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Authors

Oyegbile, Temitayo Oyefunmike
Delasobera, Bronson Elizabeth
Zecavati, Nassim

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Temitayo Oyefunmike Oyegbile, MD, PhD¹,
Bronson Elizabeth Delasobera, MD¹, and **Nassim Zecavati, MD, MPH¹**

Abstract

The objective was to characterize cognitive deficits and postconcussive symptoms in a pediatric population with no concussion, a single concussion, and ≥ 2 concussions, using a cross-sectional design. Cognitive function and postconcussive symptoms were assessed in participants (age 10-20) with no concussion ($n = 1118$), single concussion ($n = 368$), and repeated (≥ 2) concussions ($n = 252$). Analyses were adjusted for age and gender. Individuals with ≥ 2 concussions exhibited more total postconcussive symptoms; more loss of consciousness, amnesia and confusion; more headaches; and poorer cognitive function compared to no concussion and single concussion. Postconcussive symptoms may play a modulatory role in cognitive dysfunction after repeated concussions as those with loss of consciousness, amnesia, confusion, or headaches exhibited worse verbal memory, visual memory, visual-motor processing, and poorer impulse control compared to those without these symptoms. This analysis demonstrates that repeated concussions is associated with poorer cognitive function and postconcussive symptoms compared to a single concussion.

Keywords

repeated concussions, cognitive function, postconcussive symptoms, neurocognitive testing

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There is increasing evidence of the adverse effects of a single concussion on cognitive function and postconcussive symptoms including headaches, fatigue, and poor attention.¹⁻⁴ Less attention has been paid to the cognitive performance deficits after multiple concussions. Subsequent concussions after a first concussion are very common and repeated concussions are often sustained within a short period of time after sustaining the first concussion.^{3,5} Both animal and human studies indicate that there is an increased risk of brain injury while recovering from a concussion.⁶⁻¹² In spite of this, the specific cognitive dysfunction after repeated concussions are yet to be clearly delineated and the limited evidence available is conflicting.

A number of studies have noted significant postconcussive cognitive and symptom differences between no concussion testing and repeated concussions in high school and collegiate athletes,^{2-4,13} whereas others find no significant differences.^{1,14-21} Similar conflicting results have been noted in studies evaluating specific sports. Repeated headers in soccer have been associated with poorer neurocognitive function in some studies,²²⁻²⁵ whereas others found no effect of repeated headers in soccer players²⁶⁻²⁹ when compared to nonathletes. Football and ice hockey players can also incur repeated head impacts, which were found to affect postconcussive symptoms in

some studies^{30,31} whereas others found no differences after repeated head impacts compared to no concussion.³²⁻³⁴ Studies in boxing suggest similar conflicting findings as well.³⁵ These conflicting findings could be due to significant differences in past concussion histories that may be more difficult to delineate. An assessment of younger individuals with less history of prior head injuries may provide a cleaner, less-complicated picture illustrating the cognitive dysfunction after repeated concussions.

Furthermore, the effect of repeated concussions on the developing brain remains unclear. Given the recent concerns about potential risk for long-term cognitive dysfunction in athletes after repeated concussions,³⁶⁻³⁸ it is imperative that the effects of repeated concussions in the developing brain be established. In order to address the aforementioned concerns, the primary objective of this study was to characterize the

¹ Medicine & Epilepsy, MedStar Georgetown University Hospital, Washington, DC, USA

Corresponding Author:

Temitayo Oyegbile, MD, PhD, Pediatric Neurology, MedStar Georgetown University Hospital, 4200 Wisconsin Ave NW, Washington, DC 20016, USA.
Email: Too3@georgetown.edu

cognitive function deficits and postconcussion symptoms sustained after repeated concussions and compare the findings to that of a single concussion in a younger population.

