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Prevalence and types of sleep disturbances acutely after traumatic brain injury

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Abstract

Primary objective—To assess the prevalence of and risk factors for sleep disturbances in the acute post-traumatic brain injury (TBI) period.

Research design—Longitudinal, observational study.

Methods and procedures—Fifty-four first time closed-head injury patients were recruited and evaluated within 3 months after injury. Pre-injury and post-injury sleep disturbances were compared on the Medical Outcome Scale for Sleep. The subjects were also assessed on anxiety, depression, medical comorbidity and severity of TBI.

Main outcomes and results—Subjects were worse on most sleep measures after TBI compared to before TBI. Anxiety disorder secondary to TBI was the most consistent significant risk factor to be associated with worsening sleep status.

Conclusions—Anxiety is associated with sleep disturbances after TBI. Further studies need to be done to evaluate if this is a causal relationship.

Keywords

Trauma; mood disorder; sleep

Introduction

Sleep problems are common after traumatic brain injury (TBI), with prevalence estimated at 30-70% [1,2]. Sleep problems interfere with rehabilitation and quality of life [3]. Most studies have focused on sleep disturbances in the chronic TBI period [1,4]; however, it is equally important to focus on the immediate post-TBI period (within 3 months of injury), as this is a period of active functional recovery. Identification and treatment of sleep disturbances during this period may reduce TBI morbidity, including the risk of chronic sleep disorder. The aim of this study was to determine the prevalence and risk factors for sleep disturbances in the acute

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post-TBI period. This study is part of a larger ongoing study to determine prevalence and risk factors associated with the development of psychiatric disorders after TBI. The results presented here are thus preliminary.

Methods

Participants and procedures

Patients with first-time closed head injuries were recruited within 3 months of trauma. Evaluations were completed only on participants able to give informed consent; the ability of participants to give informed consent was evaluated based on their treating physicians' opinions and based on the abilities of the patients to accurately summarize the study and their roles in it. Two evaluations were done within 3 months of the TBI. The first evaluation was done within the first 2 weeks of TBI to assess lifetime history of psychiatric and sleep problems. The second evaluation assessed for psychiatric and sleep problems within the first 1-3 months post-TBI. However, for those subjects who were unable to give consent within the first 2 weeks of trauma, both the pre-TBI and post-TBI status were assessed at the time they were able to provide informed consent (within the first 3 months of trauma). Informant information was collected at each evaluation whenever possible. All patients were recruited from two hospitals: the trauma unit of the Johns Hopkins Hospital and the Brain Injury unit of Kernan Hospital, University of Maryland. All patients had varying severities of brain and body injury. For the purposes of the study, TBI was defined as having at least one of the following: (a) admitted to the hospital with clear history of loss of consciousness; (b) Glasgow Coma Score 15 or less; and/or (c) evidence of trauma on computerized tomography (CT) scans done as part of clinical workup. Other inclusion criteria included: (a) ability to provide consent personally and (b) ≥18 years of age. Exclusion criteria included (a) a prior TBI; (b) an open-head injury (e.g. a displaced skull fracture or a gun-shot wound); or (c) a history of any other type of brain illness (e.g. stroke, seizure, encephalitis). The study was approved by the Institutional Review Boards of both universities.

Measures

All participants were interviewed by a neuropsychiatrist with the Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID-IV) [5]. The severity of TBI was determined by the Glasgow Coma Scale obtained at the time of presentation to the emergency room [6]. Medical comorbidity was assessed using the General Medical Health Rating (GMHR) [7] scale, which provides an overall assessment of a person's medical problems and medications.

Sleep problems before and after TBI (based on recall of the subjects and collateral information) were determined using the 12-item Medical Outcome Scale for Sleep (MOS). The scale has good psychometric properties and has been found to be useful to assess sleep problems in adults [8]. Scoring of this instrument is in six domains: sleep disturbance, snoring, awakening with shortness of breath or with headache (SOBHA), sleep amount, sleep adequacy, and daytime somnolence. In addition, two summary index measures were used to assess overall sleep problems as part of the MOS: Sleep Problem Index 1 (short summation index includes awaken short of breath or with headache, trouble staying awake during day, trouble falling asleep, awaken during sleep and have trouble falling asleep, get enough sleep to feel rested in the morning and get the amount of sleep needed) and Sleep Problem Index 2 (thorough summation index includes all items in index 1 and time taken to fall asleep, sleep not quiet, sleepiness or drowsy during day). All domain scales and index measures were scored on a transformed 0-100 metric, with higher scores indicating more sleep problems.

