases in depression and sleep problems during acute recovery, these persisting symptoms remain highly prevalent 6 months after injury.

Sleep and global functioning during TBI recovery

We first identified relevant demographic and injury-related factors that correspond to changes in global functioning during the first 6 months of TBI recovery (Table 3, model 1). TBI patients who identified as female (b = –.39, p < .01), had loss of consciousness at time of injury (b = –.29, p = .04), and had greater severity of head injury (b = –.24, p < .01) had poorer global functioning over the first 6 post-injury months. Time remained a significant predictor, whereas TBI recovery was not associated with age or GCS rating of TBI severity at ED presentation.

We estimated global functioning as predicted by sleep disturbance, depression, and relevant covariates (Table 3, model 2). This analysis was estimated using 494 observations from 238 subjects, indicating that the average number of observations from each subject was 2.08 for this analysis. Results from the linear mixed-effects model showed that patients had poorer global functioning when sleeping more poorly (b = –.03, p < .01). Importantly, the association between sleep disturbance and global function was independent of the effects of depression, which also corresponded to poorer global function (b = –.07, p < .001). We then ran a mixed-effects logistic regression predicting risk for functional impairment (GOSE ≤ 6) based on sleep disturbance (PSQI > 8) and depression (PHQ-9 ≥ 10); see Table 3, model 3. Across the 6-month recovery period, patients were at nearly eightfold higher odds of having significant functional impairment when sleeping poorly (odds ratio [OR] = 7.69, p < .001). Notably, after accounting for the effects of sleep and depression on functioning in the linear and logistic models, women were no longer more functionally impaired during recovery than men (linear: p = .11; logistic: p = .41).

Sleep onset insomnia and short sleep

After establishing that problematic sleep is associated with functional impairment during TBI recovery, we then focused on two important aspects of compromised sleep health: insomnia symptoms and short sleep duration. Specifically, we investigated whether insomnia symptoms and short sleep uniquely correspond to global function (Table 3, model 4). A linear mixed effects model suggested that patients function more poorly when struggling to fall asleep (b = –.03, p = .05) and sleeping for shorter durations (b = .04, p = .02). A logistic model revealed that the odds of being functionally impaired were eight times greater for patients endorsing sleep onset insomnia than those without insomnia (OR = 8.33, p < .001; Table 3, model 5). An effect suggesting short sleepers (<6 hours/night) to be at greater odds for having functional impairment approached significance (OR = 2.93, p = .07).

To exploratorily test for synergistic effects of short and sleep onset insomnia on TBI recovery, we compared rates of functional impairment across four groups: (1) *good sleepers with normal sleep duration*, (2) *good sleepers with short sleep*, (3) *patients with sleep onset insomnia symptoms and normal sleep duration*, and (4) *patients with sleep onset insomnia symptoms and short sleep*. Rates of functional impairment were highest among patients with both sleep onset insomnia and short sleep (42.9%–79.1%; see Table 4 for full results). Follow-up dummy coded logistic regression models (with "good sleepers with normal sleep duration" as the reference group) showed that impairment rates were only consistently higher among patients with insomnia and short sleep, who were at 4- to 11-fold greater odds for significant impairment compared to good sleepers with normal sleep duration (Table 4). Even so, impairment rates were at times elevated among patients with sleep onset insomnia symptoms or short sleep alone.

Directionality of effects between sleep and global function

The above models showed that short and disturbed sleep were associated with functional impairment, but do not address

Table 2. Global Functioning, Depression, and Sleep Disturbance Across First 6 Months of TBI Recovery

	1 month post-injury	3 months post-injury	6 months post-injury	Change over time
GOSE ($M \pm SD$; % ≤6)	6.65 ± 1.18, 43.5%	6.84 ± 1.13, 31.0%	6.95 ± 1.16, 26.6%	χ^2 = 45.56, b = .21, z = 6.75***
PHQ ($M \pm SD$; %depressed)	6.09 ± 5.86, 22.7%	5.82 ± 6.13, 19.5%	5.05 ± 5.53, 19.4%	χ^2 = 9.27, b = –.70, z = –3.04**
PSQI				
Disturbance ($M \pm SD$); % poor	9.79 ± 4.75, 51.0%	9.42 ± 4.67, 45.0%	8.68 ± 4.89, 42.4%	χ^2 = 16.00, b = –.73, z = –4.00***
Latency ($M \pm SD$); % >30 minutes	46.37 ± 66.42, 33.3%	37.72 ± 43.49, 32.4%	35.67 ± 47.60, 25.6%	χ^2 = 3.71, b = –5.25, z = –1.93, p = .05
Sleep onset insomnia (n, %)	66/150, 44.0%	66/181, 36.5%	53/162, 32.7%	χ^2 = 7.79, OR^{-1} = 1.75, z = –2.79**
Duration ($M \pm SD$); % <6 hours	5.76 ± 1.89, 47.7%	5.91 ± 2.06, 49.7%	6.16 ± 2.04, 35.6%	χ^2 = 2.17, b = .12, z = 1.47, p = .14

