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Original Article

Gender differences in sleep symptoms after repeat concussions



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ABSTRACT

Objectives: There are notable gender differences in concussion as well as sleep. Sleep disturbance is a major symptom of post-concussive syndrome. The interplay between sleep disturbance, concussion, and gender has yet to be examined. The objective of this study was to determine whether sleep disturbance plays a role in the known gender differences associated with concussion.

Methods: Males and females (ages 10–35 years) completed a pre-concussion and post-concussion evaluation. Levels of sleep disturbance were assessed at baseline ($N = 1284$), after first concussion ($N = 432$) and after repeated concussions (one or more concussions, $N = 296$). Sleep disturbance levels were also compared among males and females with headaches, mood changes, and cognitive dysfunction. Analyses included group comparisons and correlations of post-concussive symptoms and cognitive dysfunction, respectively. Data was adjusted for age.

Results: Compared to males, females reported higher levels of sleep disturbance after a single concussion; however, levels of sleep disturbance equalized after repeated concussions. Females with higher levels of sleep disturbance had more headaches and more mood changes requiring medical treatment, compared to males. In addition, sleep disturbance was more strongly correlated with cognitive dysfunction in females compared to males.

Conclusion: Gender differences in concussion recovery after repeat concussions may be primarily due to a difference in sleep disturbance between the genders. This difference in sleep appears to moderate the levels of other post-concussive symptoms. This indicates that sleep disturbance should be closely monitored and treated in females after a concussion. Further studies are required to determine the underlying reasons for these gender differences.

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1. Introduction

Concussions affect between 1.6 and 3.6 million individuals in the United States every year [1–3]. Furthermore, in the US alone, medical costs as well as consequences from lost productivity due to concussions total an estimated \$60 billion annually [2,3]. The long-term effects of concussion on cognition and physical symptoms are becoming more evident [4–20]. Less attention, however, has been given to the effect of cumulative concussions compared to the effect of a single concussion [10–18,21–23]. Our research team recently documented that cumulative concussions progressively lead to increased cognitive dysfunction [22] and that sleep disturbance moderates this cognitive dysfunction as the number of concussions

increases [23]. Furthermore, sleep disturbance also moderates mood changes and headaches in repeat concussions [23].

It is well recognized that gender differences exist in concussion [18–21] as well as sleep disturbance [24–28]. Females are at higher risk for concussion [29]; they experience more post-concussive symptoms and these symptoms are more severe than their male counterparts [30,31]. They also take a longer time to recover from concussion [29] compared to males. On cognitive testing after a concussion, verbal memory skills are better preserved in females, while visuospatial abilities are preserved in males [21,32–34]. Overall, females have worse outcomes compared to males after a head injury [35].

In the sleep literature, there is evidence that females have more sleep disorders [24] (excluding obstructive sleep apnea [36]) and have higher levels of insomnia with poor sleep quality [28,37], subsequently resulting in more daytime fatigue, mood changes, as well as pain perception concerns [24,25]. This evidence raises the question of whether sleep disturbance following concussion affects

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females disproportionately compared to males; and if so, how this affects other associated post-concussive symptoms such as mood changes and cognitive dysfunction remains to be clarified. The aim of this study was to explore the relationship between these variables.

The objectives of this study were two-fold. First, we aimed to assess gender differences in sleep disturbance experienced as number of concussions increased. Secondly, we aimed to characterize the impact of this gender difference in sleep disturbance on other post-concussive symptoms and cognitive function.

We analyzed data collected from males and females within the Washington DC area, both before and after sustaining a concussion, to assess gender differences in sleep and concussion. Within the Washington DC area, many institutions/universities require baseline concussion testing by a physician or athletic trainer prior to the start of the sports season and require individuals to return to the clinic for evaluation and clearance after sustaining a concussion. We evaluated the sleep of pre-concussed (baseline) male and female patients and compared the findings to those who returned after sustaining one or more concussions. In this prospective study, patients were evaluated within the MedStar Georgetown University Hospital/Medstar National Rehabilitation system in the pediatric and sports medicine clinics where they completed a concussion evaluation before and after injury. The testing included a comprehensive neurocognitive battery in addition to an assessment on post-concussive symptoms. Within our unique model, these patients served as their own healthy controls. This data was collected prospectively over the past 6 years, resulting in a database of over 2000 patients.