Statistical methods

Repeated measures ANOVA was used to compare the differences in sleep disturbances between baseline (recall of pre-TBI) and the immediate post-TBI period. The second part of the analysis included multivariate linear regression to assess predictors of sleep disturbances for each of the six domains on the MOS scale. *A priori* significance levels were set at $p < 0.05$.

Results

Demographics

A total of ~1000 people admitted during the 2.5 year study period to the trauma unit at Hopkins and the Brain Injury unit at Kernan Hospital, University of Maryland were screened. Of these, only those who met the study inclusion/exclusion criteria and had both baseline and follow-up visits within 3 months of trauma were included in this analysis (*n*=54). The majority were excluded because of prior head injury. Other reasons for exclusion included age below 18, no admission to the hospital, absence of clear history of loss of consciousness and refusal to participate. Most patients did not offer reasons for lack of interest other than stating that they could not commit themselves to a research study. The mean age of the sample was 43.2 years (SD=17.7; range 18-90), mean education level 13.2 years (SD=3.1) and the mean Glasgow Coma Scale score was 12.5 (SD = 3.6; range 3-15). Sixty-five per cent of the sample had mild TBI (GCS 13-15), 11% moderate TBI (GCS 9-12) and 19% severe TBI (GCS 8 or less). The GCS of three (5.5%) participants was unknown. The duration of post-traumatic amnesia was not determined. Males accounted for 59.0% and non-Caucasians 53.7% of the sample. The majority (72.2%) were either married or had a partner, were employed (75.9%) and had an annual income of at least US$20 000 (55.6%). Over half (52%) sustained TBI in a motor vehicle accident; otherwise assault (24%), falls (22%), and unknown or 'found down' (2%) accounted for the injury. Ninety-three per cent (*n*=50) had not had any brain surgery after the trauma and 54% (*n*=29) had also sustained body trauma.

Prevalence of anxiety and depression due to TBI

Nine per cent (*n*=5) reported to a history of major depression prior to the TBI and 7% (*n*=4) reported to a history of anxiety disorder pre-TBI. The incidence of Mood Disorder Due to General Medical Condition (TBI), Major Depressive-like Episode (henceforth called MDGMC) was 13% (*n*=7) and the incidence of Anxiety Disorder due to General Medical Condition, With Generalized Anxiety (henceforth called GADGMC) was 11% (*n*=6).

Comparison of sleep scores before and after TBI

As seen in Table I, there was a significant increase after TBI in the sleep score in all domains on the MOS scale except 'Snoring' (as assessed by repeated measures ANOVA analysis).

Regression analysis to assess predictors of sleep disturbance

Seven hypothesis-driven independent variables were chosen based on literature findings on the association of these variables with sleep disturbance after TBI. They include: age [4], gender [4], MDGMC [9], GADGMC [10], GMHR score, body injury and GCS [9]. Each of the seven independent variables was separately regressed on MOS sub-component domains and the two index scores (dependent variables) (Table II). Independent variables found to be significant in univariate models were then entered into multiple regression calculations.

Sleep disturbance—Significant predictors of sleep disturbance on univariate analysis included MDGMC (p=0.026) and GADGMC (p=0.006). In the multivariate linear regression, MDGMC and GADGMC accounted for ~14% of the variance in the sleep disturbance sub-component (Adjusted R^2=0.139).

Snoring—Age alone emerged as a significant predictor (p=0.047) of scores in the snoring sub-component, explaining ~6% of the variance (Adjusted R^2=0.057). Multivariate regression analysis was not conducted.

SOBHA (awaken with short of breath or headache)—On univariate analysis, only female gender was a significant (p 0.037) predictor of the SOBHA sub-component and accounted for ~6% of variance (Adjusted R^2 = 0.064). Again, multivariate regression was not conducted.

Sleep adequacy—None of the independent variables were found to be significantly associated with the sleep adequacy sub-component score.

Daytime sleepiness—Significant predictors of daytime sleepiness included age (p=0.024) and GADGMC (p=0.009). In the multivariate model, age and GADGMC explained ~15% of the variance in daytime sleepiness (Adjusted R^2 = 0.145).