GOSE ≤ 6 represents functional impairment. PHQ ≥ 10 represents a positive screen for depression. PSQI > 8 represents poor sleep in clinical samples. n = sample size; M = mean; b = unstandardized regression coefficient; z = z-test statistic; p = significance value (reported for p-values ≥ .05).
**p < .01; ***p < .001.

Table 3. Concurrent Associations Between Sleep and Global Functioning During TBI Recovery

	b	95% CI	*z*	*p*	χ^2, *p*
Model 1: Identifying baseline covariates predicting global functioning (*n* = 238, obs = 494)					
Baseline factors					70.91, <.001
Age	.00	−.01, .01	0.00	.99	
Female gender	−.39	−.66, −.12	−2.83	<.01	
TBI severity	.02	−.13, .18	0.29	.77	
Head injury severity	−.24	−.38, −.10	−3.42	<.01	
Loss of consciousness	−.29	−.56, −.02	−2.09	.04	
Recovery factors					
Time	.21	.15, .27	6.75	<.001	
Model 2: Sleep predicting functional impairment during recovery, linear (*n* = 230, obs = 481)					
Baseline factors					259.18, <.001
Female gender	−.17	−.38, .04	−1.59	.11	
Head injury severity	−.21	−.32, −.11	−3.97	<.001	
Loss of consciousness	−.17	−.38, .03	−1.66	<.10	
Recovery factors					
Time	.14	.07, .20	4.35	<.001	
Depression	−.07	−.08, −.06	10.50	<.001	
Sleep disturbance	−.03	−.05, −.01	−3.25	<.01	
Model 3: Sleep predicting functional impairment during recovery, logistic (*n* = 230, obs = 481)					
Baseline factors		OR; 95% CI			42.32, <.001
Female gender	−.54	—	−0.82	.41	
Head injury severity	−1.19	3.33; 1.67, 6.67	−3.40	<.01	
Loss of consciousness	−1.61	5.26; 1.32, 20.00	−2.37	.02	
Recovery factors					
Time	1.22	3.38; 1.90, 6.04	4.12	<.001	
Depression	−3.86	50.00; 11.11, 250.00	−5.10	<.001	
Sleep disturbance	−2.03	7.69; 2.50, 25.00	−3.53	<.001	
Model 4: Sleep components predicting functional impairment, linear (*n* = 232, obs = 471)					
Baseline factors					269.16, <.001
Female gender	−.20	−.41, .01	−1.86	.06	
Head injury severity	−.20	−.30, −.09	−3.71	<.001	
Loss of consciousness	−.16	−.36, .05	−1.47	.14	
Recovery factors					
Time	.13	.07, .19	4.16	<.001	
Depression	−.08	−.09, −.07	−12.21	<.001	
Sleep latency (× 30 m)	−.03	−.06, .00	−1.94	.05	
Sleep duration (hours)	.04	.01, .08	2.30	.02	
Model 5: Sleep components predicting functional impairment, logistic (*n* = 151, obs = 364)					
Baseline factors		OR; 95% CI			35.59, <.001
Female gender	−1.39	4.00; .86, 20.00	−1.77	.08	
Head injury severity	−1.27	3.57; 1.49, 8.33	−2.86	<.01	
Loss of consciousness	−1.59	5.00; 1.06, 25.00	−2.04	.04	
Recovery factors					
Time	1.10	3.01; 1.60, 5.63	3.43	<.01	
Depression	−3.43	33.33; 6.25, 100.00	−4.23	<.001	
Sleep onset insomnia	−2.08	8.33; 2.50, 25.00	−3.51	<.001	
Short sleep (<6 hours)	1.08	2.93; .93, 9.25	1.83	.07	

Global functioning assessed by the GOSE. Functional impairment defined as GOSE ≤ 6. TBI severity assessed by the Glasgow Coma Scale. Head injury severity measured by the AIS, item #1. Loss of consciousness at time of injury was self-reported by patient. Depression measured by the PHQ. Sleep disturbance measured by the PSQI. Sleep latency was estimated in minutes on the PSQI, item #2. Sleep duration was measured by PSQI item #4a. Sleep onset insomnia = rating inability to fall asleep within 30 minutes on three or more nights per week, PSQI item #5a. *n* = sample size; *b* = unstandardized regression coefficient; CI = confidence interval; *z* = z-statistic; *p* = significance value, which describes whether the model explains greater variance in the outcome than a null model with no predictors. obs = number of observations in model. OR (values are inversed for negative associations to ease interpretability), not reported for parameters with *p*-values > .10.

