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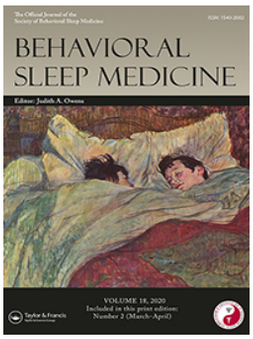

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High Sleep Disturbance and Longer Concussion Duration in Repeat Concussions

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ABSTRACT

Objectives: The relationship between repeated concussions and sleep disturbance is yet to be fully understood. The objective of this study was to examine the relationship between sleep disturbance, concussion duration, and repeated concussions by assessing postconcussive symptoms and cognition. *Methods*: Subjects (ages 13–33 years) underwent postconcussion cognitive function evaluation and reported postconcussion symptoms including severity of disturbed sleep (drowsiness, trouble falling asleep, sleeping more than usual, and sleeping less than usual), mood disturbance (sadness, irritability, nervousness, and emotional lability), and headache. Data on cognitive function and concussive symptoms were collected for 430 subjects after first concussion, 192 subjects after second concussion, and 118 subjects after three or more concussions. A subset of subjects (119) were monitored longitudinally to assess concussion duration. Analyses included group comparisons, regression, and correlation; data were adjusted for age and gender. *Results*: Sleep disturbance differed significantly by group (mean[SEM]: 1st concussion = 2.56[0.2]; 2nd concussion = 3.65[0.34]; 3+ concussions = 4.32[0.43]). Concussion history predicts concussion duration (R^2 = 0.20, F[1,116] = 27.33, p < 0.001). Furthermore, trouble falling asleep (β = 0.15) and sleeping less than usual (β = 0.15) predicted concussion duration (R^2 = 0.062, F[1,116] = 3.15, p = 0.047). Reported sleep disturbance after repeated concussions was higher in patients with higher headache (F[2,732] = 3.15, p = 0.043) and mood disturbance (F[2,733] = 3.35, p = 0.036) severity. In addition, after repeated concussions, the positive correlation between sleep disturbance and cognitive dysfunction strengthened. *Conclusions*: History of repeated concussion is associated with longer concussion duration and higher reported sleep disturbance. Furthermore, those with sleep disturbance after repeated concussion exhibit more severe headaches, mood disturbance, and cognitive dysfunction.

Abbreviations: ImPACT: Immediate Postconcussion Assessment and Cognitive Assessment (ImPACT); this is a computer-based test that assesses an individual's cognitive function and cumulatively documents current concussion symptoms. PCSS: Post Concussion Symptom Scale; this scale assesses the severity of concussion symptoms. SPSS: Statistical Package for Social Sciences. This is a statistical software package.

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This is not a clinical trial.
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Introduction

Sleep disturbance is one of the hallmark symptoms associated with concussion and postconcussion syndrome (Towns, Silva, & Belanger, 2015). Investigation of sleep disturbance as a pathway to further understand the effects of concussion has received greater consideration in recent years (Kostyun, Milewski, & Hafeez, 2015; Raikes & Schaefer, 2016; Towns et al., 2015). After sustaining a concussion, patients frequently report sleep-related symptoms, such as difficulty falling asleep or staying asleep, fragmented sleep, hypersomnia, and insomnia.

This sleep disturbance may increase the risk for other adverse secondary postconcussive outcomes (Jaffee, Winter, Jones & Ling, 2015), including higher levels of mood disorders (Schwenk, Gorenflo, Dopp, & Hipple, 2007), chronic pain (Schwenk et al., 2007), and poorer cognitive function (Asken et al., 2016; Beebe, Powers, Slattery, & Gubanich, 2017). The mechanisms underlying the link between sleep and concussion are complicated and have yet to be completely elucidated (Asken et al., 2016).