Sleep Index 1—Significant univariate predictors of Sleep Index 1 included MDGMC (p=0.04) and GADGMC (p=0.013). Approximately 15% (Adjusted R^2 = 0.146) of the variance in Sleep Index 1 was accounted for by MDGMC and GADGMC.

Sleep Index 2—MDGMC (p=0.021) and GADGMC (p=0.004) were also significant univariate predictors of the Sleep Index 2 summary score. In the multivariate model, MDGMC and GADGMC accounted for 22% of the variance (Adjusted R^2=0.218). In the multivariate model, the association between MDGMC and Sleep Index 2 was attenuated and only trended towards significance (p=0.086).

Discussion

This report found that sleep problems in the acute post-TBI period (within 3 months of injury) generally worsened compared to recall of sleep problems before the injury in most domains (other than snoring). Sleep problems in the immediate TBI period can be secondary to numerous factors: injury to sleep regulating centres [11], pain, comorbid medical problems, side effects of medications, or a symptom of a mood and/or anxiety disorder [12]. From this report, new onset anxiety disorder with generalized anxiety features that developed for the first time after TBI (GADGMCC) was the most consistent correlate of various specific sleep disturbances and of the global measures of sleep problems (Sleep Problems Index 1 and 2). Mood disorder with major depressive-like episode that developed for the first time after TBI also appeared to be related to overall sleep problems, but the relationship was not as consistent.

Other TBI studies have also found a significant association between sleep problems and anxiety/depression [10,13]. In a retrospective analysis of 60 patients 3 months to 2 years post-TBI, Verma et al. [10] found that patients with sleep onset insomnia had higher anxiety scores as assessed by the Hamilton Anxiety Scale (HAS) and sleep maintenance insomnia was associated with higher Beck Depression scores. Similarly, Parcell et al. [13] have also found increased levels of anxiety and depression as measured by the Hamilton Anxiety and Depression scale (HADS) in chronic TBI patients compared to age and gender matched controls. However, both these studies did not use structured psychiatric interviews to diagnose depression or anxiety. While scales such as the HAS and HADS measure the severity of anxiety or depression, they are not diagnostic of these disorders. This is particularly important in brain injured patients who present with a number of somatic symptoms which could be secondary to the brain injury itself. Despite this important finding of anxiety as a predictor of sleep disturbance, the authors are unable to comment on the direction of the relationship as anxiety can be both a cause and consequence of sleep disturbance.

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Severity of TBI (as assessed by GCS) has previously been reported in the TBI literature as a significant factor in sleep disturbances [4], but it was not significant in this study. These findings are, on the other hand, supportive of a study by Castriotta et al. [14], who found no relationship between severity of TBI and daytime sleepiness in a study of 87 chronic TBI patients using objective measures to assess sleep disturbances. Similarly, Baumann et al. [15] found that in a sample of 76 TBI patients in the chronic stage of injury, there was a high prevalence of sleep disturbance but no association between sleep problems and severity or localization of TBI.

This study also did not find the presence of body injury or medical comorbidity to be significantly correlated with sleep disturbances. However, other studies have found medical problems and pain to be significant contributors to sleep problems [1,14,16]. The lack of association between medical burden and sleep disturbance in this study could be because the presence of pain, number of medications and nature and severity of medical problems were grouped under one category, the GMHR scale. Future studies should better define medical problems and also rate the severity of pain.

This study also did not find any association between sleep adequacy and any of the demographic or clinical variables. This may be due to not specifically collecting data on variables that correlate with poor sleep adequacy in the general population, including increased use of health services [17], use of hypnotic agents [18], impaired functional capabilities and poor health-related quality of life [19].

Additionally, some of the other sleep variables such as snoring were only associated with increase in age in this study. Studies in the general population have found older age to be a risk factor for snoring [20]. However, other well known risk factors for snoring such as body mass index and oropharyngeal abnormalities were not analysed in this study [21]. Additionally, brain pathology causes of snoring, such as stroke, are often localized to the brainstem [22]. Neuroimaging was not part of this research study and hence one is unable to comment on the brain pathology associated with post-TBI snoring.

Female gender was the only significant predictor of shortness of breath and headache in this study. Even though it is well known that females tend to somatize more males [23-25] and post-traumatic headaches are more common in women [26], other mechanisms affecting this variable (such as pulmonary, cardiac, or muscular factors; use of analgesics) should be looked into.