temporal precedence or directionality. Leveraging the time-nested structure of our data, we examined directionality between sleep and global functioning by lagging predictors in two separate models. First, we estimated global functioning as predicted by lagged values for sleep disturbance, while controlling for relevant covariates (Table 5, model 1). Analyses revealed that greater sleep problems predict poorer global functioning months later (b = −.04, p = .01). A logistic mixed effects model showed that having sleep onset insomnia symptoms increased the odds by 7 for functional impairment at the next follow-up assessment (OR = 7.14, p = .01; Table 5, model 2). We then explored the opposite direction to determine whether global functioning predicts future sleep (Table 5, model 3). Results showed that greater functional impairment augured poorer sleep at the next follow-up assessment (b = −.86, p < .01). Notably, depressive symptoms also predicted poor sleep later on, suggesting that

Table 4. Rates of Functional Impairment Based on Short Sleep and Sleep Onset Insomnia

	Rates of functional impairment		
	1 month	3 months	6 months
No insomnia, normal duration	14/56; 25.0%	12/72; 16.7%	12/79; 15.2%
Short sleep, no insomnia	8/28; 28.6%	14/42; 33.3%; OR = 2.50*	9/29; 31.0%; OR = 2.51**
Insomnia, normal duration	14/22; 63.6%; OR = 5.25**	6/18; 33.3%	10/24; 41.7%; OR = 3.99**
Short sleep insomnia	34/43;79.1%; OR = 11.33***	25/47; 53.2%; OR = 5.68***	12/28; 42.9%; OR = 4.19***

Functional impairment defined as GOSE score of ≤ 6. Sleep duration was measured by PSQI item #4a, with estimates of <6 hours/night constituting short sleep. Sleep onset insomnia = rating inability to fall asleep within 30 minutes on three or more nights per week, PSQI item #5a.
*$p < .05$; **$p < .01$; ***$p < .001$.

Table 5. Sleep Predicting Future Functional Impairment During Recovery

	b	95% CI	*z*	*p*	χ^2, *p*
Model 1: Sleep predicting future global functioning during recovery (*n* = 156, obs = 247)					
Baseline factors					72.01, <.001
Female gender	−.36	−.62, −.09	−2.65	<.01	
Head injury severity	−.22	−.35, −.09	−3.41	<.01	
Loss of consciousness	−.19	−.44, .06	−1.48	.14	
Recovery factors					
Time	.12	−.03, .26	1.56	.12	
Depression, lagged	−.03	−.05, −.01	−3.13	<.01	
Sleep disturbance, lagged	−.04	−.06, −.01	−2.56	.01	
Model 2: Logistic model of sleep predicting future functional impairment (*n* = 126, obs = 214)					
Baseline factors		OR; 95% CI			16.04, .02
Female gender	−1.69	5.26; .83, 33.33	−1.76	.08	
Head injury severity	−.92	2.50; 1.02, 6.25	−2.00	<.05	
Loss of consciousness	−1.54	4.76; .79, 25.00	−1.70	.09	
Recovery factors					
Time	.49	—	.91	.36	
Depression, lagged	−.99	—	−1.28	.20	
Sleep onset insomnia, lagged	−1.96	7.14; 1.56, 33.33	−2.54	.01	
Short sleep, lagged	−.87	—	−1.18	.24	
Model 3: Global functioning predicting future sleep (*n* = 154, obs = 246)					
Baseline factors					85.72, <.001
Female gender	2.66	1.43, 3.89	4.26	<.001	
Head injury severity	−.23	−.84, .39	−.72	.47	
Loss of consciousness	.70	−.49, 1.88	1.16	.25	
Recovery factors					
Time	.09	−.70, .88	.22	.82	
Depression, lagged	.19	.08, .29	3.53	<.001	
Functional impairment, lagged	−.86	−1.48, −.24	−2.73	<.01	

Global functioning assessed by the GOSE. Functional impairment defined as GOSE ≤ 6. TBI severity assessed by the Glasgow Coma Scale. Head injury severity measured by the AIS, item #1. Loss of consciousness at time of injury was self-reported by patient. Depression measured by the PHQ. Sleep disturbance measured by the PSQI. Sleep latency was estimated in minutes on the PSQI, item #2. Sleep duration was measured by PSQI item #4a. Sleep onset insomnia = rating inability to fall asleep within 30 minutes on three or more nights per week, PSQI item #5a. *n* = sample size; *b* = unstandardized regression coefficient; CI = confidence interval; *z* = z-statistic; *p* = significance value, which describes whether the model explains greater variance in the outcome than a null model with no predictors. obs = number of observations in model. OR (values are inversed for negative associations to ease interpretability), not reported for parameters with *p*-values > .10.

functional impairment and depression both uniquely associated with future sleep problems during TBI recovery.