To begin to understand the potential underlying mechanisms, an assessment of the association between sleep and repeated concussions would be valuable. The evidence for adverse effects of repeated concussions has been steadily mounting (Guskiewicz et al., 2003; Oyegbile, Delasobera, & Zecavati, 2017, 2018). In addition, repeated concussions are often sustained within a short period of time after sustaining the first concussion (Guskiewicz et al., 2003; Levy, Ozgur, Berry, Aryan, & Apuzzo, 2004). As a consequence, repeat concussions may be associated with more significant sleep disturbance and consequently a worsening of postconcussive symptoms (Bryan, 2013; Gouttebarge, Aoki, Lambert, Stewart, & Kerkhoffs, 2017). Limited attention has been given to the relationship between sleep disturbance, concussion duration, and repeated concussions (Eisenberg, Andrea, Meehan, & Mannix, 2013). The literature suggests that sleep disturbance after repeated concussions may have more adverse effects than that of a single concussion (Gouttebarge et al., 2017), leading to a longer concussion duration. However, this relationship is yet to be clearly characterized.

In order to address the aforementioned concerns, the primary objective of this study was to characterize the relationship between repeated concussion, sleep, and concussion duration. Furthermore, another objective was to evaluate if sleep disturbance may play a role in the intensity or severity of other postconcussion symptoms after sustaining repeated concussions.

We evaluated sleep symptoms of 740 concussed patients seen at MedStar Georgetown University Hospital and associated clinics within the MedStar National Rehabilitation Network. The testing included a comprehensive neurocognitive battery, in addition to an assessment of self-reported sleep symptoms and postconcussive symptoms. A subset of patients were monitored longitudinally to determine the duration of the concussion.

Methods

Study setting and design

All patients were seen at the MedStar Georgetown University Hospital or Medstar National Rehabilitation Hospital system, both of which are academic institutions located in Washington, DC. Our concussion data were drawn from individuals who presented to our clinic with a suspected concussion. Concussions were diagnosed by one of five physicians who were either (a) primary care sports medicine specialists or (b) pediatric neurologists in the outpatient sports medicine or pediatric neurology concussion clinics. Criteria used to diagnose patients with concussion included the Post Concussion Symptoms Scale (PCSS) as well as physical examination, which included visual and ocular motor testing (VOMS), cervical exam, and balance evaluations. Diagnosis was generally based on comparison to pre-injury testing (if available), the history of trauma, the PCSS score, and abnormality in physical or neurological exam. Prior number of concussions was assessed based on history from the patient and medical records. The data was collected over a six-year period for the purposes of research and this study was approved by the Georgetown

University Institutional Review Board (IRB ID# 2015-0807 AND IRB ID# 2016-1528). The original study was designed as a cross-sectional project (IRB ID# 2015-0807) with a subset of subjects evaluated longitudinally (IRB ID# 2016-1528) to assess for concussion duration.

Participants

Patients ranged in age from 13 to 33 years and median age was 19.2 years. The group was 59% male. Upon sustaining a concussion, most (~92%) of the patients were seen within three days of the injury. The patient cohort consisted primarily of young adults. A subset of the patients was monitored longitudinally to assess concussion duration in days. These patients were randomly selected to be representative of all concussion history groups. Patients were assigned randomized subject ID numbers to protect their identifying information in compliance with the institutional review board requirements.

Data collection

Postconcussion symptoms were assessed through clinical examination and a neurocognitive battery test: Immediate Postconcussion Assessment and Cognitive Assessment (ImPACT). This is a computer-based test that assesses an individual's cognitive function and cumulatively documents current concussion symptoms measured by the Post-Concussion Symptoms Scale (PCSC; details discussed elsewhere, Tanveer, Zecavati, Delasobera, & Oyegbile, 2017). Briefly, the software uses a postconcussion symptom scale, which assesses the severity of concussion symptoms including headache after the concussion(s) using a 7-point Likert scale whereby 0 is asymptomatic and 6 is the most severe. This Likert scale also assesses mood symptoms (sadness, irritability, nervousness, and emotional lability). Using yes-or-no questions, the need for medical management of headaches and a psychiatric condition (anxiety, depression) was also assessed ("Treatment of headaches by physician?" and "Treatment for psychiatric condition [depression, anxiety]"). Finally, six neurocognitive test modules measuring the cognitive domains of visual memory, verbal memory, reaction time, and visual motor processing speed are administered via computer testing.