2. Methods

2.1. Study setting and design

Patients were seen for pre-concussion evaluations at the MedStar Georgetown University Hospital or Medstar National Rehabilitation Network from January 2010 to May 2016. When patients returned with a possible concussion, the concussion was diagnosed by one of the five physicians who were either primary care sports medicine specialists or pediatric neurologists in the outpatient sports medicine and/or pediatric neurology concussion clinic. These patients underwent clinical re-evaluation and repeat concussion testing following the diagnosis of a concussion. This study was approved by the Georgetown University Institutional Review Board (IRB ID# 2015-0807).

2.2. Participants

Patients ranged in age from 10 to 35 years at the time of the initial cognitive testing and they completed the subsequent cognitive testing at the clinic within 1 day–4 weeks after injury. Most (~87%) of the patients were seen within 3 days of the injury. The patient data consisted primarily of college-age patients. Patients were assigned randomized subject ID numbers to protect their identifying information in compliance with the institutional review board requirements.

2.3. Data collection

Pre-concussion and post-concussion symptoms were assessed through clinical examination and a neuropsychological test: Immediate Post-concussion 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. The test was administered via a web-enabled desktop computer and with the assistance of a clinical nurse, medical assistant, athletic trainer, or medical resident/fellow who had undergone test administration training.

This test is a neuropsychological screening test that helps healthcare providers oversee the recovery progress in injured individuals within a clinical setting. The neurocognitive assessment consists of a demographic questionnaire, concussion symptom inventory, and neurocognitive performance test. The data obtained from the neurocognitive component examined variables such as reaction time, processing speed, verbal memory, visual memory, and total symptoms score [11].

Briefly, the testing has been shown to be specific and sensitive, as well as reliable and valid [11–14]. The reliability, validity, and testing instructions have been rigorously studied. Furthermore, this testing shows construct validity [12], indicating that the test battery is an accurate and reliable measure of neurocognitive performance.

Six neuropsychological test modules measuring the cognitive domains of attention, memory, reaction time, and processing speed are administered via computer testing. The testing takes less than 25 min. Final scores from each of the modules are presented in four composite cognitive domains: verbal memory, visual memory, processing speed, and reaction time. Higher scores on verbal and visual memory as well as motor processing speed indicate a better performance. Verbal and visual memory scores are presented as a percentage. Motor processing speed is presented as a composite score. A lower score on reaction time indicates a better performance. All reaction time scores are presented in seconds.

In addition to the cognitive testing, the software uses a 22-item scale, the Post-Concussion Symptom Scale, which is used to test the severity of concussion symptoms. Patients rate their current symptom severity on a seven-point Likert scale, where 0 is asymptomatic and 7 is the most severe. All 22 items are then summed to produce the total symptom score evaluating headache, nausea, vomiting, balance problems, dizziness, fatigue, trouble falling asleep, sleeping more than usual, sleeping less than usual, drowsiness, sensitivity to light, sensitivity to noise, irritability, sadness, nervousness, feeling more emotional, numbness or tingling, feeling slowed down, feeling mentally foggy, difficulty concentrating, difficulty remembering and visual problems.

Data were obtained from a prospective dataset of concussion injury reports from patients seen by Georgetown University Physicians utilizing the testing database.