Rates of insomnia and short sleep in functionally impaired TBI patients

Lastly, we conducted post hoc descriptives to provide estimates of sleep onset insomnia and short sleep in functionally impaired versus unimpaired TBI patients (see Table 6 for results). Across all 6 months, rates of sleep onset insomnia symptoms were consistently higher among patients with functional impairment than those with without functional impairment. By comparison, rates of short sleep were higher among the functionally impaired at 1- and 3-months post-injury, but not at 6 months.

Discussion

In a sample of 238 ED patients diagnosed predominantly with mild TBI, the present study characterized changes in sleep and global functioning and their bidirectional temporal relations with one another across the first 6 months of TBI recovery. Although sleep quality and global functioning improve during the acute and post-acute recovery period, a key finding from our study indicates that sleep problems predict poor functional

Table 6. Comparing Rates of Sleep Problems in the Functionally Impaired vs. Good Recovery

	Rates of sleep problems (impaired vs. unimpaired)		
	1 month	3 months	6 months
Sleep onset insomnia	68.6% vs. 22.5%*	55.2% vs. 27.6%*	51.2% vs. 26.1%*
Short sleep	60.0% vs. 36.7%*	68.4% vs. 41.0%*	48.8% vs. 30.8%*

Impaired subjects were identified by scoring 6 or below on the GOSE. Sleep duration was measured by PSQI item #4a. Sleep onset insomnia = rating inability to fall asleep within 30 minutes on three or more nights per week, PSQI item #5a.
*Statistically significant z-test comparing sleep problem proportions.

outcomes in the future. Evidence suggested that functional impairment was associated with both sleep onset insomnia symptoms and short sleep duration, and that insomniacs sleeping fewer than 6 hours/night recovered poorly from TBI. However, not only did sleep problems augur poor global functioning, but a temporal association in the opposite direction was supported as well, such that functional impairment predicted future sleep difficulties. Together, these data emphasize the importance of sleep health in recovery from TBI, and identify insomnia and short sleep as targets for intervention to improve functional outcomes.

Functional impairment in short sleep and insomnia

Rates of functional impairment decreased considerably from 44% to 27% across the first 6 post-injury months. Although sleep quality improved slightly during the first 6 months after injury, with rates of poor sleep decreasing from 51% to 42% and sleep onset insomnia decreasing from 44% to 33%, impairments of sleep remained highly elevated among these patients. Consistent with prior research highlighting the costs of poor sleep during TBI recovery [34], disruptions in sleep were associated with functional impairment. When TBI patients reported having poor sleep, their odds for being rated as functionally impaired increased nearly eightfold. Notably, the effects of sleep on TBI recovery were independent of the effects of head injury severity and loss of consciousness on functional outcomes.

Analysis of insomnia symptoms and sleep duration on global functioning suggested that both difficulty falling asleep and short sleep independently increased risk for impairment. Across the first 6 post-injury months, sleep onset insomnia rates were 51%–69% among the functionally impaired compared to just 23%–28% among the unimpaired. A similar trend was observed across the first 6 months for short sleep such that functionally impaired patients had rates of short sleep at 49%–68% compared to just 31%–41% for unimpaired patients. Important to highlight here is that the relationship between sleep onset insomnia symptoms and functional impairment was stronger and more robust than the association of short sleep with functional impairment. Pre-sleep cognitive-emotional arousal is often a key ingredient in sleep onset insomnia [56–58]. Thus it is possible that psychological correlates including nocturnal rumination and worry may contribute to the relationship between sleep onset insomnia symptoms and functional impairment.

Impairment rates in the first 6 months after injury were highest among short sleeping insomniacs at 43%–79% as compared to individuals with good sleep (≤25%), short sleep alone (≤33%), or insomnia alone (≤64%), which may reflect short sleep augmenting the effects of insomnia on functional impairment. These potentially synergistic effects between insomnia and short sleep on poor recovery from TBI is consistent with the expanding literature on the serious negative health outcomes associated with short sleep insomnia [37–40, 59].