Methods

Study Setting and Design

All participants were seen at the MedStar Georgetown University Hospital or Medstar National Rehabilitation Hospital system, both of which are academic institutions located in Washington, DC. The coaches of the sports teams require the teams to undergo a yearly preconcussion evaluation prior to starting the sports season. This served as our baseline (no concussion) data. Our postconcussion data were drawn from individuals who presented to our clinic with a concussion (some returns from the preconcussion group and some new to the clinic). Concussions were diagnosed by one of the 5 physicians who were either primary care sports medicine specialists or pediatric neurologists in the outpatient sports medicine and/or pediatric neurology concussion clinics. Criteria used to diagnose participants with concussion included the Post-Concussion Symptoms Scale as well as physical examination that included vision and balance evaluations. The data were collected over a 6-year period for the purposes of research, and this study was approved by the Georgetown University Institutional Review Board (IRB ID 2015-0807). The study was designed as a cross-sectional project, and because of patient confidentiality concerns, a direct repeated measures study was not conducted.

Participants

Participants ranged in age from 10 to 20 years. The participant data consisted primarily of high school and college-age participants. Participants were assigned randomized subject ID numbers to protect their identifying information in compliance with the institutional review board requirements. The inclusion criteria included a clear history of their concussion history, diagnosis of concussion after the preconcussion testing, and completion of the Post-Concussion Symptoms Scale and ImPACT testing. Exclusion criteria included age above 20 years and unclear concussion history.

Data Collection

Preconcussion and postconcussion symptoms were assessed through clinical examination and a neurocognitive battery test: Immediate Postconcussion Assessment and Cognitive Testing (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 (details discussed elsewhere³⁹). Briefly, the program assesses the severity of concussion symptoms 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. This is then summed up to produce the total symptom score. Symptoms of confusion, loss of consciousness and amnesia immediately following sustaining the concussion/s are also assessed in the ImPACT testing. In addition, the need to seek treatment for headaches was also assessed. Finally, the ImPACT testing included 6

neurocognitive test modules measuring the cognitive domains of visual memory, verbal memory, reaction time, and visual motor processing speed are administered via computer testing. The test also provides a composite Impulse Control score, which is a measure of number of errors during testing.

Briefly, the testing has been shown to be specific and sensitive as well as reliable and valid^{8,40-42} for individuals within 72 hours from a concussion without a history of learning disabilities and ADHD. As a result, individuals who self-reported a history of ADHD and learning disabilities were excluded from the study.

Data were obtained from a prospective data set of concussion injury reports from participants 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). Univariate analysis of covariance was used to evaluate for the relationship between repeated concussions, cognitive function, and postconcussive symptoms by assessing cognitive function and postconcussive symptoms after no concussion (baseline), a single concussion, and repeated concussions. Repeat concussion was defined as individuals with 2 or more concussions. The variables included concussion history (0, 1, or ≥ 2 concussions), total symptom score (an aggregate of Post-Concussion Symptoms Scale), confusion, loss of consciousness, amnesia, headache (all by self-report), and 4 cognitive composite scores (visual memory, verbal memory, reaction time, and visual motor processing speed). An aggregate variable, memory Index, included visual and verbal memory. An additional variable, seeking treatment for headache, was also included in the analyses and used as a proxy for severity as a mild headache disorder is less likely to warrant any significant treatment as compared to a severe headache. Age and gender were included as covariates to address potential confounding effects in all analyses, including the correlational analyses. The alpha level was set at $P = .05$, with a targeted minimum Cohen d effect size of 0.2. least significant difference post hoc tests were used for individual comparisons. Partial correlations were also used, with age and gender as covariates.

Results

Demographics

Our study included a total of 1738 testing sessions, 1118 preconcussion sessions conducted as a no concussion (baseline), 368 individuals were evaluated after a single concussion, and 252 individuals were evaluated after 2 to 8 concussions (see Table 1). This data set included individuals with 0 to 8 concussions. Upon sustaining a concussion, most ($\sim 92\%$) of the participants were seen within 3 days of the injury. The ages ranged from 10 to 20 years; the average age was 17.0 years. The group was 61% male. Sports injuries were the most common cause of concussions 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.