2.4. Analyses

All data obtained were collated using the Statistical Package for Social Sciences (SPSS) software (Version 21.0, IBM, Chicago, IL). Items were recoded to numeric values to conduct statistical computations. Cognitive scores were initially log-transformed. Univariate analysis of co-variance was used to evaluate gender differences effects of repeated concussions on sleep disturbance by assessing no concussion (baseline), first concussion and repeated concussions. Repeated concussion was defined as two or more concussions. This data set included individuals with anywhere from zero to eight concussions in their lifetime. In addition, correlational analysis was utilized to characterize relationships between sleep disturbance cognition scores, mood and other concussion symptoms. The independent variable was gender and the dependent variables were concussion history, concussion

symptoms (mood and headaches) and the four log composite scores (verbal, visual memory, and motor processing speed, and visual motor). Sleep disturbance was an aggregate score which compiled five variables – drowsiness, trouble falling asleep, sleeping more than usual, sleeping less than usual, and fatigue. Age was included as a covariate to address potential confounding effects in all 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. Least Significant Difference (LSD) post hoc tests were used for individual comparisons. Partial correlations were also utilized.

3. Results

3.1. Demographics

A total of 1284 individuals underwent baseline testing, 432 individuals returned for evaluation after one concussion and 296 individuals returned for evaluation after two to eight prior concussions. Age range was 10–35 years and median age was 19.7 years. The group was 57% male. Sports injuries were the most common cause of concussion in our study. The 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.

3.2. Sleep disturbance and repeat concussions

Post-concussive sleep disturbance differs between males and females overall ($F(2,2004) = 13.28, p < 0.001$). After a single concussion, females have significantly increased sleep disturbance while males experience minimal change in sleep ($p < 0.001$). After repeat concussions, however, males and females have similar levels of sleep disturbance ($p = 0.262$) (see Fig. 1).

When separated out by age, specifically above and below age 15 years old, there were clear differences. Below age 15 years, there were no significant gender differences between baseline, a single

concussion and repeated concussions ($p = 0.912$). The findings above age 15 years were identical to the above findings ($p < 0.001$).

3.3. Sleep disturbance and headaches

Among concussed individuals, females with sleep disturbance were more likely to develop significant headaches compared to male counterparts ($F(1,766) = 4.68, p = 0.031$) (Fig. 2). Males and females who did not experience significant sleep disturbance reported minimal headaches. However, among those who experienced headaches, females have significantly higher levels of sleep disturbance compared to males.

3.4. Sleep disturbance and mood changes

Among concussed individuals, females who were more likely to require medical treatment for a post-concussive mood disorder (psychiatric disorder/anxiety/depression) had higher levels of sleep disturbance compared to males ($F(1,703) = 4.44, p = 0.038$) (Fig. 3). Males and females who did not experience significant sleep disturbance were less likely to seek out treatment for a mood disorder. However, among those who required medical treatment for a mood disorder after sustaining concussion, females experience significantly higher levels of sleep disturbance compared to males.

3.5. Sleep disturbance and cognitive dysfunction

Among concussed individuals, both males and females exhibited cognitive dysfunction after concussion. Interestingly, when separated out by gender, females show a stronger correlation between sleep disturbance and cognitive function compared to males. Females with higher levels of sleep disturbance have significantly slower reaction times ($r = 0.316, p < 0.001$) and slower visual motor speed ($r = 0.338, p < 0.001$) compared to males. In addition, females with greater levels of sleep disturbance performed worse on verbal ($r = -0.284, p < 0.001$) and visual ($r = -0.256, p < 0.001$) memory scores compared to males (Table 1).