The major limitations of this paper are that a subjective measure was used to assess sleep disturbance and the assessment of baseline sleep disturbances may have been subject to recall bias. Another limitation is the lack of information on presence/absence of pain, nature and severity of medical problems and medications used by the subjects before and after injury. It is well known that these factors contribute to sleep problems in both TBI and non-TBI patients [1,16,27]. Even though the GMHR is a global measure of medical problems, its use has not been validated in the TBI population and may not capture the different components of medical burden (nature and severity of medical problems, types and frequency of medication use, presence/severity of pain).

Despite these limitations, the study has several strengths. It is one of the few studies to analyse sleep problems in the acute TBI period other than Keshavan et al. [28] and Dikmen et al. [29]. This study is the first to evaluate sleep problems in the pre- and post-TBI period in adults with varying TBI severity. Parsons and Van Beek [30] have done similar comparisons of pre-TBI and post-TBI sleep problems, but restricted their study to mild TBI in the age group 16-30. This study is also the first to look at new-onset anxiety and depressive disorders using structured psychiatric interviews. Other strengths include the use of validated measures and the use of regression to determine predictors

Conclusion

Sleep problems are common after TBI. This study indicates that anxiety disorder that develops for the first time after TBI is a significant predictor of sleep disturbance in the acute TBI period, underscoring the importance of psychiatric evaluation in people with sleep problems post-TBI. Future studies need to focus on sleep problems as a predictor of TBI mood disturbances and if treatment of sleep problems can reduce psychiatric morbidity. In particular, the direction of causality between sleep and mood disorder needs to be elucidated in order to know whether anxiety can lead to sleep disturbances after TBI or the other way around. This can best be done with future prospective studies.

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Table I

Comparison of MOS sleep scores before and after TBI

Variable		*M*	SD	*F*	*p*-value
Sleep disturbance	V0	17.5	15.9	6.0	0.018
	V1	27.7	24.1		
Snoring	V0	18.4	30.2	0.72	0.400
	V1	14.5	26.9		
SOB/HA*	V0	0.39	2.8	12.6	0.001
	V1	14.1	27.5		
Sleep adequacy	V0	26.7	28.2	5.5	0.023
	V1	38.6	31.1		
Daytime sleepiness	V0	17.3	17.5	10.8	0.002
	V1	31.8	26.9		
Sleep Problem Index 1	V0	14.4	14.0	16.8	<0.001
	V1	28.0	22.3		
Sleep Problem Index 2	V0	17.2	12.7	13.2	0.001
	V1	29.3	20.5		

V0=Baseline recall of sleep status before TBI; V1=Assessment of sleep status within 3 months after TBI.

*SOB/HA=Shortness of breath/headache.

Table II

Association between participant characteristics and sleep domains and summary scores

Independent variables	Sleep disturbance B	Sleep disturbance SE	Snoring B	Snoring SE	SOBHA B	SOBHA SE	Sleep adequacy B	Sleep adequacy SE	Daytime sleepiness B	Daytime sleepiness SE	Sleep Index I B	Sleep Index I SE	Sleep Index II B	Sleep Index II SE
Age	0.01	0.19	0.42*	0.20	-0.04	0.22	-0.05	0.25	0.47*	0.20	0.12	0.18	0.11	0.16
Female	4.91	6.61	-3.67	7.44	15.63*	7.31	4.06	8.82	8.25	7.42	8.56	6.14	7.12	5.61
MDGMC	21.12*	9.21	6.96	10.81	10.68	11.01	11.49	12.76	18.42	10.62	17.86*	8.76	18.69*	7.87
GADGMC	27.42**	9.46	12.72	16.17	8.94	16.75	21.00	16.90	38.86**	14.37	25.62*	9.79	26.35**	8.70
GMHR	-5.28	3.44	-2.60	3.92	-0.87	4.03	-0.22	4.68	-5.85	3.89	-3.70	3.27	-3.65	2.97
Body injury	-5.21	6.54	-1.15	7.38	5.63	7.51	-9.30	8.65	-5.41	7.39	-2.79	6.18	-5.35	5.59
GCS	-0.69	0.97	-0.17	1.12	-0.08	1.14	0.70	1.31	-0.05	1.11	-0.68	0.91	-0.45	0.83

SOBHA=Shortness of Breath/Headache; MDGMC=Major Depressive-like Episode due to General medical disorder; GADGMC=Generalized Anxiety Disorder due to General Medical Condition; GMHR=General Medical Health Rating; GCS=Glasgow Coma Scale.

* $p<0.05$;

** $p<0.01$.