Table 1. Demographics Table.

	No concussion	1 concussion	≥2 concussions
Sample size	1118	368	252
Mean age, y (SD)	17.1 (1.2)	17.0 (1.4)	17.1 (1.4)
Percentage aged ≤11 y	1	0.8	0
Gender, % male	60%	62%	60%
Sport (most frequent)	Football	Football	Football

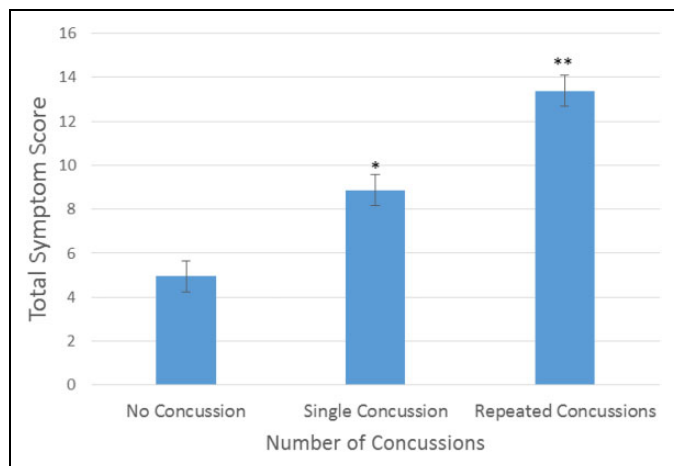


Figure 1. Increasing total symptom score as number of concussions increases.

Repeated Concussions and Concussion Symptoms

The severity of concussion symptoms was associated with number of concussions. As expected, individuals with a single concussion have a higher total symptom score ($F[2, 1732] = 54.6, P < .005$) compared to no concussion. In addition, individuals with ≥ 2 concussions have even higher total symptom scores compared to no concussion ($P < .001, d = 0.64$) and compared to individuals with a first concussion ($P < .001, d = 0.35$) (Figure 1).

Headaches were more common in individuals with ≥ 2 concussions (46%) compared to those with a single concussion (27%) and those with no concussion (17%) (RR = 1.5, 95% CI = 1.24, 1.81, $P < .001$) (Table 2). The incidence of headaches was also higher after a single concussion compared to no concussion ($F[2, 1730] = 61.5, P < .001$). Furthermore, the incidence of headaches was even higher after ≥ 2 concussions compared to a single concussion ($P < .001, d = 0.3$) and compared to no concussion ($P < .001, d = 0.62$).

Individuals with ≥ 2 concussions particularly have more severe headaches ($F[2, 1726] = 59.84, P < .001$) and require more tailored headache treatment (medications etc) ($F[2, 1726] = 22.66, P < .001$), compared to no concussion ($P < .001, d = 0.6$) and compared to individuals with a single concussion ($P < .001, d = 0.3$).

Furthermore, individuals with ≥ 2 concussions are more likely to have suffered from loss of consciousness

Table 2. Individuals With ≥ 2 Concussions Have a Higher Frequency of Headaches Than 1 Concussion and No Concussion.

	No headache	Headache	% frequency	Subtotal
No concussion	956	162	16.9%	1118
1 concussion	268	100	27.2%	368
≥ 2 concussions	137	115	45.6%	252
Total	1361	377		1738