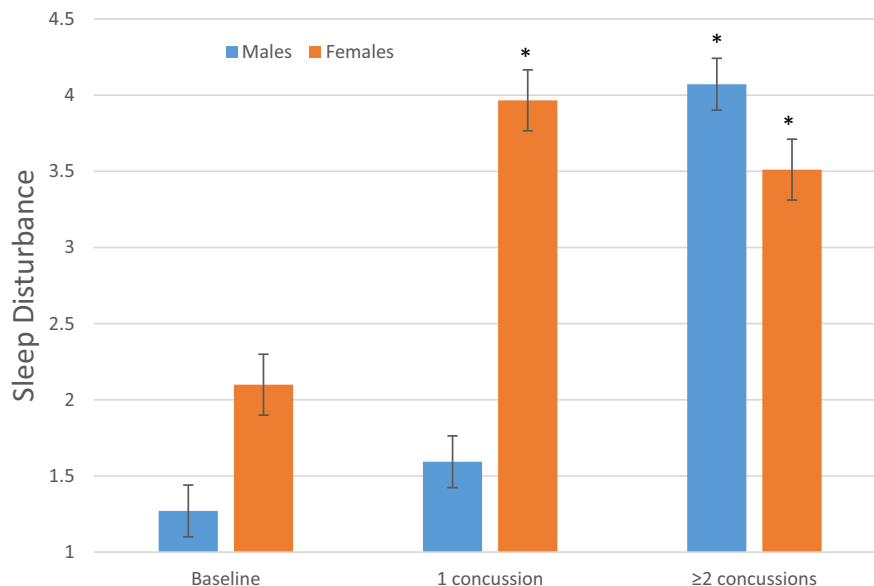


Fig. 1. Gender differences in sleep disturbance with accumulating concussions. * $p < 0.001$.

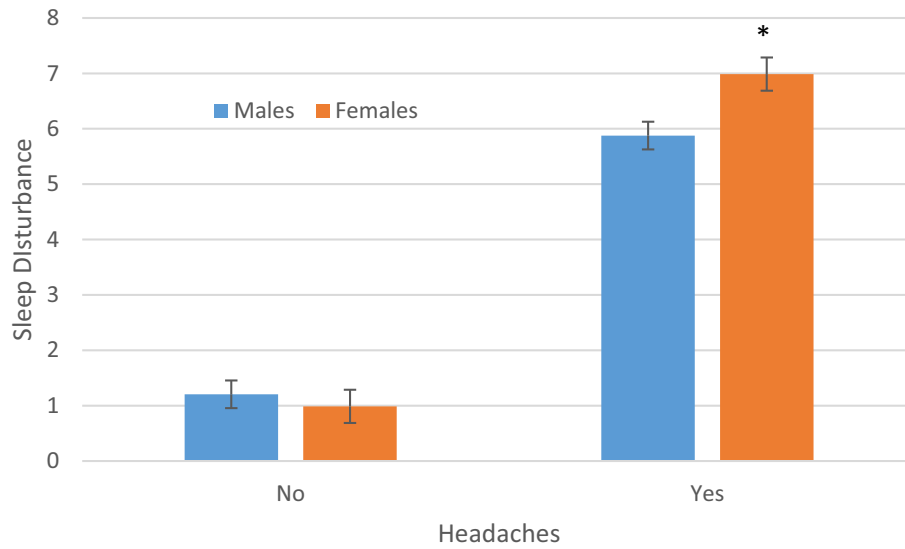


Fig. 2. Sleep disturbance is higher among females with headaches.* $p < 0.05$.