ImPACT has been shown to be specific, sensitive, reliable, and valid (Iverson, Lovell, & Collins, 2003, 2005; Rose, Weber, Collen, & Heyer, 2015; Schatz, Pardini, Lovell, Collins, & Podell, 2006) for individuals within 72 hr from a concussion and without a history of learning disabilities or ADHD. As such, individuals with ADHD and learning disabilities were excluded from the study.

Data were obtained from a prospective data set of concussion injury reports from patients seen by Georgetown University Hospital physicians utilizing the testing database.

Analyses

All data obtained were collated using the Statistical Package for Social Sciences (SPSS) software (Version 21.0, IBM, Chicago, IL). Items were coded into numeric values to conduct statistical computations. Stepwise linear regression was used to evaluate the relationship between repeat concussions, concussion duration, and sleep disturbance. Concussion history was categorized into first concussion, second concussion, or three or more concussions. Univariate analysis of covariance and stepwise linear regression were used to evaluate the relationship between sleep disturbance and headache or mood disturbance severity. In addition, correlational analysis (partial correlation correcting for age and gender) was utilized to characterize relationships between sleep disturbance, concussion history, and cognitive dysfunction. The variables included concussion history (1st, 2nd, or ≥ 3rd concussion), sleep disturbance, headache severity, mood disturbance severity, and four cognitive composite scores (visual memory, verbal memory, reaction time, and visual-motor processing speed).

Total sleep disturbance, aggregated into one score, comprised four variables: (a) drowsiness, (b) trouble falling asleep, (c) sleeping more than usual, and (d) sleeping less than usual. These four individual sleep

symptoms were also used for the stepwise linear regression analysis to determine the distinct effect of each symptom. Headache severity was assessed two ways: (a) headache severity via the 7-point Likert scale and (b) treatment for headache by a physician as a proxy for severity of the headache. Mood disturbance severity was assessed two ways: (a) mood disturbance severity using an aggregate score comprised of four variables: sadness, irritability, nervousness, and emotional lability, and (b) treatment for anxiety or depression by a physician as a proxy for severity of the mood disturbance.

Age and gender were included as covariates to address potential confounding effects in the analyses, including the correlational analyses. The alpha level was set at $p = 0.05$, with a targeted minimum Cohen's d effect size of 0.2. LSD post-hoc tests were used for individual comparisons. Partial correlations were also utilized, with age and gender as covariates.

Results

Demographics

A total of 740 individuals underwent testing; 430 individuals were evaluated after one concussion, 192 individuals were evaluated after two concussions, and 118 individuals were evaluated after 3–8 concussions (see Table 1). This data set, therefore, included individuals with 1–8 concussions. Age range was 13–33 years and median age was 19.2 years. A separate supplemental analysis showed that the results presented below did not differ significantly if the age range was reduced to the adolescent (young-adult) age range (16–23) only. This group was 60% male. Sports injuries were the most common cause of concussion. Sports included lacrosse, soccer, American football, cheerleading, field hockey, equestrian, softball, road and mountain biking, volleyball, baseball, basketball, swimming, tennis, martial arts, rugby, ice hockey, boxing, track and field, skiing, wrestling, rowing, cross country, diving, and boating.

Repeated concussions and sleep disturbance

Individuals with more concussions had significantly higher total sleep disturbance scores ($F[2,739] = 8.07$, $p < 0.001$). More specifically, there were lower levels of sleep disturbance after one concussion compared to those with two concussions ($p < 0.008$) and ≥ 3 concussions ($p < 0.001$; see Table 1).