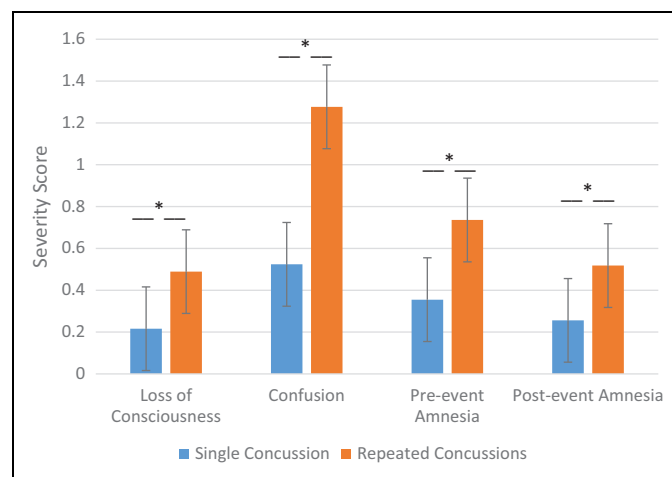


Figure 2. Individuals with repeated concussions experience more loss of consciousness, confusion, and amnesia compared to a single concussion. (* $P < .05$).

($F[1, 725] = 21.22, P < .001, d = 0.49$), confusion ($F[1, 725] = 82.53, P < .001, d = 0.82$), amnesia of the event ($F[1, 725] = 43.37, P < .001, d = 0.54$) and amnesia after the event ($F[1, 725] = 23.87, P < .001, d = 0.4$), compared to individuals with a single concussion ($P = .003$) (see Figure 2).

Repeated Concussions and Cognitive Function

Cognitive function is also significantly associated with repeated concussions. In a comparison of no concussion testing to a single concussion and ≥ 2 concussions, we found an association with memory ($F[2, 1730] = 5.101, P = .002$; Figure 3). Specifically, memory index scores are lower after a single concussion ($P = .044, d = 0.3$) and ≥ 2 concussions ($P = .003, d = 0.4$). There was no difference in memory index scores between a single concussion and ≥ 2 concussions ($P > .05$). No significant differences were noted between a single concussion and repeated concussions in other cognitive measures.

Correlational analyses using age and gender as covariates showed that individuals with higher total symptom scores performed poorer on verbal memory ($r = -0.318, P < .001$), visual memory ($r = -0.316, P < .001$), visual-motor scores ($r = -0.293, P < .001$), reaction time ($r = 0.267, P < .001$), and impulse control ($r = 0.141, P < .001$).

Among all concussion symptoms, headache was the most common symptom associated with multiple concussions.

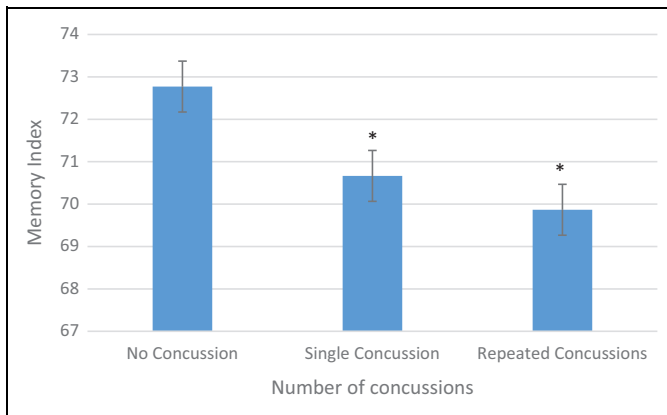


Figure 3. Poorer memory scores after a concussion compared to no concussion (* $P < .05$).

Among participants with ≥ 2 concussions only, those with headaches performed worse in multiple domains of cognitive testing compared to those without headaches. Individuals with ≥ 2 concussions and postconcussive headaches exhibited worse verbal memory composite scores ($F[1, 248] = 20.3, P < .001, d = 0.52$), visual memory composite scores ($F[1, 248] = 11.2, P < .001, d = 0.54$), visual motor processing composite scores ($F[1, 248] = 9.3, P = .003, d = 0.61$), and impulse control composite scores ($F[1, 248] = 15.5, P < .001, d = 0.55$) compared to concussed individuals without headaches.