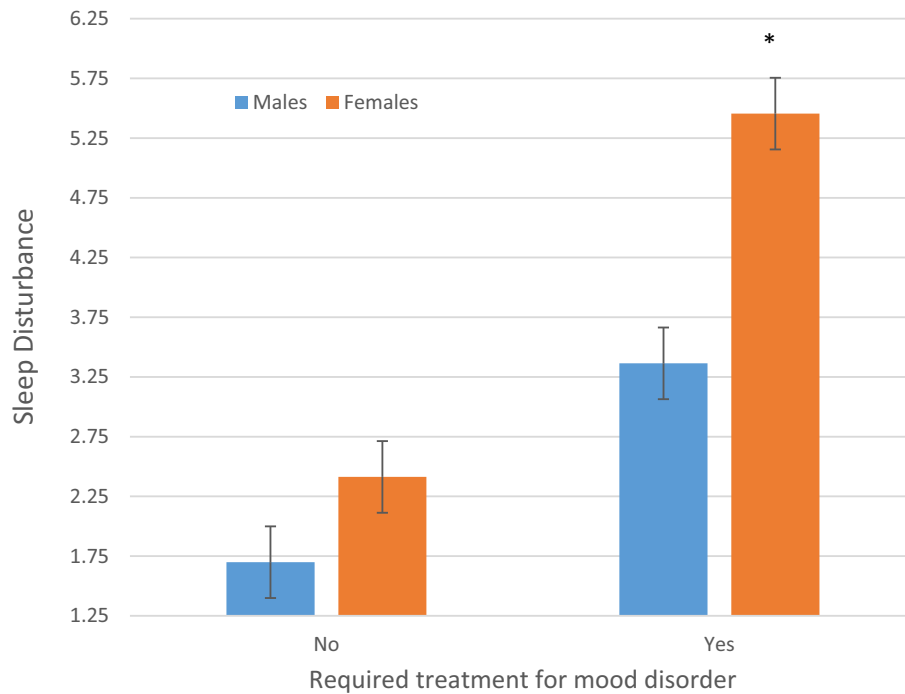


Fig. 3. Sleep disturbance is higher among females requiring medical treatment for a mood disorder. * $p < 0.05$.

Table 1

In females, poor sleep is more strongly associated with poor cognitive scores, compared to males.

	Male	Female
Reaction time	0.149*	0.316**
Visual motor speed	0.181*	0.338**
Visual memory	-0.117*	-0.284**
Verbal memory	-0.191*	-0.256**

Controlling for age.
* $p < 0.05$, ** $p < 0.001$.

4. Discussion

The goal of this study was to characterize the gender differences in sleep disturbance following concussion. Our findings indicate that there are indeed gender differences in self-reported sleep disturbance after a concussion, which may subsequently affect other post-concussive symptoms. Prior studies have indicated that females may be more susceptible to severe post-concussive symptoms after sustaining a concussion and recovery is prolonged [29–31]. Our findings here suggest that sleep disturbance may play a key role in moderating these post-concussive symptoms.

We show here that females report significant sleep disturbance after sustaining a single concussion while males may not report sleep disturbance until cumulative concussions have been sustained. Females with sleep disturbance are more likely to experience significant headaches and mood changes requiring medical treatment. This suggests that high levels of sleep disturbance may negatively impact the sensation of pain, which may perhaps promote poorer mood. Gender differences among these associations may be due to there being stronger associations between these variables among females compared to males. In addition, cognitive dysfunction in females after sustaining a concussion is more dependent on associated sleep disturbance than among male counterparts. It is important to note that these findings are correlational only and future studies will be important to determine causal relationships.

The underlying etiology behind these gender differences remains unclear, however our findings provide new insight into the potential reasons behind this gender difference. Sleep changes following a concussion may play a key role in modulating recovery in women suggesting that female athletes are more vulnerable to co-morbid post-concussive conditions such as mood disorders and cognitive dysfunction, when sleep is significantly disrupted. Awareness of the variability of post-concussion symptoms between men and women can aid providers in accurately diagnosing and treating post-concussion syndrome. As is the practice at our institution, we recommend a multi-disciplinary approach to the patient that includes psychiatry, neurology, sleep medicine and physical medicine/rehabilitation with special attention to gender-based differences in symptoms.

Studies have suggested that the gender difference may be related to estrogen levels [38] or may be due to the decreased female head–neck segment compared to males which can result in greater angular acceleration to the head after concussive impact [39]. Further investigation is necessary to determine causality.

Our novel findings indicate that the gender differences noted after concussion [18,20,21] may be due primarily to sleep disturbance, which can in turn affect multiple other post-concussive symptoms. Concussion has become a significant public health concern especially among athletes who sustain multiple cumulative concussions [40–42]. The main focus has been on primarily male-dominated sports such as football. There is growing evidence and awareness of concussion in women highlighting the need for more aggressive surveillance and treatment as this may be a sub-population where the effects of concussion may be more severe and more prolonged. Our evidence also indicates that it may be beneficial to adjust or modify post-concussive symptom assessments for males and females with a particular focus on sleep disturbance among females who sustain concussion. Our findings add to the mounting evidence that concussion evaluation must be performed on an individual basis, taking into consideration factors such as gender [30] to facilitate accurate screening, diagnosis and treatment.

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Conflict of interest

The authors have no financial disclosures to report.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <https://doi.org/10.1016/j.sleep.2017.09.026>.

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