When separated into individual sleep symptoms, only drowsiness ($\beta = 0.16$) was associated with repeat concussions ($R^2 = 0.04$, $F[1,739] = 20.2$, $p < 0.001$).

Repeat concussions, sleep disturbance, and concussion duration (longitudinal subset analysis, *N* = 119)

In a subset of the patients assessed longitudinally, linear regression indicated that number of prior concussions predicted the duration (in days) of concussion and explained 20% of the variance ($R^2 = 0.20$, $F[1,116] = 27.33$, $p < 0.001$; $\beta = 0.45$; see Table 1).

While the *total* sleep disturbance score did not directly predict duration of concussion ($p = 0.12$), when separated into individual sleep symptoms, this subset showed that trouble falling asleep

Table 1. Demographics table.

	1st Concussion	2nd Concussion	3+ Concussion
Sample size	430	192	118
Age, Y (*SD*)	19.3 (4.8)	19.1 (4.8)	19.1 (2.5)
Gender, % M	61%	59%	59%
Sport (most frequent)	Football	Lacrosse	Football
Total Sleep Disturbance Score (SE)	2.56* (0.2)	3.65** (0.34)	4.32** (0.43)
Concussion Duration in Days (SE)	70.2* (19.3)	93.72** (20)	206.61*** (22.4)

Note. *SD*, Standard Deviation, *SE*, – Standard Error.1, 2 & 3 stars differ significantly, $p < 0.01$

(β = 0.15) and sleeping less than usual (β = 0.15) predicted the concussion duration (R^2 = 0.062, F[1,116] = 3.15, p = 0.047).

Sleep disturbance and headache severity

Individuals with higher headache severity scores and ≥ 3 concussions experienced significantly worse sleep disturbance compared to those with individuals with higher headache severity scores and only one concussion (p = 0.013). Furthermore, individuals who required medical treatment of headaches had significantly worse sleep disturbance compared to those who had headaches but did not seek medical treatment of the headaches (F[2,732] = 3.15, p = 0.043, Figure 1).

When separated into the individual sleep symptoms, a stepwise linear regression showed that drowsiness (β = 0.50), trouble falling asleep (β = 0.25), and sleeping more than usual (β = 0.06) predicted higher headache severity scores and explained 51% of the variance (R^2 = 0.51, F[1,733] = 260.7, p < 0.001).

Sleep disturbance and mood disturbance severity

Individuals with higher mood disturbance scores and ≥ 3 concussions experienced significantly worse sleep disturbance compared to those with higher mood disturbance scores and only one concussion (p = 0.011). Furthermore, individuals who required medical treatment of depression or anxiety had significantly worse sleep disturbance compared to those who did not seek medical treatment for a depression or anxiety (F[2,733] = 3.35, p = 0.036), signifying that those with higher levels of sleep disturbance had more severe depression and anxiety (Figure 2).

When separated into the individual sleep symptoms, a stepwise linear regression showed that trouble falling asleep (β = 0.28), drowsiness (β = 0.24), and sleeping more than usual (β = 0.13) predicted higher mood disturbance scores and explained 29% of the variance (R^2 = 0.29, [1,734] = 33.8, p < 0.001).

Sleep disturbance and cognition

Overall, sleep disturbance was significantly more likely to be associated with cognitive dysfunction after repeated concussions. After three or more concussions, there were stronger correlations between sleep disturbance and cognitive dysfunction when compared to a first or second