Bidirectionality between global functioning and problematic sleep during TBI recovery

A unique strength of the current study is the repeated follow-up assessments allowing for examination of temporal precedence between sleep anomalies and functional impairment. Analysis revealed a bidirectional relationship wherein poor sleep quality and insomnia symptoms predicted poorer global functioning months later, and functional impairment augured future sleep issues. It is important to emphasize here that the relationships between sleep and global function were independent of depression-effects. In other words: although depression is common after TBI and is associated with both poor sleep and functional impairment, our data show that poor sleep is associated with poor global function, and vice versa, independently of depression. Even so, our data also show that greater depressive symptoms predict both future sleep difficulties and negative functional outcomes, thus highlighting the critical interrelatedness of sleep, depression, and TBI recovery. As depression and poor sleep are endemic to patients with TBI, optimizing functional outcomes will likely involve the assessment and treatment of both of these conditions for those afflicted. Interestingly, female TBI patients had poorer functional outcomes than male TBI patients in our study. However, after accounting for the effects of sleep and depression on functional impairment, women and men no longer differed in global functioning. These data offer early evidence suggesting that post-TBI sleep issues and depression are salient risk factors for poor TBI recovery that may be especially relevant to women with TBI.

Limitations and future directions

The present study should be interpreted in light of certain limitations. Firstly, our sample does not include TBI patients who do not seek medical attention, thus our study likely suffers from a selection bias favoring more severely symptomatic sufferers of mild TBI. Along these lines, it should be emphasized that the majority of the patients in this study were diagnosed with mild TBI, thus our findings may not generalize to patients with moderate or severe TBI. Secondly, while 238 subjects allow for adequate statistical power to detect effects, the rates of functional impairment for various sleep groups as well as the rates of insomnia and short sleep between functionally impaired and unimpaired TBI patients may not accurately represent rates in the larger population of TBI patients. Furthermore, as this study

was observational by design, we are unable to firmly establish causality between sleep problems and functional impairment.

We would also like to emphasize that our evaluation of insomnia focused on nocturnal symptoms, whereas the disorder also requires distress and daytime sequelae for diagnosis. Clinician interviews are necessary for proper evaluation of sleep disorders. Along these lines, reliance on self-reported sleep parameters and, in particular, individual items to capture insomnia symptoms and sleep duration may be biased among TBI patients, especially for those sleeping poorly. While subjective sleep ratings correspond to objective sleep measures [60, 61], the gold standard of sleep assessment involves the combination of subjective ratings and objective sleep measures (e.g. actigraphy, polysomnography). Measuring sleep both objectively and subjectively is highly recommended in trauma patients who may have difficulty accurately estimating their sleep [15, 62]. Importantly, objective measurement of short sleep is strongly recommended in sleep research and some data show that classifying short sleep based on subjective estimates results in erroneous non-significant results [37], which could have potentially hindered our ability to detect effects associated with short sleep in the present study. With the increased availability of cost-effective wearable sleep technology, future investigations are well-positioned to utilize both continuous subjective and objective sleep measures to monitor post-acute and long-term trends in sleep after TBI, which may offer greater insights into the directionality of sleep, mood, and global functioning in this population. Lastly, it should be noted that other pre- and post-TBI factors unaccounted for in this study may contribute to the association between poor sleep and functional impairment during recovery, such as prior history of TBI, pre-injury history of sleep disorders and the use of sleep aids, antidepressants, and possible trauma to other body parts. Research is needed to identify how genetic factors, psychosocial morbidity, insufficient services or social support, psychiatric history, personality factors, and poor coping skills may influence sleep and function among patients with TBI.

Conclusions

Our data indicate that sleep and functional impairment share a bidirectional relationship during recovery from TBI. Main findings include sleep onset insomnia as a key risk factor for functional impairment, in addition to evidence suggesting that short sleep may impede recovery as well, particularly when combined with insomnia complaints. Patients sleeping poorly in the weeks following TBI are at elevated risk for negative functional outcomes and may represent a population to target for rehabilitation optimization. Indeed, a growing number of researchers have proposed that addressing sleep difficulties early after TBI may improve functional outcomes [3, 10]. As our data suggest that sleep is slow to improve during the acute recovery period following TBI, cognitive-behavioral interventions (such as cognitive behavioral therapy for insomnia, CBTI) and/or pharmacotherapy targeting insomnia symptoms and insufficient sleep may improve clinical outcomes for patients recovering from TBI. It is likely that a better understanding of the causal mechanisms facilitating the effects of problematic sleep on functional impairment may pave the way for more effective interventions and treatment optimization.

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