Discussion

The primary goal of this cross-sectional study was to characterize the relationship between repeated concussions, postconcussive symptoms, and cognitive function in a pediatric population. Our findings clearly indicate that the severity of postconcussive symptoms and cognitive deficit is indeed associated with the number of concussions. Individuals with repeated concussions experience more total symptoms than those with a single concussion. Loss of consciousness, confusion, and amnesia around the time of the injury are more likely to be experienced after repeated concussions than after a single concussion. In addition, frequency and severity of headaches are higher in those with repeated concussions compared to a single concussion. These findings corroborate the prior literature that report worsening postconcussive symptoms associated with repeated concussions.^{2,4,13}

In addition to postconcussive symptoms, individuals with repeated concussions also experience worsening cognitive function compared to no concussion. We report here that individuals with a history of repeated concussions exhibit poorer memory, compared to no concussion and compared to a single concussion. Others have reported similar findings indicating that the major cognitive domains may be adversely affected after repeated concussions.^{1,2,13} Interestingly, upon further analysis of our data, we found that the postconcussive symptoms may play a role in the degree of cognitive dysfunction, such that after repeated concussions, individuals with worse

postconcussive symptoms display poorer cognitive outcomes compared to a first concussion. This suggests that there is likely a higher level of injury/pathology to the brain from multiple concussions, leading to worse symptoms and poor cognitive performance. Injury to developing brains can have long-term consequences as is seen in multiple neurologic disorders such as pediatric epilepsy.⁴³ Given the fact that this study showed clear worsening of symptoms after repeated pediatric concussions, it begs the question if these symptoms have long-term consequences or if the brain is able to recover quicker and more completely than an adult brain based on concepts such as cerebral reserve.^{43,44} Further research is necessary to determine the underlying mechanisms behind the worsening symptoms and cognitive deficits in developing brains after repeated concussions and determine if the long-term consequences are worse than that of a single concussion.

Within the current literature, several studies support our findings, however, the evidence is conflicting. Our findings provide further evidence that there are significant postconcussive cognitive and symptom differences between no concussion testing and repeated concussions in developing brains. Further research is required to understand the specific effect of repeated concussions on the brain, specifically within a pediatric population.

Our data are clearly limited by the fact that the postconcussive symptom variables are primarily self-reported measures. However, the clear relationship of our self-reported variables with objective cognitive findings indicate that repeated concussions may have a big impact on the developing brain. A small number of children under age 11 were tested even though ImPACT and Post-Concussion Symptoms Scale testing has been validated for ages ≥ 11 (see Table 1); the lower percentage should not make a significant difference to the overall results. The causal relationship between postconcussive cognitive symptoms, cognitive deficits, and repeated concussions needs to be further clarified using more objective measures. Another limitation of the study is that time between each repeat concussion could not be clearly delineated as number of concussions was based on participant report and clinic visit data. Potentially, there may be a long-term impact of repeat concussions on the developing brain. Further research is necessary in this area.

Overall, there is limited evidence about the cumulative adverse effects of repeated concussions on cognitive function and postconcussive symptoms in the developing brain. This report strengthens existing evidence that repeated concussions do indeed have a larger impact on the brain compared to a single concussion. These findings suggest that more precautions need to be taken after a single concussion to facilitate complete recovery and that education needs to be provided to concussed individuals about the risks of repeat concussions. At this point, the duration of the cognitive dysfunction remains unknown. Given the fact that repeated concussions can result in a prolonged recovery period,³ it is plausible that repeated concussions may have a prolonged impact on cognitive symptoms as well. Future studies in this area will be beneficial to

understand the full impact of repeated concussions on the developing brain.

Authors' Note

Corresponding author and statistician completed the statistical analyses.

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Author Contributions

TOO was responsible for study concept and design and analysis and interpretation of data. BED acquired the data and along with NZ, critically revised the manuscript for important intellectual content. NZ contributed to study concept acquisition of data.


Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORCID iD

Temitayo Oyefunmike Oyegbile, MD, PhD  <http://orcid.org/0000-0003-3844-315X>

Ethical Approval

This research project was conducted in an ethical manner ensuring confidentiality of all participants while closely adhering to the outlined protocol approved by the Georgetown University IRB.

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