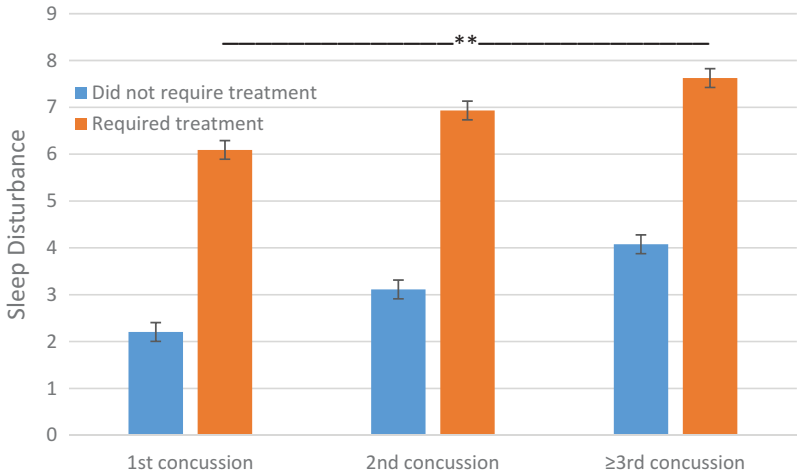

Figure 1. The relationship between sleep disturbance and postconcussive headache severity (treatment requirement by a physician) strengthens with repeated concussions (*p < 0.05, **p < 0.001).

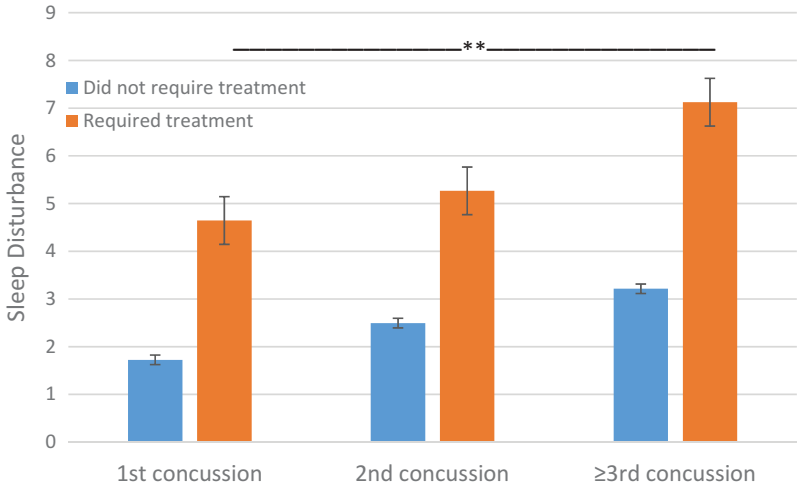

Figure 2. The relationship between sleep disturbance and mood disturbance severity (treatment requirement by a physician) strengthens with repeated concussions (*$p < 0.05$, **$p < 0.001$).

Table 2. Sleep disturbance is more strongly associated with poorer cognitive scores after repeated concussions.

	1st Concussion	2nd Concussion	3+ Concussions
Visual Memory	−0.285*	−0.304*	−0.490**
Verbal Memory	−0.179	−0.206	−0.472**
Reaction Time	0.237*	0.127	0.439**
Visual Motor Speed	0.194*	0.294*	0.453**

Note. Memory scores: higher score means better performance; Time/speed scores: higher time means poorer performance. Controlling for age and gender. *$p < 0.05$, **$p < 0.001$.

concussion (Table 2). Specifically, individuals with ≥ 3 concussions exhibit higher levels of sleep disturbance, a finding that was associated with significantly lower visual ($R = -0.490$, $p < 0.001$) and verbal ($R = -0.472$, $p < 0.001$) memory scores, compared to those with a first or second concussion. In addition, individuals with ≥ 3 concussions exhibit higher levels of sleep disturbance, which was associated with significantly slower reaction time performance ($R = 0.439$, $p < 0.001$) and slower visual motor speed ($R = 0.453$, $p < 0.001$), compared to those with a first or second concussion.

When separated into the individual sleep symptoms, a stepwise linear regression indicated that drowsiness ($\beta = -0.28$), sleeping less than usual ($\beta = -0.08$), and trouble falling asleep ($\beta = -0.09$) best predicted poorer cognitive function ($R^2 = 0.14$, $F[1,739] = 41.5$, $p < 0.001$).

Discussion

This study establishes a relationship between sleep disturbance, concussion duration, and repeated concussions. In addition, this study examines the interaction between repeated concussions and sleep disturbance in relationship to headache severity, mood disturbance severity, and cognitive dysfunction. Our data show that concussion duration is associated with concussion history, such that individuals with repeated concussions experienced a longer concussion duration. Although total sleep disturbance scores did not directly correlate with concussion duration, specific self-reported sleep complaints—trouble falling asleep and sleeping less than usual—were associated with concussion duration.

Overall, after repeat concussions, the self-reported sleep complaints of trouble falling asleep and drowsiness appear to be consistently associated with headache severity, mood disturbance severity, and cognitive dysfunction. Although the exact causal relationships are yet to be delineated, it is possible that after repeated concussions, sleep may become more disrupted. This may be due to trouble falling asleep, which may lead to daytime drowsiness, as well as subsequent worsening in postconcussive symptoms and poorer cognitive performance. These risk factors may lead to delayed resolution of the concussion symptoms and consequently, longer concussion duration.

This study corroborates prior documentation of the association between sleep, concussion duration, repeated concussions, and postconcussive symptoms (Bryan, 2013; Eisenberg et al., 2013; Gouttebarge et al., 2017; Guskiewicz et al., 2003; Oyegbile et al., 2017). The prior evidence has established relationships between repeated concussions and concussion duration (Eisenberg et al., 2013; Guskiewicz et al., 2003), or repeated concussions and sleep (Bryan, 2013; Oyegbile et al., 2017), or repeated concussions and mood disturbance (Gouttebarge et al., 2017). This study takes one step further by investigating the relationships among all these variables, which provides new insight into our understanding of concussion and its pathophysiology.

Interestingly, those with greater sleep disturbance after repeated concussions were more likely to experience and seek out medical treatment for severe postconcussive headaches. They were also more likely to experience severe mood disturbance, such as sadness and emotional lability, as well as seeking treatment for anxiety and depression. Finally, our data show a significant positive relationship between postconcussive self-reported sleep disturbance and cognitive dysfunction, with this association becoming magnified with repeated concussions. Even though the clinical guidelines for concussion treatment are continually evolving, it is clear that sleep disturbance history in the evaluation of concussion may be underutilized. The current study findings indicate that concussion evaluation programs should include sleep data in concussion evaluations in order to improve clinical follow-up assessments. In addition, this study indicates that clinicians and providers of concussion care may be able to better identify concussion patients who are at higher risk of untoward outcomes based on postconcussive sleep disturbance, headache, and mood disturbance severity.

Our data set is limited by the fact that our sleep variable was a self-reported measure. Furthermore, many of our correlating variables were also subjective and we could not control for factors such as pain, concomitant injury, and sedating medications. Also, total sleep disturbance did not significantly correlate with concussion duration, possibly due to the small subsample size. Another limitation of the study is that time between each repeat concussion could not be clearly delineated, as number of concussions was based on patient report and clinic visit data. Further longitudinal research is necessary in this area to clarify our understanding of the significance of sleep disturbance in repeated concussions.

In conclusion, repeated concussions are associated with higher levels of sleep disturbance and prolonged concussion duration. Individuals with higher levels of sleep disturbance and repeated concussions also experience more severe headaches, greater mood disturbance, and significant cognitive dysfunction. Overall, our findings indicate that the relationship between repeated concussions and sleep disturbance merits further investigation to adequately understand how these two issues are intertwined. A better understanding of these complex variables would enable providers to better diagnose, treat, and provide interventions to improve neurologic outcome following concussion.

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Author Contribution

Corresponding author Dr. Temitayo Oyegbile and consulting statistician Dr. Jaeil Ahn completed the statistical analyses.

Disclosure statement

All authors have no financial support for this study and no conflicts of interest. This is no off-label or investigational use.

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